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Contents

ORIGINAL ARTICLES

- Tobacco use among Pre-university Students in Kannur, Kerala:
A Cross-sectional Study
Sushrit A Neelopant, D Shilpa 1
- Carotid Intima-media Thickness and Epicardial Fat Thickness in
Patients with and without Metabolic Syndrome: A Correlative Study
S Renjeesh, M Mahesh, S Mamatha 6
- Role of Ultrasonogram in Detection of Congenital Anomalies and
Prevalence of Anomalies in High-risk Pregnancies
Mahalakshmi Aravazhi, Thangamani Balasubramaniam, Shantha Devi Sambath 10
- Evaluating the Etiology and Disease Specific Clinical Profiles of
Acute Undifferentiated Febrile Illness
Shashidhara Kuppegala Chikkaveeraiah, Abhijit Bhograj, Rajashekar Reddy, Arun Kumar 14
- Comparative Study Evaluating Safety and Efficacy of Bicalutamide
(150 mg) Monotherapy versus Orchidectomy and Bicalutamide (50 mg)
in the Treatment of Locally Advanced/Metastatic Prostate Cancer
Laxmi Agnihotri, Money Gupta, Vishal Mandial, Anil Kayastha 18
- Esophageal Atresia and Tracheoesophageal Fistula: Study of Various
Factors Affecting Leak Rate
Money Gupta, Laxmi Agnihotri, V J S Virdi, Vishal Mandial, JK Mahajan 23
- Changes of Macular and Retinal Nerve Fiber Layer Thickness Measured
by Optical Coherence Tomography in Diabetic Patients with and without
Diabetic Retinopathy
Raghavendra Ramappa, Reji Koshy Thomas 27
- Evaluation of the Mode of Failure of Glass Fiber Posts: An *In Vitro* Study
Kiran Kulkarni, S R Godbole, Seema Sathe, Shreyas Gotoorkar, Pooja Jaiswal, Prithwish Mukherjee 34

- Surgical Fibrolysis and Skin Grafts in the Management of Oral Submucous Fibrosis
Subodh Nanavati, Pallavi Nanavati, Maulik Nanavati 40
- Burr Hole Irrigation of Hematoma Cavity with and without Drainage in the Treatment of Chronic Subdural Hematoma: A Comparative Study
Dipu Bhuyan, Pradipta Ray Choudhury, Mrinal Bhuyan 50
- Clinical Profile of Conjunctival Lesions: A Prospective Study
Sundeep, B V Vinutha, H Niveditha, K Divya, Minal Kothari 55
- Malaria Positive Cases with Reference to Liver Function Test among Patients Attending in Teerthanker Mahaveer Medical College and Research Centre, Moradabad, Uttar Pradesh, India
Kamal Kishor Dhariyal, Umar Farooq, Sudhir Singh, Mohd Shariq, Navdeep Kaur, Amit Kumar Bharti 59
- Cardiac Complications of Diabetes Mellitus: A Prospective Study
Varun Shetty, H R Jain, G S Singh, S Shetty 64
- Serum Fibrinogen Levels and its Relation to Hypertension
Adil Majeed, Aamir Rashid, Rashid Maqbool, Waseem Rashid, Mukhtar Ahmed, Ujala Gulzar 69
- Spectrum of Malformation of Cortical Development with Clinico-radiological Correlation
Alok Kumar, Rahul Ranjan, Supriya Katiyar, Gaurav Arya, Dayaram Yadav 73
- Epidemiology of Secondary Peritonitis: Analysis of 545 Cases
Partha Sarathi Ghosh, Ramanuj Mukherjee, Snigdha Sarkar, Sandip Kumar Halder, Debasis Dhar 80
- Effect of Modifiable Risk Factors on the Prevalence of Type 2 Diabetes in the Tribal Adult Population of Boko Bongaon Block of Kamrup District of Assam
Deep Prakash Paul, Jutika Ojah 86
- Presumptive Coliform Count in Water Sample Collected from Different Sites of a University, Moradabad, Uttar Pradesh, India
Mohd Shariq, Sudhir Singh, Umar Farooq, Kamal Kishor Dhariyal, Komal Singh, Navdeep Kaur 91
- Surgical Site Infection Following Cesarean Section in a Teaching Hospital
C P Vijayan, Simi Mohandas, Asha G Nath 97

- Incidence of Odontogenic Sinusitis – Experience in a Tertiary Care Centre
B G Prakash, Suhasini Biyyapu 102
- Surgical Management of Isolated Tibial Shaft Fractures with Closed Intramedullary Interlocking Nail
Kadiri Venkata Ranganath, H S Arun, S Hariprasad 107
- Incidence of Enterococcal Urinary Tract Infection and its Sensitivity Pattern among Patients Attending Teerthanker Mahaveer Medical College and Research Centre, Moradabad, India
Amit Kumar Bharti, Umar Farooq, Sudhir Singh, Navdeep Kaur, Raees Ahmed, Komal Singh 112
- Risk Factors Associated with Clinically Significant Macular Edema in Patients with Type 2 Diabetes Mellitus
Gagan Sathya Prakash, Minal Kothari 117
- Comparative Evaluation of Techniques in Supraclavicular Brachial Plexus Block: Conventional Blind, Nerve Stimulator Guided, and Ultrasound Guided
Jagdish Dureja, R C Siwach, Jaswant Singh, Gunjan Chaudhry, Pranav Bansal 122
- Comparison of Conventional Cephalometric Method of Landmark Identification with Digital Monitor Image and Film-based Digital Image
Sagar A Mapare, Ranjit O Pawar 126
- Efficacy of Vaginal Misoprostol in Second-trimester Abortion
Atima Bharti, Seema Kumari 130
- Ophthalmic Manifestations in Human Immunodeficiency Virus Patients at Presentation in a Tertiary Care Hospital
A Yogeswari, S B Sivathanu, Heber Anandan, M Rekha Sravya 136
- Internal Root Morphology of Maxillary First and Second Molars of South Indian Population by Canal Staining and Clearing Technique
Kishore Gopalakrishna Naik, Nasil Sakkir, Vamsi Kalyan Yaragonda, Mohamed Asifulla, Shuaib Farooq Razvi 140
- Effect of Vaginal Administration of Nitric Oxide Donor Isosorbide Mononitrate on Cervical Ripening Before Induction in Term Pregnancy: A Randomized Controlled Study
Muthuramu Poovathi, Dhivya Kanagasabhai 145

- Scenario of Palliative Radiotherapy at a Cancer Centre in Kashmir
Syed Arshad Mustafa, M Ismail, Saquib Zaffar Banday, Aamir Rashid Patigaroo, Malik Tariq Rasool, Mushood G Nabi 149
- Effect of Alcohol Consumption on Indices of Serum Iron and Ferritin in a Tertiary Care Hospital of Rural, Maharashtra
Makarand Mane, Priyanka Mane, Piyush Prajapati, Shivaraj Afzalpurkar, Aditya Aundhakar 156
- Mantle Cell Lymphoma and Variants: A Clinicopathological and Immunohistochemical Study
Kanwardeep Singh Kwatra, Preethi A M Paul, Dilshad Dhaliwal, Nalini Calton, Joseph M John 162
- Prevalence of Fear of Hypoglycemic Attack in Patients with Uncontrolled Diabetes Mellitus and Correlation Analysis in Diabetes
A D Mahabalshetti, S I Ramdurg, M Dhananjaya 169
- Prediction of Mesiodistal Width of the Mandibular Permanent Canines and Premolars by Utilizing the Mesiodistal Width of Mandibular First Permanent Molars and Incisors
Ranjit O Pawar, Shweta R Bhat 174
- Biofilm Production and Antibiotic Susceptibility Pattern of Coagulase Negative Staphylococci from Various Clinical Specimens in a Tertiary Care Hospital
Priyanka M Mane, Makarand B Mane, S T Mohite, S R Patil, S K Pawar, G S Karande 180
- Assessment of Vascularity of Femoral Head after Post-traumatic Fracture Neck of Femur of Variable Period
Pankaj Jyoti Sonowal, Arnab Karmakar, Dibyendu Biswas, Debasis Mukherjee, Hibjul Ali Khan 183
- Significance of Silver Binding Nucleolar Organizer Regions in Oral Squamous Cell Carcinomas
Ritu Sharma, Gaurav Kumar 189
- Variation in Drainage of Frontal Sinus: A Study on Cadavers
A Sharma, Joseph Abraham, K V Amrutha 194
- Children with Poor School Performance for Specific Learning Disability
M Veena Kumari, Sayid M Barkiya 197

- Correlation of Central Corneal Thickness and Axial Length in Myopes, Emmetropes, and Hypermetropes
Trupti Solu, Pathik Baravaliya, Isha Patel, Santosh Kamble, Chetan Savaliya, Bhavesh Golakiya 202
- Relationship between Employee Empowerment and Organizational Stress: A Research on Hospital Employees
Mustafa Demirkıran, Serap Tařkaya 206
- Targeting Emmetropia in a Pseudophakic Eye: A Prospective Study
C Doshi Vidhan, U Shanbhag Nita, S Karandikar Sumita, D Wanage Taran 213
- Comparative Study of Role of Fentanyl and Dexmedetomidine as an Adjuvant to Bupivacaine in Controlling Post-operative Pain
Vishwanath Kumar, Rakesh Kumar, Neha Priya 221
- Outcome of Modified Papineau Technique with Vacuum-assisted Closer System in the Treatment of Chronic Osteomyelitis and Infected Nonunion of Tibia
S K Kaushik, Bipin Solanki, V P Pathania, Apser Khan 227
- Knowledge, Attitude, and Practices on Vaccination among Mothers of under-5 Children, Attending Immunization Out Patients Department at Gwalior, Madhya Pradesh
Priyesh Marskole, Ritesh Rawat, Priyanka Chouhan, Priyanka Sahu, Rahul Choudhary 231
- Comparison of Bolus Bupivacaine, Fentanyl, and Mixture of Bupivacaine with Fentanyl in Thoracic Epidural Analgesia for Upper Abdominal Surgery
Sachin Gajbhiye, Neeraj Narang, R Mahendra, Ruchi Singh, R B Godwin, Mohammad Ilyas 234
- Observation on Effects of Lumbar Epidural Analgesia for Painless Labor
Shaily Sengar, Raman Ohary 240
- Effects of Deviated Nasal Septum on Sinus Mucosa: A Cadaveric Study
Mani Arora, Sadakat Ali, A K Choudhary, K Gopal 244
- Effect of Oral Awareness Intervention on Dental Caries Prevalence among 3-6 Years Old School Children in Mumbai City
Raju Padmini Jagdish, Sanghvi Apeksha Mahendra, Kalra Dheeraj, Rajeev Haveri, Nagda Rahul Javerchand 248

Incidence of Infectious Complications in Central Venous Catheterization: Internal Jugular versus Subclavian Route <i>Ashita Mowar, H S Nanda, R K Goyal</i>	251
Pulse Therapy - A Boon to Pemphigus: A Case Series from a Rural Tertiary Care Center <i>Uma Selvaraj, Sudha Alagarsamy, Revathy Mathan</i>	257
Profile of Rat Killer Poisoning Cases in a Tertiary Care Hospital at Mysore <i>D K Suneetha, J Inbanathan, Sowmya Kannoth, P K Reshma, M S Shashank</i>	260
Evaluation of Cardiac Autonomic Dysfunction in Human Immunodeficiency Virus Infection and its Correlation with CD4 Levels <i>M Mahesh, M Shashidhara</i>	264
High-sensitivity C-reactive Protein? Is It Significant in Tuberculous Spondylitis <i>V Srinivasa Rao, KVV Sathyanarayana Murthy</i>	270
Complement Levels in Chronic Obstructive Pulmonary Disease: Correlation with Pulmonary Function and Radiological Emphysema Score <i>M Mahesh, Manoj Yalamudi, S Lokesh</i>	276
Microscopic Study of Left Middle Cerebral Artery in Different Age Groups <i>M B Prasanna, Cessy Job, P A Nandagopalan</i>	281
Randomized Controlled Study to Compare the Efficacy of Intravenous Palonosetron and Intravenous Ondansetron in Preventing Post-operative Nausea and Vomiting in Laparoscopic Surgeries <i>K Sureshkumar, A Sivashanmugam, N Giri Murugan, Suneeth P Lazarus, M Nithish Mukunthan</i>	284
Fetal Biometry in Late 3 Trimester for Gestational Age Indian Standards <i>Haridas Govinda Warriar, K M Ashokan</i>	291
Coronary Artery Involvement in Diabetic and Non-diabetic Patients with Acute Coronary Syndrome <i>M K Malthesh, T M Mohammed Sakib, P Mallesh</i>	295
Awareness of Anemia among Pregnant Women and Impact of Demographic Factors on their Hemoglobin Status <i>Thangamani Balasubramanian, Mahalakshmi Aravazhi, Shantha Devi Sampath</i>	299

CASE REPORTS

- Custom-made Pressure Earring for Sustained Compression on Auricular Keloid: A Case Report
Teny Fernandez, Sheela Virginia Rodrigues, K Harshakumar, S Lylajam 302
- Management of Homicidal Cut Throat Open Airway Injury: A Case Report
K S Smitha, S S Nethra, Raghavendra Rao 306
- Carcinosarcoma of Breast: A Rare Case Report with Review of Literature
Nabatika Mohanty, Tapan Kumar Sahoo 309
- Rehabilitation of an Acquired Skull Defect Using Custom Made Titanium Cranial Prosthesis: A Case Report
Teny Fernandez, K Harshakumar, S Lylajam 313
- Gaze Palsy with Diplopia in Hyper Homocysteinemia: A Rare Neuro-ophthalmic Presentation
Sandhya Ramachandra, Shruti Singh, Sahana P Raju 316
- Mesothelial Cyst of Left Round Ligament, Misdiagnosed as a Left-sided Ovarian Cyst Presenting with Pain Abdomen: A Rare Case Report
Bhavana Gupta 320

Tobacco use among Pre-university Students in Kannur, Kerala: A Cross-sectional Study

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Abstract

Introduction: The data available on tobacco use by school children are weak, except in very few developing countries. Studies show that the more adolescents are exposed to tobacco marketing, the more likely they will smoke as adults.

Objectives: To estimate the prevalence of tobacco use among pre-university students in Kannur, Kerala and to estimate the knowledge about the ill effects and law to control tobacco products.

Materials and Methods: It was a cross-sectional study. The study subjects were the students of two higher secondary schools of Kannur, Kerala. The sample included all the students of the 11th and 12th class of the selected schools which amounted to 775. A questionnaire based on the WHO Global Youth Tobacco Survey questionnaire was administered to fetch socio-demographic profile and data related to tobacco use and knowledge, attitude, and practices toward act to control tobacco products.

Results: Out of 775 students, males were 43.35% and females 56.65%. Mean age was 16.32 ± 0.656 years. 11.7% students tried smoking or chewing tobacco at least once. Among boys, the prevalence of tobacco use of any form is 19.04%. Among females, the prevalence of smoking is 5.92%. 88.12% were aware of the act regarding tobacco products. Majority of the students were aware of the prohibition of smoking in public places (90.12%). Majority of the study participants said that tobacco has ill effects (97.16%). Majority of the students do not know about tobacco use by other students of their class (69.29%).

Conclusion: Prevalence of tobacco use especially smoking form in higher secondary school students is high.

Key words: Pre-university students, Smoking, Tobacco use

INTRODUCTION

Tobacco products are made totally or partially from dried leaves of the plant *Nicotina tabacum*, as a raw material, which is intended to be smoked, chewed, or snuffed. All these products have Nicotine, a highly addictive psychoactive agent. Tobacco use is one of the main risk factors for a number of chronic diseases including cancer, lung diseases, and cardiovascular diseases.¹ Tobacco is cultivated in many regions around the world and can be legally bought in most of the countries.² Beedi, cigars, cigarettes, and hookah

are few smoking forms of tobacco and chewing tobacco, dipping tobaccos, gutka, and snuff are non-smoking forms. While the prevalence of tobacco use has declined in some high-income countries, it is increasing in some low and middle-income countries, especially among young people and women.² Among these different forms of tobacco, the common products available and used are beedis, cigarettes, chewing forms, and gutka. The increase in usage of these products occurs due to various reasons. For example, the sale of single cigarettes is an important way of attracting children who cannot afford to buy a whole packet of cigarettes.

Studies show that the more adolescents are exposed to tobacco marketing, the more likely they will smoke as adults. In many countries, the vast majority of adult smokers begin smoking before the age of 18.³ In India alone, nearly 1 in 10 adolescents in the age group 13-15 years have ever smoked cigarettes and almost half of these reports initiating tobacco use before 10 years of age.⁴

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There are only a few studies on prevalence and initiation of smoking and smokeless tobacco use among children in our country.^{5,6} The risks of tobacco use are highest among those who start early and continue its use for a long period.⁷ The early age of initiation underscores the urgent need to intervene and protect this vulnerable group from falling prey to this addiction.⁸ The most common reasons cited for children to start using tobacco are peer pressure, parental tobacco habits, and pocket money given to children.⁹

The present cross-sectional study was undertaken to determine the prevalence and age at initiation of tobacco smoking or tobacco chewing among school children in Kannur city in south India.

MATERIALS AND METHODS

A cross-sectional study was conducted among students of two pre-university schools of Kannur, Kerala. Two schools were selected by random sampling from the city. The principals of the schools were informed in writing about the importance of the survey. The schools were given prior intimation about the date of study to have a maximum number of participants. However, the topic of the study was not informed to the students. Students were told to participate in the study voluntarily and informed consent from the students and school authorities was obtained. The study participants were explained about how to fill up the questionnaire and to provide authentic information. They were assured that all information would be kept confidential.

The sample included all the students of the 11th and 12th class of the selected schools who were present on the days of study. Sample from the first school was 387. Absentees were 33. A sample size of the second school was 388. Absentees were 32. Hence, the total sample size amounted to 775. The response rate was 100% among the students who were present on the day of data collection.

A pre-tested, anonymous, self-administered, and semi-structured questionnaire was prepared based on the WHO Global Youth Tobacco Survey⁴ questionnaires, which included age, gender, type of family, and questions related to tobacco use and knowledge, attitude, and practices toward act to control tobacco products. No changes were made in questions, but some were excluded. The questionnaire was translated into Malayalam and was reviewed by two Malayalam teachers. A pilot study was done on 50 students to see the feasibility of the study.

The data were collected on age, gender, type of family, and weekly pocket money. Data were also collected regarding the use of tobacco, age at initiation, smoking habits of

parents and siblings, peer influence, places of tobacco consumption, purchase of tobacco for elders at home and teachers, etc. 'Ever use of tobacco' was defined as the use of tobacco even once including current tobacco use. Tobacco consumption was broadly classified into three categories: Smoking, chewing, and more than one form of tobacco use. Tobacco smoking includes cigarettes, beedis, and others such as hookah, chillum, and ganja. Smokeless tobacco use includes gutka, khaini, and zarda.

Data were entered in excel sheet after coding. Analysis was done using SPSS V. 17.0 trial version. The categorical outcomes were summarized by rates. Numerical outcomes were summarized by mean and standard deviation.

RESULTS

Out of 775 students, males were 336 (43.35%) and females were 439 (56.65%). Mean age of the students was 16.32 ± 0.65 years (range - 15-18 years). The majority of the students were from nuclear family ($n = 587$, 75.74%). 23.3% of them were from joint families and only 7 (0.09%) were from broken families.

In our study, the majority of the students (579, 74.72%) spent up to Rs. 100 a week as per their wish. 90 (11.7%) students tried smoking or chewing tobacco at least once. Among boys, the prevalence of tobacco use of any form is 19.04% and prevalence of only smoking is 18.15%. Among females, the prevalence of smoking is 5.92%.

Most of the students who used tobacco were cigarette smokers ($n = 85$, 94.45%). Only 2 of them were beedi smokers, 2 were maava users, and only 1 student used both cigarette and chewing forms of tobacco.

In our study, the majority (64, 71.11%) students started using tobacco when they were more than 15-year-old. Out of 90 ever users of tobacco, 40 (44.44%) did not use tobacco in last 30 days, 30 (33.33%) used for 1-5 days, 8 (8.89%) used for 6-15 days, 4 (4.44%) used for 16-29 days, and 8 (8.90%) used tobacco on all 30 days. About one-fourth of the ever users of tobacco (24.5%) used tobacco products in school premises. Less than half of the students were willing to quit tobacco (46.67%).

In the present study, about two-thirds ($n = 32$, 68.08%) of the study subjects said that their friends knew about their habit, in 12.77% family members knew, only 3 (6.38%) said that their teachers knew, and 6 (12.77%) said that nobody knew about their habit of tobacco. Among the users of tobacco, only 47 have got advice from somebody. Out of these 47, 8 (17.02%) said they had got from a program, 12 (25.53%) had got advice from their friends, 8 (17.02%)

got from family members, 6 (12.77%) got from teachers, 7 (14.89%) got from all of the above, and 6 (12.77%) have not got any advice regarding the cessation of tobacco use.

Among 775 students, most of the students ($n = 668$, 86.19%) do not have someone who uses tobacco products at home and 107 (13.81%) have family members using tobacco products and among them majority 85 (79.44%) said their father uses tobacco, 5 (4.67%) said their uncle uses tobacco, 13 (12.15%) said their grandfather uses tobacco products, and 4 (3.74%) said their brother uses tobacco products.

In the present study, 24 students (22.43%) said they have not seen any family member using tobacco for the past 7 days, 45 (42.06%) have seen 1-3 times, 22 (20.56%) have seen 4-6 times, and 16 (14.95%) have seen more than 7 times. When asked about the mode of starting the habit of using tobacco, 25 (27.78%) said they started with their own wish, 10 (11.11%) by peer pressure, 28 (31.11%) by seeing parents, and 27 (30.0%) due to the influence of the media.

In our study, majority 37 (41.11%) of the study subjects got the tobacco products from a nearby shop, 16 (17.78%) from a street vendor, 25 (27.78%) got from friends, and 12 (13.33%) got through other ways like stealing.

Among the current 47 users, 20 (42.55%) said they have been refused to buy tobacco products and more than half of them (27, 57.45%) said that they have not been refused to buy tobacco products by the vendors due to their age.

In our study, 683(88.12%) students are aware of the act regarding tobacco products and 92 (11.88%) are not aware. Among those, who are aware, 126 (16.25%) got the information from newspaper, 147 (18.99%) from television, 32 (4.12%) from friends, and 378 (48.77%) from multiple sources. The majority of the students were aware of the prohibition of smoking in public places (699, 90.12%) and remaining 76 (9.88%) were not aware. More than half of the students 409 (52.65%) were of the opinion that the pictorial warnings on the tobacco products will not help quit tobacco. 173 (22.32%) said the pictorial warnings will help quit tobacco, 193 (24.91%) said they do not know whether the warnings will help or not.

About the chance of using a tobacco product on offering by a friend, 63 (8.13%) said they will definitely use, 35 (4.52%) said probably yes, 54 (6.97%) said probably no, and 623 (80.38%) said they will not use definitely. The majority of the study participants said that tobacco has ill effects ($n = 753$, 97.16%); 22 (2.84%) gave the opinion that tobacco products have no ill effects.

More than two-third of the students knew the ill effect of tobacco as cancer (516, 68.53%) and 141 (18.46%) of students did not mention any ill effect of tobacco. Regarding the easiness of obtaining tobacco products, 85 (10.97%) said it is very difficult to get, 76(9.81%) said fairly difficult, 386 (49.81%) said fairly easy, and 228 (29.41%) said very easy to obtain. Majority 537 (69.29%) of the students do not have knowledge about the use of tobacco by the other students of their class. Among the remaining students, 33 (4.26%) were of the opinion that most of the class use tobacco, 29 (3.74%) said half of the class, 92 (11.87%) said some of them in the class, and 84 (10.84%) none of the students use tobacco. The majority of students 676 (87.23%) have the opinion that use of tobacco products does not make them more attractive and 99 (12.77%) thinks it makes them attractive (Tables 1 and 2, Figures 1-4).

DISCUSSION

The data available on tobacco use by school children are weak, except in very few developing countries. This study was conducted as means of providing baseline information on higher secondary students and their tobacco use.

This study demonstrates that the prevalence of tobacco use among 15-18 years old pre-university students (corresponding to grades 11-12) in Kannur, is high. However, the prevalence is less than in the studies conducted in Gujarat,¹⁰ Karnataka, Uttar Pradesh,¹¹ and other North-Eastern states.¹⁰ But still, this is of concern because, younger the age of initiation of tobacco use, more likely are they become addicted and die due to the diseases caused by tobacco. The strategies to

Table 1: Money spent by the students a week as their own wish

Money spent weekly as per wish	Number of students (%)
No money	127 (16.38)
Below 50 rupees	462 (59.63)
50-100 rupees	117 (15.09)
100-200 rupees	42 (5.42)
More than 200 rupees	27 (3.48)

Table 2: ill effects of tobacco use known by the study participants

ill effects of tobacco use known to the students	Number of students, %
Cancer	516, 68.53
Bronchial asthma	56, 7.44
Bronchitis	9, 1.19
Death	29, 3.85
Coronary artery disease	4, 0.53
Do not know	141, 18.46

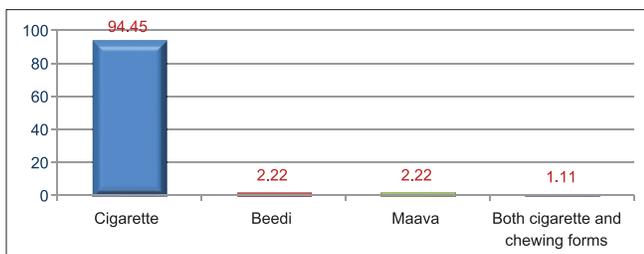


Figure 1: Different types of tobacco use among the study participants (n = 90)

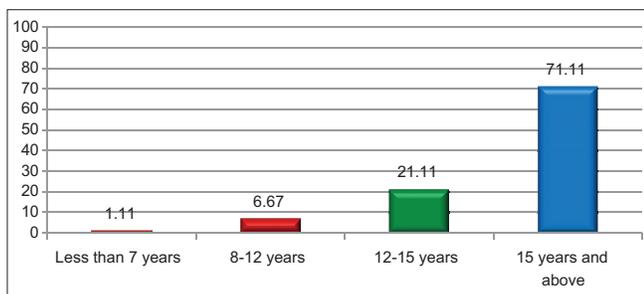


Figure 2: Age at which the participants started using tobacco (n = 90)

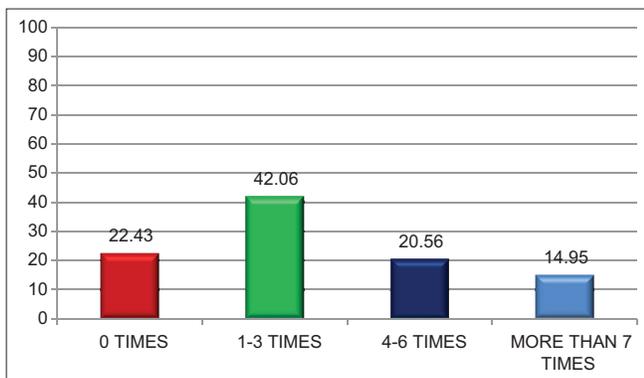


Figure 3: Number of times family members used tobacco in last 1 week (n = 90)

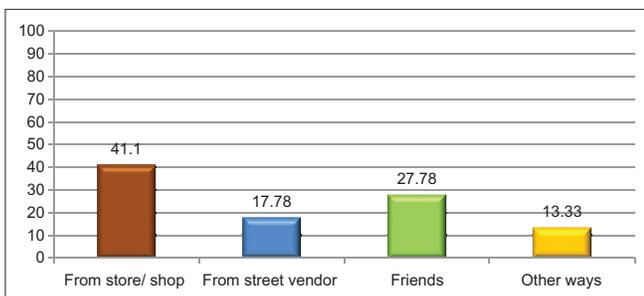


Figure 4: Major source of obtaining tobacco product (n = 90)

reduce initiation of tobacco use needs to be targeted more toward younger age groups.

Cigarette smoking outside the school campus was reported by a high percentage of the youth in the present study. It

is not known whether this smoking was practiced in the presence of family members. Most of them do not have difficulty in procuring the tobacco products despite their young age, and this indicates that laws restricting sale of tobacco products to minors were not implemented adequately. The share of students who wanted to give up tobacco varied considerably. A similar difference was evident in receiving help or advice to give up tobacco usage. This indicates that the programs and interventions targeting young people need to expand their focus to include prevention of initiation as well as offering tobacco cessation programs in young.

There are numerous recent reports, predicting a rise in oral cancer incidence in India. This is based on the observation of an increase prevalence of oral submucous fibrosis, especially in younger individuals, caused by industrially manufactured smokeless tobacco products.^{12,13} In the present study, the tobacco chewers are very less in number, which differs from the nation-wide trend.

Possibly little can be done about exposure at home except to educate the public on the needs to restrict smoking at home for health reasons, but for preventing contact in public places, there is already imposed ban by Hon'ble Supreme Court of India on smoking in public places, along with ban on selling tobacco products to minors. This needs to be implemented robustly while the public needs to be informed about the dangers of tobacco smoke.

In western set up, intervention programs have been successful, at least in delaying initiation of tobacco use. A comprehensive school tobacco control strategy comprising a combination of tobacco-free school policies and an evidence-based syllabus linked to community-wide programs involving families, peers, and organizations with counter-marketing campaigns and community-based activities have succeeded in reducing tobacco in schools.¹⁴ There is greater potential for school-based awareness programs in Kannur city as well as the whole of India followed by cessation initiatives.

CONCLUSION

The prevalence of tobacco use especially smoking form in higher secondary school students is high. The findings of this study will help to design, implement, and evaluate tobacco control and prevention programs in a standard format. It also offers a unique tool to improve the information base on tobacco use among young people, which will support medium-term and long-term programing and advocacy actions for youth-targeted tobacco control.

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Carotid Intima-media Thickness and Epicardial Fat Thickness in Patients with and without Metabolic Syndrome: A Correlative Study

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Abstract

Introduction: The presence of metabolic syndrome (MetS) in an individual confers increased the risk of cardiovascular disease. It is an important risk factor for mortality, morbidity, and decreased life span. There are a very few studies from India regarding the correlation of carotid intima-media thickness (CIMT) and epicardial thickness in MetS patients.

Objectives: To investigate the relationship, if any, between CIMT and epicardial fat thickness (EFT) in patients with and without MetS.

Materials and Methods: This was a prospective cross-sectional hospital based study. A total of 60 patients were studied. 30 with MetS and 30 without MetS anthropometric measurements were recorded, and patients underwent transthoracic echocardiography and ultrasound of carotids. EFT and CIMT were measured, and results were analyzed statistically.

Results: 60 patients were studied. 30 were MetS and 30 were non-MetS. 32 were male and 28 were female. The mean CIMT (mm) among MetS patients was (male-1.80, female-2.02) and non-MetS was (male-1.45, female-1.42). The mean EFT among MetS patients (mm) was (male-8.17, female-9.67) and non-MetS (male-4.52, female-4.38), respectively. The differences were statistically significant. In the MetS group, CIMT and EFT showed a significant correlation which was not so in non-MetS group. In the MetS, CIMT showed a positive correlation with body mass index (BMI) and waist circumference (WC) and no positive correlation with waist-hip ratio (WHR) and cholesterol levels. Among the non-MetS patients, CIMT showed no positive relation with BMI, WC, WHR, and cholesterol levels. Among the MetS patients, EFT showed a positive relation with BMI and WC and no positive relation with WHR and cholesterol levels. Among the non-MetS patients, EFT showed no positive relation with BMI, WC, WHR, and cholesterol levels.

Conclusion: EFT and CIMT were significantly correlated among MetS while not significantly correlated among non-MetS patients, suggesting that EFT can be used as an alternative for CIMT in predicting cardiometabolic risk.

Key words: Carotid atherosclerosis, Cardiac imaging, Syndrome X, Visceral fat

INTRODUCTION

The metabolic syndrome (MetS) refers to the presence of three or more abnormalities (impaired glucose metabolism, elevated blood pressure, hypertriglyceridemia, low-

density lipid cholesterol [LDL] and high-density lipid cholesterol [HDL], and central obesity) in the same person.¹ Several studies showed high prevalence of the MetS in different high-risk populations,^{2,3} but the magnitude of the MetS became apparent when in an apparently healthy population a prevalence of nearly 24% was found.⁴

MetS is an important risk factor for high risk of mortality, prolonged morbidity, and decreased life span. MetS is a powerful predictor of cardiovascular (CV) events such as the risk of myocardial infarction (MI), stroke, and peripheral arterial disease.

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Epicardial adipose tissue (EAT) is defined as adipose tissue situated within the pericardium. EAT is of interest because of its close anatomic relationship with the myocardium. EAT is believed to have an independent correlation with coronary artery disease (CAD),⁵ and EFT is also correlated with abdominal visceral fat volume and EFT measured by echocardiography correlates with magnetic resonance imaging (MRI) measurement.⁶ It is also associated with obesity-related insulin resistance and fasting glucose.⁷ It is strongly correlated with waist circumference (WC) and carotid intima-media thickness (CIMT),⁸ and it reduces on weight reduction.⁹ It is directly related to total cholesterol, LDL, triglycerides, ApoA, ApoB, visceral fat hormones and inversely related to HDL.¹⁰ It is directly related to severity of CAD and number of vessels involved in CAD, where EFT is proportionately higher in multivessel CAD than 1- or 2- vessel CAD.¹⁰ It is more informative than abdominal obesity as predictor of coronary atherosclerosis.¹⁰

Over the past years, a large number of trials have been performed in which CIMT was used as an alternative end point for CV morbidity and mortality to study the efficacy of certain interventions. The main advantage of using CIMT as an end point in a trial over morbidity and mortality as end points is the considerable reduction in sample size and possibly shorter duration of follow-up.¹¹ Studies of the association between CIMT and coronary atherosclerosis, as assessed by coronary angiography, show generally modest positive associations.^{12,13}

The literature from India in this regard is sparse. Hence, this study was taken up.

MATERIALS AND METHODS

This was a prospective, comparative, non-interventional, case-control study carried out between October 2013 and October 2015 in the Department of Medicine, JSS Hospital, a tertiary care teaching hospital in Mysore city. A total of 60 patients of both sexes aged between 18 and 65 years were studied. Patients satisfying three or more MetS alterations such as central obesity, hypertriglyceridemia, LDL-HDL cholesterol, and hypertension impaired fasting glucose or previously diagnosed. Type 2 diabetes was included. Excluded were those with hypothyroidism, chronic kidney disease, chronic liver disease, past neck surgery, and pregnancy.

Echocardiography was performed using Philips HD 11 XE Machine by a single observer for all the subjects. EFT was measured from parasternal long and short axis B-mode still free images perpendicularly to the free wall of right ventricle at end-systole in three cardiac cycles, using the

aortic annulus as the anatomic reference for the parasternal long axis view and the papillary muscle level for short axis view. Epicardial fat thickness (EFT) was measured at end-systole.⁶

Ultrasound carotid was performed using Philips HD 11 XE Machine by a single observer. The CIMT was measured on the far wall at 1 cm from the bifurcation of the common carotid artery as the distance between the lumen-intima interface and the media-adventitia interface. Blood sugar levels were estimated using the glucose oxidation method. HbA1c was done using HPLC method. Insulin levels were measured using chemiluminescence immunoassay method. Lipid profile was done using Agappe lipid profile kit.

Statistical Analysis

Descriptive statistics was used to identify frequencies and the mean scores of the sample. Independent sample *t*-test was computed to compare variables with each other. The relationship between the variables was explored using bivariate correlational analysis using SPSS version 16.0.

RESULTS

Among the 60 subjects, 32 (53.3%) were males and 28 (43.6%) were female. The age ranged from 18 to 60 years. 1 (1.6%) from the age group of 18-20, 4 (6.6%) from the group of 21-30, 10 (16.6%) from 31 to 40 group, 20 (33.3%) from 41 to 50 group, and those from 51 to 60 were 25 (41.6%). 32 (53.3%) were males and 28 (43.65%) female. 30 (50%) were MetS patients and 30 (50%) were non-MetS patients.

Comparison of EFT among MetS and non-MetS Group (Table 1) revealed that the mean scores of MetS group was higher ($M = 8.77$, standard deviation [SD] = 1.89) than the control group ($M = 4.45$, SD = 0.99). These differences in the mean scores of the two groups were found to be statistically significant.

On comparing the CIMT among MetS and non-MetS group (Table 2), it was observed that the mean scores of MetS group was higher (mean [M] = 1.89, SD = 0.30) than the control group ($M = 0.30$, SD = 0.09). However, this difference was not found to be significant. This indicates that there is no difference in the CIMT level of MetS and controlled group participants.

The bivariate correlational analysis was done to find the relationship between EFT and CIMT of MetS patients (Table 3). The results showed that there was a positive and significant correlation between EFT and CIMT of MetS patients with a $P = 0.00$ and $r = 0.789$.

Table 1: Comparison of EFT between MetS and non-MetS group

Group	N	Mean	SD	t	Significant
MetS	30	8.77	1.89	11.06	0.00
Non-MetS group	30	4.45	0.99		

EFT: Epicardial fat thickness, MetS: Metabolic syndrome, SD: Standard deviation

Table 2: Comparison of CIMT between MetS and non-MetS group

Group	N	Mean	SD	t	Significant
MetS	30	1.89	0.30	7.902	0.00
Non-MetS	30	1.44	0.09		

CIMT: Carotid intima-media thickness, MetS: Metabolic syndrome, SD: Standard deviation

Table 3: Bivariate correlation between EFT and CIMT of MetS patients

Pearson correlation	CIMT
EFT	0.789**
Significant two-tailed	0.00
n	30

CIMT: Carotid intima-media thickness, MetS: Metabolic syndrome, EFT: Epicardial fat thickness, **p value of .00 and r value of .789

DISCUSSION

The association of obesity with CV disease depends both on the amount of body adiposity and its distribution. Those with increased fat in the abdominal region have atherogenic lipid profiles and are at increased CV risk. The loss of elasticity in medium and large arteries is an early manifestation of atherosclerosis. This study aimed to evaluate whether EAT, as determined by echocardiography, is related to CIMT, an index of subclinical atherosclerosis.

Aydin *et al.* conducted a study on 2102 participants. CIMT was measured in all of the participants. The study sample was divided into 4 groups; Group 1 subjects with a body mass index (BMI) < 25.0 kg/m², Group 2 BMI between 25.0 and 29.9 kg/m², Group 3 BMI between ≥ 30 kg/m² and 39.9 kg/m², and Group 4 BMI ≥ 40 kg/m². CIMT was higher in the individuals with MetS compared to their normal counterparts. Furthermore, the subgroup analysis showed that CIMT values in Group 1, Group 2, and Group 3 were significantly higher in subjects with MetS compared to their normal counterparts, whereas the values were similar in Group 4. They concluded that CIMT of overweight, obese, and normal weight individuals without MetS were lower than their counterparts with MetS. In our study, the CIMT in MetS patients was higher when compared with the normal individuals, but the difference was not statistically significant.

Reinehr *et al.* had analyzed the relationships between MetS and IMT in 461 overweight adolescents aged 10-18 years. Overweight adolescents with MetS demonstrated increased IMT values compared with overweight adolescents without MetS. The use of dichotomized variables reduced the diagnostic accuracy. Thus, in clinical practice, treatment of overweight adolescents should be based on weighing CV risk factors themselves, rather than on the dichotomous variable MetS.

In our study, the IMT of the common carotid-internal carotid artery measured by carotid artery Doppler with a minimum of 0.6 mm and maximum of 1.6 mm.

Jeong *et al.*¹⁴ in their study of 203 IHD patients which included MI, stable angina, and unstable angina and tried to correlate it with the Carotid Intima Media Thickness. The mean age was 63.1 ± 10.4 years. In 108 male patients, the mean value of EFT was 6.38 mm (1.10-16.55 mm). They had found that the incidence of CAD increases with increase in EFT. There was no significant difference in the EFT as per the patient's clinical diagnosis was concerned. They had found a significant correlation of EFT with age, C-reactive protein, BMI, and WC. In our study, the EFT found to be increased in patients with MetS (male-8.17, female-9.67) when compared with non-MetS patients (male-4.52, female-4.38) and the EFT was significantly and positively related with BMI and WC and no correlation with WH ratio and cholesterol levels and our findings correlated with Jeong *et al.*¹⁴

Iacobellis and Leonetti studied 30 obese subjects and compared EFT with Insulin resistance. They found that the thickness of EFT in the free wall of right ventricle ranged from 4 to 17.4 mm. The EFT was significantly correlated with WC, BMI, and fasting glucose levels. The present study also showed that EFT is significantly correlated with WC in obese subjects. They concluded that EFT was significantly correlated with obesity-related insulin resistance.

One of the strengths of this study is that all the echocardiographic measurements were done by a single physician trained in echocardiography. However, this study is not without limitations. The number of subjects studied could have been large. Furthermore, MRI was not used which gives a better estimate of EFT.

In the evaluation of cardiological disorders, echocardiography is used for the assessment of left ventricle function and other parameters. The cardiac patient being evaluated by the cardiologist/physician undergoes routine echocardiography and in the same setting ejection fraction can be measured by the same specialist, thus avoiding the need for another

scan (ultrasonography abdomen) by another specialist (radiologist).

CONCLUSION

The CIMT and EFT were significantly correlated in patients with MetS when compared with non-MetS patients, suggesting that MetS patients are prone for cardio MetS risks when compared with non-MetS patients. EFT can be used as an alternative for CIMT in predicting CV risks.

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Role of Ultrasonogram in Detection of Congenital Anomalies and Prevalence of Anomalies in High-risk Pregnancies

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Abstract

Introduction: In any antenatal population, about 2-3% of the foetus are affected by congenital anomalies it is mainly due to intrinsic genetic pathology and abnormal embryogenesis during the early gestational period.

Objective: To categorize the type of major congenital anomalies in routine second and third trimester ultrasonogram (USG) and its association with high-risk pregnancy.

Methods: This is a cross-sectional study carried out in the Department of Obstetrics and Gynaecology at Government Theni Medical College and Hospital, Tamil Nadu. The study population includes about 6250 antenatal mothers in the second and third trimester, who were subjected to USG by expert radiologists and the ultrasound findings were analysed on a statistical basis in structured data collection form.

Results: About 6250 antenatal mothers of the 2nd and 3rd trimester were subjected to USG out of which 122 mothers were found to have an anomalous foetus. (1) The antenatal prevalence of congenital anomalies was 1.95%, (2) The mean gestational age and mean maternal age at diagnosis was 24 weeks (Standard deviation [SD] \pm 5.15) and 28.5 years (SD \pm 6.10), respectively. Central nervous system was the most common system affected out of which maximum anomaly was anencephaly.

Conclusion: USG is a cost-effective, non-invasive and sensitive tool in detecting the congenital anomalies antenatally in the hands of an experienced radiologist. Besides the first-trimester USG, the second trimester scan is mandatory in detecting anomaly in the growing foetus, as the majority of congenital anomalies are detected between 20 and 22 weeks of pregnancy.

Key words: Anencephaly, Congenital anomalies, Second and third trimester

INTRODUCTION

In any antenatal population, about 2-3% of the foetus are affected by congenital anomalies it is mainly due to intrinsic genetic pathology and abnormal embryogenesis during the early gestational period. The factors such as racial, social, environmental, and economical factors are responsible for the type and prevalence of the anomalies in a different population.

The most common anomalies noticed are in the nervous system, cardiovascular system and genitor-urinary system.

Although there are many investigations for detection of the anomalies, ultrasonogram (USG) is the gold standard until now in modern obstetrics. Therefore, routine anomaly USG is advised as early as 11-14 weeks and again at 20-22 weeks of gestation which detect almost 95% of the major anomalies.

In India because of the increasing awareness of detection of anomalies by ultrasonogram, the percentage of mental and physical handicap is in the declining phase. Detection of anomalies in the earlier gestation age is essential to reduce the maternal risk during expulsion process and to improve future obstetric outcome. The main aim of the study is to evaluate the prevalence of the anomalies in high-risk maternal population.

METHODS

This is a cross-sectional study performed in the Department of Obstetrics and Gynaecology at Government Theni

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Medical College and Hospital. About 6250 antenatal mother of 2nd and 3rd trimester were screened for the congenital anomalies by an expert radiologist from January 2015 to December 2015.

Form B consent is obtained from all the antenatal mothers. Expert trans abdominal USG was carried on sonoray DS30 machine using 3.5-5 MHz ultra-serve curvilinear probe.

A proforma containing age, parity, investigations for the maternal disease was used.

RESULTS

During the study period of January 2015 to December 2015, a total of 6250 antenatal mothers of second and third trimester were screened. About 122 numbers of congenital anomalies were detected. The antenatal prevalence of congenital anomalies was found to be 1.95%. Of the antenatal mothers screened, the majority were between 20 and 35 years of age (94) followed by those <20 years of age (24). The mean maternal age at diagnosis was 28.5 years. Most of the women were illiterate accounting 73%, and those who had primary education represented 20%. The majority of the women were primi (50.8%) followed by second gravida (40.16%). The majority of the cases were detected at 2nd trimester, i.e., 76 cases (62.29%) the mean gestational age during the time of diagnosis was 24 weeks of gestation (Table 1).

Out of the study population ($n = 122$), 105 (86%) fetuses with congenital anomaly were alive at the time of scanning and the rest 17 (14%) numbers were intrauterine death. 4 Women had twin pregnancy with anomalous fetuses. Out of which one was conjoint twins. 20 fetuses had multiple anomalies (Table 2).

Out of 122 anomalous fetuses, central nervous system (CNS) defect was the most common accounting 38.5% of which maximum number had anencephaly (23.77%) followed by genitourinary system 26.22% we notice a high sensitivity in the detection rate of CNS, genitourinary and cardiac anomalies (Table 3, Figure 1 and 2).

Out of 122 anomalous, 56 cases were high-risk pregnancies.

Teenage pregnancy (24 cases) accounts for 42.8% of the total high-risk cases followed by diabetes, seizure, hypertension, elderly age (Table 4).

DISCUSSION

Routine B mode transabdominal USG has made it possible to detect increased number of birth defects antenatally

Table 1: Socio-demographic variables in anomaly positive cases (n=122)

Variables	Category	Numbers (%)
Age group	Adolescent (<20 years)	24 (19.6)
	Middle age (20-35)	94 (77)
	Elderly (>35)	4 (3.27)
Literacy	Illiterate	89 (72.95)
	Primary education	24 (19.67)
Occupation	Graduation	9 (7.37)
	Unemployed	109 (89.3)
	Employed	15 (12.29)

Table 2: Obstetric characteristics of anomaly positive population (n=122)

Variables	Category	Numbers (%)
Parity	0	62 (50.8)
	1	49 (40.16)
	2	9 (7.37)
	3	2 (1.63)
Gestational age	2 nd trimester	76 (62.29)
	3 rd trimester	46 (37.7)
Viability	Alive	105 (86)
	IUD	17 (14)

Table 3: Prevalence of anomalies in different organ systems

Category	Total (%)	Anomaly	Number (%)
CNS	47 (38.5)	Hydrocephalus	12 (9.8)
		Anencephaly	29 (23.77)
		Meningomyelocele	4 (3.2)
		Spina bifida	2 (1.6)
		Polycystic kidney	2 (1.6)
Genito urinary system	32 (26.22)	Obstructive uropathy	30 (24.6)
		Shunt diseases	13 (10.6)
Cardiac	13 (10.6)	Polycystic kidney disease	2 (1.6)
		Obstructive nephropathy	30 (24.6)
GI	10 (8.1)	Skeletal dysplasia	8 (6.5)
		Hydrops foetalis	1 (0.8)
Musculo skeletal	8 (6.5)	Conjoint syndrome	1 (0.8)
		Down's syndrome	3 (2.4)
		Single umbical artery	7 (5.7)
		Others	12 (9.8)

GI: Gastrointestinal

Table 4: Association between high-risk cases and congenital anomalies

High-risk	Numbers (%)
Teenage	24 (42.8)
Diabetes	9 (16.07)
Hypertension	5 (8.9)
Elderly	4 (7.1)
Previous Iscs	10 (17.85)
Seizure	4 (7.1)

Total number of high-risk cases reported 56

The antenatal prevalence of congenital malformation in the present study was 1.95% which is comparable with the observations of Wong *et al.* (2004)¹ which is 1.4% and

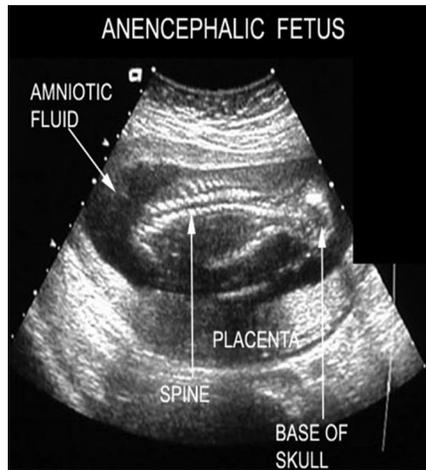


Figure 1: Ultrasound picture of an anencephalic foetus detected in second trimester

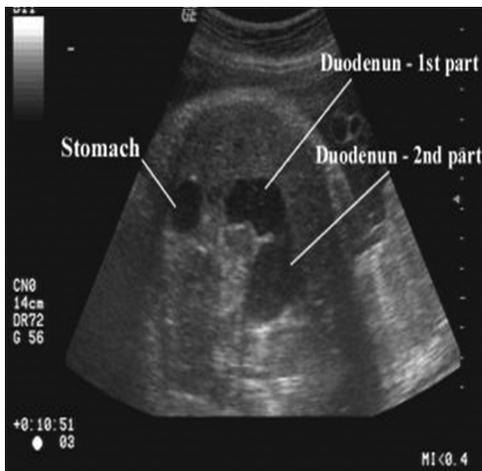


Figure 2: Ultrasound picture of a foetus showing double bubble sign in duodenal atresia

nakling et al (15) 2005² which is 1.5%, Patel ZM *et al* 2005³, which is 1.6%. The routine ultrasonogram in antenatal mothers detects about 40% of anomalies compared to 28% those who undergo ultrasonogram on risk basis which is comparable with observations of Boyd PA *et al.* 2005⁴, Temtamy S *et al* 1998⁵; and Biri A *et al* 2005⁶.

The detection rate of anomalies by ultrasonogram is depend upon the prevalence of anomalies in the study population, the experience of the sonologist, the gestational age at the time of scanning, maternal age and medical risks.

Though elderly age group and higher parity are considered as risk factors for congenital anomaly, in our study the incidence was observed higher in younger age group and primigravida. This may be due to earlier age of marriage and early pregnancy in our screening population similar observations were present in the study of Lin AE *et al.*,

1999⁷ and Centers for Disease C 2006;54⁸. In present study, congenital malformations of the central nervous system were the highest (38.5%) followed by malformations of the genitourinary system (26.22%). Similar findings were observed by Sallout *et al.*,⁹ Perveen *et al* (2007)¹⁰ and Mahela S *et al.*, 2016¹¹.

Due to early marriage and early pregnancy, poor literacy, poor intake of folate, there is increased prevalence of CNS malformations in our study population. Single umbilical artery was a common anomaly detected in miscellaneous group which is around 5.7% of the total anomalies. It is comparable to Canfield *et al.* 2006¹². Lee RS 2006;118¹³, Alia N *et al* 2010¹⁴ and Souka AP *et al* 2006;194¹⁵.

CONCLUSION

Prevalence of congenital anomalies in our study is 1.95%. CNS is the most common system involved of which anencephaly is the maximum. Health education and creating awareness regarding the importance of detection of anomalies will be the first step in preventing and reducing adverse perinatal outcome in such pregnancies.

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Evaluating the Etiology and Disease Specific Clinical Profiles of Acute Undifferentiated Febrile Illness

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Abstract

Background: To evaluate the etiology and disease specific clinical profiles of acute undifferentiated febrile illness (AUF) in JSS Medical College, Mysore in south India, a tertiary medical center.

Methods: This 2 years prospective, observational study was conducted in JSS Medical College in 150 patients. Clinical evaluation and relevant investigations like Blood culture; malarial parasites and febrile serology (acute and convalescent) were performed.

Results and Observation: A total of 150 AUF patients were evaluated: scrub typhus (19); malaria (3); enteric fever (2); dengue (11); leptospirosis (19); hantavirus (1), acute bacterial infections (14), HIV (1), hepatitis (1), and unclear diagnoses (79).

Conclusion: This study reports discovery of dengue, typhus fever, leptospirosis, and rare disease like Hanta and more number undiagnosed cases ranging from 15% to 42% in local community. This shows that further research is required in identifying the etiology of undifferentiated fevers.

Key words: Acute undifferentiated febrile illness, Fever, Thrombocytopenia

INTRODUCTION

The acute undifferentiated febrile illness (AUF) is commonly seen in developing countries especially in tropical regions. The etiology is usually unknown and presents without disease specific focal signs and symptoms. These infectious diseases traverse the most of the boundaries established by medical specialists with multiorgan involvement leading to increased morbidity and mortality in spite of to the availability of newer investigations.

The prevalence of dengue, leptospirosis, malaria, hepatitis, and scrub typhus has reached endemic proportions. With respect to the local prevalence of AUF patients with

hematological complications, if not managed well can become fatal.

A study in a dengue endemic area of Vietnam demonstrated the inability of physicians to accurately diagnose the disease, regardless of their level of training or years of clinical experience.¹ This difficulty was not due to the lack of advanced laboratory equipment. Similar problems are faced by clinicians in the developed world as they struggle to find a specific etiology for AUF acquired in the tropics. The cause of systemic febrile illness could not be identified by physicians at academic travel medicine clinics in more than half of travelers returning to the United States from South America.² In another series, no etiology could be determined in at least one-fourth of hospitalized febrile travelers returning to the United Kingdom from the tropics.² Given their similar clinical presentations, many researchers have commented on the difficulty in distinguishing between dengue fever and leptospirosis. In places where dengue is recognized as a significant health problem, leptospirosis may be overlooked as the cause of AUF, delaying antibiotic administration and leading to increased complications and death.³

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Forming guidelines in approach of management with relation to treatment, transfusion and, diagnosis - serology, virology test for AUFI are required to come to a better understanding of the etiology is utmost need. Despite the existence of safe and effective interventions, many people lack access to needed investigations, prevention methods and treatment.

As an average, every 5th or 6th admission in JSS hospital is a case of AUFI. We conducted this study to evaluate the local prevalence, clinical presentation, and seasonal variation of several type of AUFI to correlate with the symptoms and signs and with specific investigations to make a proper diagnosis and early treatment.

METHODS

The study was performed at the medical wards in JSS Medical college hospital, Mysore, Karnataka, India, a tertiary medical care center. Patients who are more than 14 years of age with acute undifferentiated fever with thrombocytopenia of <14 days during the period between July 2009 and July 2011. Patients with fever >14 days, with localized focus of infection in skin, soft tissue, autoimmune diseases, connective tissue, vasculitides, idiopathic thrombocytopenic purpura, leukemia, malignancy are excluded from the study.

Once the patients enrolled into the study, a detailed history was elicited and a thorough clinical examination was done. Data were collected in a prewritten proforma; Patients were screened with hemoglobin, total leukocyte count, differential leukocyte count, Platelet count, hematocrit, peripheral blood smear, dengue NS1Ag, IgG ELISA, IgM ELISA, quantitative buffy coat (QBC) for malaria parasite, serology for enteric fever, scrub typhus, leptospirosis, liver function tests (LFT), and a chest radiograph were done in all patients. The blood c/s, urine c/s, ultrasound abdomen, computed tomography scan was done whenever it is indicated. Kits used were from standard diagnostics SD. Elisa kits were used for HIV, HbsAg, dengue (NS1 Ag, IgM, IgG), *Leptospira* (IgG), rapid tests were done for influenza, hanta virus, weil felix for scrub typhus, QBC and blood picture for malaria, blood culture for widal positive typhoid cases.

In whom a final definite diagnosis was reached, were treated for the disease. Platelet transfusions were done if platelet count was <10,000/cumm or who had bleeding manifestations irrespective of their platelet count. Prior approval was obtained from Ethical Committee of the JSS Medical College Hospital, Mysore and informed consent was obtained by the study participants.

RESULTS AND OBSERVATION

A total number of 150 patients with AUFI admitted to JSS Hospital over 2 years were studied. In our study, 81 were male and 69 were female patients (Figure 1). The mean age was 35.2 years with a range of 16-70 years. Undifferentiated fever was seen in 97 and others with specific etiology were 53. The Malaria was seen in 3, typhoid in 2, typhus in 16, dengue in 8, leptospirosis in 17, hanta in 1, HIV in 1, Hep B in 1, combined illness like Typhus with dengue fever was seen in 2, typhus with leptospirosis was seen in 2, and dengue with leptospirosis was seen in 1 (Table 1).

Clinical manifestation of thrombocytopenia in the form of petechia, hematemesis, malena, menorrhagia, was there in 38 patients, and there was no similar clinical manifestation in the remaining 112 patients. The most common presentation was fever with a headache of 7 days duration which was observed in 46% of the patients. Symptoms

Table 1: Comparison of different studies done in AUFI*

Name of illness	Percentage of points			
	Suttinont study	Stephen study	Anurgha study	shashidhara study
Leptospirosis	36.9	13.2	3	12.6
Scrub typhus	16.0	5.9	47.5	12.6
Viral infection	10.7	-	-	-
Dengue	5.2	5.3	7	7.3
Japanese encephalitis	0.4	1	-	-
Influenza	4.6	-	-	-
Hanta virus	-	-	0.3	0.6
Q fever	0.8	-	-	-
Malaria	-	12.5	17.1	2
HIV	-	-	-	0.6
Hepatitis B	-	-	-	0.6
Enteric fever	-	-	8	1.3
Acute bacterial infection	1.2	-	-	9.3
Unknown	31.7	41	15	52.6

*AUFI: Acute undifferentiated febrile illness

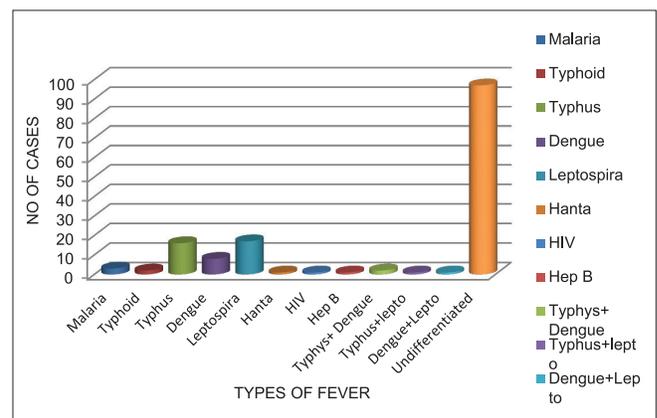


Figure 1: (Different types of fever in our study)

such as Headache, vomiting, lymphadenopathy, skin rashes, hepatosplenomegaly leukopenia, raised LFT were independently associated with scrub typhus. Headache, vomiting, petechia hepatosplenomegaly, leukopenia, raised LFT is associated with leptospirosis. Conjunctival suffusion, abnormal LFT, hepatosplenomegaly was associated with dengue fever. Bleeding manifestation in the form of hematemesis was seen in one patient.

DISCUSSION

The purpose of this study was to identify the various aetiologies and clinical presentations of AUFI in and around Mysore district in, south India, with the goal of assisting local health professionals in diagnosing, treating, and preventing these diseases.

In our study, the younger and middle-aged patients were more affected as compared to patients above 55 years. Results seen in our study are not unlike those found in other tropical regions of the developing world, although the relative incidence of specific pathogens varies considerably.

In a significant number of cases, thrombocytopenia leads to various bleeding manifestations and influenced the clinical profile of this febrile illness. The mean platelet count at presentation was in the range of 20-30000. In the majority of patients, thrombocytopenia was transient and asymptomatic. Platelet transfusion was given in one patient each in dengue, typhus fever and typhoid fever, 5 in leptospirosis, 15 in undifferentiated fever when platelet count has fallen below 10,000/cumm or patient with bleeding manifestations irrespective of platelet count.

In our study, we observed a combined illness in three patients such as typhus with dengue fever was seen in 2, typhus with leptospirosis was seen in 2, and dengue with leptospirosis was seen in 1. Although dual infections were indicated by the results of the serology in the present study, the possibility that these apparently multiple infections represent false-positive results, caused by cross-reacting antibodies or non-specific polyclonal immunoreactivity, cannot be excluded. This infers that advanced investigations are essential to isolate the organism and make a proper diagnosis and identify the causative organism.

Out of 150 patients, 146 of them had a good recovery and 4 patients expired due to septicaemia and multiorgan dysfunction syndrome. Sharp decline of platelet counts was noticed during the course of hospital in these 4 cases.

In our study the *Leptospira*, typhus and dengue were common and enteric fever, malaria were less and the proportion of undiagnosed cases were very high but similar

when compared to the other studies. Our study showed one positive case of hantavirus which was not commonly observed in our area.

A similar study done by the Anugrahchrispal done in Vellore, Tamilnadu, south India for 1 year observed predominantly scrub typhus and malaria and enteric fever and one case of hanta virus with less no of undiagnosed cases.⁴

A similar study conducted by Suttinont, *et al.* done in five hospitals at different provinces in Thailand.⁵ The leptospirosis and rickettsioses, especially scrub typhus, dengue infection or influenza and double infections were thus found to be major causes of AUFI in Thai agricultural workers.

Stephen *et al.* conducted similar study⁶ in Ecuadorean Amazon basin, by Viral isolation, reverse transcription-polymerase chain reaction (RT-PCR), along with other investigations and found, predominantly leptospirosis, malaria, rickettsioses, dengue and Q fever, and few cases of brucellosis, Ilhéusencephalitis, and venezuelan equine encephalitis, Oropouche, and St. Louis encephalitis virus infections. None of these pathogens, except for malaria, had previously been detected in the study area. Hence, their presence was unknown to local clinicians and public health authorities. Which once again confirm that advanced investigations are essential to isolate the organism and make a proper diagnosis and identify the causative organism.

The leptospirosis, malaria, scrub typhus, murine typhus, *Rickettsia typhi*, and dengue have been identified as major causes of AUFI in Thailand, Malaysia, and Nepal.^{1,6,7} Dengue was found to cause one-third of all cases of acute undifferentiated non-malarial fever in an area of Vietnam.⁸ In South America, spotted fever group rickettsia, leptospirosis, and coxiella burneti have been identified as major identifiable causes of AUFI in a subtropical area of northwestern peru.⁹ Dengue, malaria, and *Leptospira* were found in AUFI patients in the Amazon basin of Peru.

The above studies have shown leptospirosis, malaria, scrub typhus, murine typhus, *R. typhi*, and dengue were being the major causes of AUFI throughout the world and other illness dependent on the demographic area and its endemicity, vector control and level of hygiene in the area. Stephen study has shown increased no of viral fever and less number of undiagnosed cases as compared to other studies due to special test done like viral isolation or RT-PCR test.

Even when dengue fever and leptospirosis are suspected, currently available rapid serologic tests cannot reliably

detect IgM antibodies until at least the 6th or 7th day of clinical illness thus making it more complex for the treating physician. The advanced investigations such as virus isolation and identification of viral particle are more specific and sensitive. These tests are costly and may give false positive results because of contamination and fail to differentiate between primary or secondary infection. They require advanced laboratories and experts in the concerned field to analyze the tests.

This study helps to initiate empirical treatment for leptospirosis, q fever or other rickettsial disease with doxycycline after ruling out malaria and treating with quinolones or cephalosporin whenever the enteric fever is the differential diagnosis of the fever in the approach to treat AUFI. This is cost-effective and useful in treating AUFI in remote areas of developing countries where advanced investigations are unavailable.

CONCLUSION

Most of AUFI are self-limiting but accurate diagnosis and proper treatment are important in reducing the duration of fever and in preventing potentially lethal complications leading to multiorgan failure.

This study reports for the 1st time a number of important pathogens that have been overlooked in our area. The discovery of dengue, typhus fever and leptospirosis and rare disease like hanta in local community prompted the Local clinical laboratories now offer serologic testing for these diseases. Such testing is admittedly of little utility early in the course of AUFI, but can be useful to establish the etiology during outbreaks and for patients who present after several days of illness.

The type of disease and the incidence also depends on the demographic area and its endemicity, vector control and level of hygiene in the area. With Time clear patterns will emerge, with cumulative experience and advanced

investigations, will go a long way to helps us to tackle this problem of undifferentiated fevers head on. It is imperative to maintain a sound epidemiological database of AFIs so that evidence-based diagnostic criteria and treatment guide can be made.

Including our study, the other studies have shown undiagnosed cases ranging from 15% to 42%. This shows that further research is required in identifying the etiology of undifferentiated fevers which are more of viral origin than bacterial.

The drawback of our study is there were less number of cases, and we have not done nucleic acid detection or isolation in cell culture and identification using immunofluorescence.

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Comparative Study Evaluating Safety and Efficacy of Bicalutamide (150 mg) Monotherapy versus Orchidectomy and Bicalutamide (50 mg) in the Treatment of Locally Advanced/Metastatic Prostate Cancer

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Abstract

Background: Prostate cancer is one of the leading causes of death in men. The approach to prostate cancer diagnosis and treatment is changing rapidly across the spectrum of the disease. We studied, locally advanced and metastatic cancer prostate in our study. Suppressing both testicular and adrenal androgen known as combined androgen blockade (CAB), allows for a better initial and longer response compared with those methods that inhibit the production of only testicular androgen. We assessed the safety and efficacy of two methods of CAB for locally advanced/metastatic Ca prostate, i.e., orchidectomy with bicalutamide 50 mg versus bicalutamide 150 mg daily (without orchidectomy).

Materials and Methods: The present study included 50 prospective patients of locally advanced or metastatic Ca prostate. A detailed history regarding symptoms of Ca prostate, complete physical examination, digital rectal exam (DRE), and baseline investigations that included hemogram, urine R/E, urine C/S, liver function tests, renal function tests, prostate-specific antigen level, radiological included whole body X-rays, transrectal ultrasound/imaging computed tomography scan, and bone scan were done. Sextant prostate biopsy - Gleason grading and other metastatic evaluation were carried out before starting of the treatment. A comparative analysis of the effect of 2 different treatments was assessed by eastern cooperative oncology (Group) performance grading criteria, symptoms-general, urinary and side effects of medication, morbidity, and progress of disease.

Results: We observed that monotherapy (150 mg) and surgical castration + bicalutamide (50 mg) in men with locally advanced prostate cancer offers better tolerability and higher health-related quality of life.

Conclusion: Anti-androgen therapy in combination with surgical castration is given to enhance survival and to maintain or improve the quality of life of patients with advanced prostate cancer. Bicalutamide appears to have a more favorable tolerability profile than either therapy on the basis of current evidence.

Key words: Complete androgen blockage, Bicalutamide, Monotherapy in Ca prostate

INTRODUCTION

The prostate gland is an exocrine organ weighing 20-25 g, located deep in the pelvic between the bladder and the

external urinary sphincter in male anterior to the rectum and behind symphysis pubis. Prostate cancer is one of the leading causes of death in men. The incidence of prostate cancer in India is 1.4 to 7.9/100000 populations.¹ The approach to the prostatic cancer diagnosis and treatment is changing rapidly across the spectrum of the diseases.

The traditional treatment for locally advanced and metastatic adenocarcinoma prostate has been bilateral orchidectomy. Over the past 50 years, numerous medications have been developed and tested that achieve a medical castration

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with no overall change in the survival. It is well known that most of the prostatic carcinomas are hormone dependent and that approximately 70-80% of man with metastatic Ca prostate respond to a various form of androgen deprivation. Although testosterone is the major circulating androgen produced by testicles, the adrenal glands secrete the androgen dehydroepiandrosterone, dehydroepiandrosterone sulfate, and androstenedione. Suppressing both testicular and adrenal androgen known as combined androgen blockade (CAB), allows for a better initial and longer response compared with those methods that inhibit the production of only testicular androgen. Complete androgen blockade can be achieved by combining an anti-androgen with the use of a luteinizing hormone-releasing hormone agonist or orchidectomy. Non-steroidal anti-androgen such as bicalutamide in higher doses offers an effective alternative to CAB with potential quality of life benefits.

Aims and Objectives

1. To compare the safety and efficacy of bicalutamide - 150 mg monotherapy versus orchidectomy and bicalutamide - 50 mg.
2. To monitor the effect of treatment and progression of disease.
3. To study the complications and side effects of the disease.
4. To formulate our recommendation for the treatment of locally advanced/metastatic Ca prostate based on our observation.

MATERIALS AND METHODS

The present study included 50 prospective patients of locally advanced or metastatic Ca prostate.

The following inclusion and exclusion criteria were applied.

Inclusion Criteria

1. Locally advanced/metastatic prostate cancer patients diagnosed/confirmed histologically/cytologically.

Exclusion Criteria

1. The presence of any other cancer of organs or any other concomitant disease that would interfere with the treatment of/ or patient compliance.
2. Any severe renal or hepatic dysfunction - serum creatinine > 2.5 mg/dl, serum bilirubin, and/or serum transaminases > 50% of upper normal limits
3. Patient's performance status of 3-4 (as per Eastern Cooperative Oncology Group [ECOG] criteria).

Methods

1. A detailed history regarding symptoms of Ca prostate, complete physical examination, digital rectal exam

(DRE), and baseline investigations that included hemogram, urine R/E, urine C/S, liver function tests (LFT), renal function tests, prostate-specific antigen (PSA) level, radiological included whole body X-rays, transrectal ultrasound (TRUS)/imaging computed tomography (CT) scan, and bone scan were done. Sextant prostate biopsy - Gleason grading and other metastatic evaluation were carried out before starting of the treatment.

2. An informed and written consent was taken before the start of the treatment.
3. Proven cases of Ca prostate with locally advanced or metastatic disease were subjected to two different Groups of 25 patients in each group.
4. Group A: Bicalutamide 150 mg as monotherapy. Group B: Those who underwent orchidectomy and bicalutamide 50 mg being added. Bicalutamide was started daily with or without meal on the same hour of the day.
5. Serum PSA level estimation was done.
6. A comparative analysis of the effect of 2 different treatments was assessed by ECOG performance grading criteria, symptoms-general, urinary and side effects of medication, morbidity and progress of disease.
7. All these biochemical investigations were done on the 4th, 5th, 6th, 9th, 12th, 15th, and 18th months after the start of the treatment.
8. TRUS/TRUS Guided Biopsy: TRUS was done at the start and 12 months of treatment comparing the volume of prostate.
- 10 X-ray of the whole body and CT scan of abdomen and pelvis were done at the start and 12 months of treatment to assess invasion of periprostatic tissue, lymph node involvement, and metastasis in another organ.
- 11 Bone scan was done at the start and 12 months of treatment.
- 12 Follow-up: All Patients were followed with all hematological and biochemical parameters on the 4th, 5th, 6th, 9th, 12th, 15th, and 18th months after the start of the treatment. They were evaluated by asking about improvement in their performance as compared to previous grade (as per guidelines for ECOG performance grading) and simultaneously evaluated clinically also. All Patients were following up for 18 months. None of the patients were lost to follow-up since all of them being Ex-service Man of the Army were covered under Ex-Serviceman Contributory Health Scheme and reported regularly for follow-up, and there was no mortality during the study.
- 13 Data-analysis: Paired *t*-test and Chi-square test were applied to derive at the value of significance, *P* value.

RESULTS

In the present study, the range of age of patients was 59-82 years with mean of 67.4 and 70.28 in Group A ($n = 25$) and Group B ($n = 25$), respectively. The mean age of patients was 67.4 years in Group A and 70.28 years in Group B with a range of 59-82 years (Table 1).

Table 2 depicts the history observed in Group A and Group B in 0 month and 18 months, respectively.

Decrease in the grade of DRE in Group A was from mean of 3.12-1.92 and in Group B was from 3.08 to 1.68 (Table 3).

In Group A, PSA falls from mean of 44.48-13.796 after 18 months of treatment. In Group B, PSA falls from mean of 57.94-3.4804 after 18 months of treatment. Decrease in volume of the prostate gland in Group A was from mean of 64.88 to 35.52 g and in Group B was 69.48-40.08 g. No change in hematological and biochemical parameters occurred after 18 months (Table 4).

Table 5 depicts initial total workup in both the groups; Group A and Group B.

In Groups A and B, each having 25 patients all were in Grade 2 of ECOG scale initially. Out of 36% of cases in

Group A and in Group B, 32% of cases reached to Grade 0 of ECOG performance grading; 44% of Group A and 64% of Group B in Grade 1; 12% of Group A and 4% of Group B in Grade 2; and 4% of Group A deteriorate to Grade 4 after 18 months of treatment (Table 6).

Breast pain and tenderness in 40% of cases in Group A only and no patient with breast pain in Group B. Gynecomastia occurred in 28% of cases in Group A and 4% of cases in Group B. Hot flashes in 8% of cases in Group A and 32% of patients with Group B (Table 7).

The follow-up period was 18 months.

We have compared each parameter at the start and 18 months of commencement of treatment. We discontinued the treatment in Group A after 18 months in 28% of cases because of severe breast pain and gynecomastia and offered them orchidectomy and low doses of bicalutamide (50 mg).

Table 1: Age range

Age	Minimum years	Maximum years	Mean
Group A ($n=25$)	59	78	67.4
Group B ($n=25$)	57	82	70.28

Table 2: History

Symptoms	Group A		Group B	
	0 month	18 months	0 month	18 months
Hematuria	6	1	5	Nil
Bladder outlet obstruction	12	2	14	3
Urinary tract infection	7	1	5	Nil
Bony pain	4	1	3	Nil
Lower extremity edema	Nil	Nil	Nil	Nil
Paraplegia (spinal cord compression)	Nil	Nil	Nil	Nil

Table 3: Physical examination: DRE-decrease in grades

Group	Baseline		18 months	
	A	B	A	B
Minimum (grade)	2	2	1	1
Maximum	4	4	3	3
Mean	3.12	3.08	1.92	1.68

Table 4: Investigation

Investigations	Group A		Group B	
	0 month	12 month	0 month	12 month
Mean hypoechoic lesion by TRUS	1.92	1.25	1.72	1.0
Periprostatic tissue involvement	25	12	25	14
Lymph node involvement	07	03	09	04
CT scan abdomen and pelvis: Distant metastasis	03	03	04	04
Bone scan showing bony meats	05	03	06	03
Mean PSA	44.48	57.94	13.7960	3.4804
Mean tumor size in grams by TRUS	64.88	69.48	35.52	40.08

TRUS: Transrectal ultrasound, CT: Computer tomography, PSA: Prostate-specific antigen

Table 5: After initial total workup we found

Group	Locally advanced	Metastatic	Total
A	15	10	25
B	13	12	25

Table 6: ECOG grading after 18 months of treatment

Grade	Group A		Group B	
	No. of patients	%	No. of patients	%
0	12	48	15	60
1	7	28	9	36
2	5	20	1	4
3	0	0	0	0
4	1	4	0	0
Total	25	100	25	100

ECOG: Eastern Cooperative Oncology Group

Table 7: Adverse effects

Complications	No. of patients in Group A (n=25)	%	No. of patients in Group B (n=25)	%
Breast pain	10	40	Nil	Nil
Gynecomastia	7	28	1	4
Hot flushes	2	8	8	32
GIT disturbances	Nil	Nil	Nil	Nil
Cardiovascular	Nil	Nil	Nil	Nil
Respiratory	Nil	Nil	Nil	Nil
CNS	Nil	Nil	Nil	Nil
Skin	Nil	Nil	Nil	Nil

CNS: Central nervous system, GIT: Gastrointestinal

DISCUSSION

The methods for treatment of locally advanced and metastatic carcinoma prostate have increased manifold over the last decade or so, especially when it has been observed that it can be offered without orchidectomy.

This is a prospective study which was aimed at evaluating the safety and efficacy of bicalutamide 150 mg monotherapy versus orchidectomy and bicalutamide 50 mg in the treatment of locally advanced/metastatic prostate cancer.

A prospective study done by Iversen *et al.* compared monotherapy 150 mg with castration on patients with non-metastatic locally advanced prostate cancer, minimal follow-up of 6.3 years, follow-up were not significantly different with bicalutamide or castration in men with locally advanced prostate cancer. There was no significant difference between bicalutamide and castration for overall survival. With respect to health-related quality of life factors - health-related quality of life (HR-QOL), bicalutamide recipients had a significant greater sexual interest ($P = 0.029$) and physical capacity, $P = 0.049$, at 12 months than men who had been castrated. No other significant differences were seen in any of the other HR-QOL parameters (emotional well-being, vitality, social function, pain activity limitation, bed disability, and overall health).²

In our study, there was significant fall in PSA value after the start of treatment in both groups separately but to compare between two groups were insignificant. Newling *et al.* found that only moderate correlation between the effect of bicalutamide on PSA progression and objective overall survival.³

Iversen *et al.* data from the bicalutamide (Casodex) early cancer program - analysis of combined data by stage at median follow-up showed that the risk of objective progression and PSA doubling was reduced with bicalutamide, irrespective of lymph node status.⁴

In our study, there was 20-60% decrease in volume of prostate gland compares to study done by Bosch *et al.* in 1989; Matzkin *et al.* in 1990; and Whittington *et al.*, 1999 in these studies there was 30% reduction in the volume of prostate.

In our study, hot flushes were present in 8% of cases in Group A and 32% of cases on Group B and study by Iversen *et al.* and Kolvenbag *et al.* showed that hot flushes occurred in 5-28% of cases with bicalutamide 150 mg monotherapy and 24-76% of cases with combined therapy.

Breast tenderness in 40% of cases in Group A and none in Group B. Study by Iversen *et al.* and Kolvenbag *et al.* showed that breast pain and tenderness in 49% of cases in Group A and 4% of cases with combined therapy.

Gynecomastia in 28% of cases in Group A and 4% of cases in Group B which was within the range studied done by Iversen *et al.* and Kolvenbag *et al.* showed 16-60% in bicalutamide 150 mg monotherapy and 6% of cases with combined therapy.^{5,6}

Testosterone stimulates renal erythropoietin production, and castration is accompanied by a decrease in hemoglobin of 1-3 g/dl. If anemia becomes symptomatic, it can be effectively treated with recombinant erythropoietin and studied by Holzbeierlein *et al.* However, in our study, we have not found patients with symptomatic anemia.^{4,7}

In our study, there was no abnormality found in LFT, but the incidence of abnormal LFT reported as adverse events in Early Prostate Cancer program with bicalutamide monotherapy was 3.1%.⁸

We requested for complete radiographic evaluation. Bone scan of patients to look for metastatic disease at baseline and 12 months of treatment. The bone scan found to have very sensitive methods for assessment of axial skeletons but have a very high level of false positives undergoing staging evaluation, detecting not only metastatic disease but also healing fractures, arthritis, bony infections, and magnitude of other inflammatory conditions. We confirmed the suspicious lesion on the bone scan by plain bone films. Chest radiograph is necessary in initial staging, as 6% of patients may have pulmonary metastasis at the time of presentation according to Lindell *et al.* However, in our study, we have not found any patients with pulmonary metastasis.⁹

We discontinued the treatment of Group A because of severe breast tenderness and gynecomastia in 7 patients (28%) of patients and offered them orchidectomy and low doses of bicalutamide after 18 months of follow-up.

Studies by McLeod *et al.* in which they discontinued the treatment in 29.3%.

This is a prospective study conducted on 50 patients.

The most common adverse events associated with bicalutamide monotherapy were breast pain and gynecomastia.

Bicalutamide 50 mg is an effective, oral once-daily, non-steroidal anti-androgen, available for the use in combination therapy.

The problem of bicalutamide monotherapy lies mainly in its more unfavorable side effects pattern but the advantage of reversibility of these side effects with discontinuation of treatment.

The cost of combined therapy with bicalutamide per months of survival benefits is reasonable and compared with other cancer therapies.

Combination therapy in an important option in the treatment of patients with advanced prostate cancer.

The palliation of prostate cancer by castration was a key clinical advanced in the 20th century oncology. While the androgen deprivation therapy by bicalutamide on symptomatic prostate cancer is dramatic. When androgen deprivation therapy is undertaken, impact on QOL can be minimized through prevention or early identification of treatment side effects.

Hence, when treatment option being offered bicalutamide as combined therapy or monotherapy should be considered as an alternative to other available hormonal therapies.

The debate concerning the benefits of combination therapy will continue; nevertheless, this approach is an important option in the treatment of patients with advanced disease, as highlighted in many clinical studies.

Anti-androgen therapy in combination with surgical castration is given to enhance survival and to maintain or improve the quality of life of patients with advanced prostate cancer.

CONCLUSION

In our study, we conclude that compared to Monotherapy (150 mg) and surgical castration + bicalutamide (50 mg) in men with locally advanced prostate cancer offers better tolerability and higher HR-QOL. Bicalutamide appears to have a more favorable tolerability profile than either therapy on the basis of current evidence.

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Esophageal Atresia and Tracheoesophageal Fistula: Study of Various Factors Affecting Leak Rate

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Abstract

Introduction: Esophageal atresia (EA) and tracheoesophageal fistula (TEF) is the most common congenital anomalies encountered in pediatric surgery.

Materials and Methods: This prospective study was performed in patients of EA and distal TEF undergoing corrective surgery over a period of 2-year. The study comprised 40 consecutive patients of EA and distal TEF. In this prospective randomized trial, we analyzed the risk factors leading to anastomotic dehiscence in patients after surgery. Various risk factors associated with increased incidence of anastomotic leakage such as increased age at presentation, weight at presentation, associated anomalies, gap length, lower pouch mobilization, tension at anastomosis, and post-operative ventilation has been implicated to a variable extent.

Results: We analyzed the risk of anastomotic leakage associated with each factor and compared with overall leak rate. We found that anastomotic tension was the most significant risk factor followed by lower pouch mobilization and long gap. The anastomotic tension was the most significant risk factor followed by lower pouch mobilization and long gap for leak.

Conclusion: Age at presentation and birth weight had an impact on survival but not on anastomotic healing. Lower pouch mobilization and gap length increase the chances of anastomotic dehiscence. Overall leak rate was 25% study series.

Key words: Anastomotic leak, Anastomotic tension, Esophageal atresia, Gap length, Post-operative ventilation

INTRODUCTION

Esophageal atresia and tracheoesophageal fistula (EA and TEF) is one of the most common congenital anomalies encountered in pediatric surgery. The most common abnormality is a blind upper pouch with a fistula to the trachea or bronchus from the lower esophagus, occurring in approximately 87% of the patients. EA and TEF are frequently associated with anomalies of

the musculoskeletal, cardiovascular, gastrointestinal, and genitourinary systems. Prognosis of a patient with EA and TEF depends on the weight of the patient, day of presentation, associated anomalies, and ventilatory dependence.¹ Esophageal gap length, anatomy of the defect and physiological status are the other factors guiding the therapy.²

The complications of esophageal anastomosis are major or minor leaks, recurrent TEF, and significant strictures. Depending on the criteria used for the definition of leakage, the incidence varies widely from 4% to 36%.³⁻⁶ The anastomotic leak rate as reported in several Indian series varies from 16% to 35%.^{4,5,7} Mortality rates after anastomotic leak, however, are very high in developing countries (60-80%) as compared to the developed countries (0-25%).⁶ Factors, which increase the risk of

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anastomotic leakage are the use of silk sutures, tension at anastomosis, interference with blood supply of anastomosis from over-zealous dissection of the distal esophagus and a wide gap.^{3,6} A gap of more than 3 cm between the upper and lower pouches before mobilization is considered as a long gap.⁵ Leak rate in this group has been reported to be 100%.³

In this study, we studied various factors affecting leak rate in EA and TEF and studied their effect on survival of such patients.

MATERIALS AND METHODS

This study was performed prospectively in 40 patients of EA and distal TEF.

Inclusion Criteria

1. Weight more than 2 kg and full term gestation
2. Aged 3 days or less at the time of admission
3. Preoperatively maintained adequate oxygen saturation without mechanical ventilation
4. Patients did not have associated major cardiac or other life-threatening anomalies.

Exclusion Criteria

Patients with long gap and patients dying within 72 h of surgery were excluded.

A detailed clinical performa was filled up for each patient incorporating details such as weight, sex, day of presentation, birth history, antenatal diagnosis, associated anomalies, immediate postnatal management, history of feeding, respiratory distress, pre-operative pneumonia, pre-operative ventilator dependence, and inotropic support requirement. A thorough clinical examination was performed for proper assessment of other systems to rule out cardiac, gastrointestinal anomalies and major pneumonia. The patients were resuscitated and prepared for surgery as per the standard protocol. A right posterolateral thoracotomy was done through the fourth or fifth intercostal space. Esophageal anastomosis was performed using 5/0 Vicryl sutures. Post-operative ventilation was used whenever indicated. Anastomotic healing was checked by the clinical examination of the chest, respiratory rate, ventilatory parameters, chest tube inspection and radiological examination of the chest. A contrast swallow was performed on 5th post-operative day, and the oral feeds commenced once a leak free patency of the esophagus was established. A statistical analysis was done by χ^2 test and Fisher's exact test.

The Institute Ethical Committee had approved the study.

RESULTS

Table 1 denotes the Risk factors for anastomotic leak. The anastomotic tension was the most significant risk factor followed by lower pouch mobilization and long gap for leak (Figure 1).

DISCUSSION

Since, the first successful repair of EA and TEF in 1941 by Haight, the outcome has gradually improved.⁸

Although the overall mortality has declined, anastomotic leakage and its complication still continue to occur. The main determinant of prognosis of patients of EA and TEF is anastomotic leak which, in turn, is influenced by the anastomotic tension.^{6,9}

This prospective randomized controlled study of 40 cases of EA and TEF, we studied the various factors affecting anastomotic leak and their effect on survival of patients.

Table 1: Risk factors for anastomotic leak

Characteristics	Individual leak rate No. (% age)	Overall leak rate (% age)	P value
Age >1 day (n=19)	4/19 (21)	25	0.721
Weight <2.5 kg (n=30)	7/30 (23)	25	0.689
Presence of associated anomalies (n=15)	4/15 (26.6)	25	1.0
Gap length			
2-3 cm (n=19)	6/19 (31.5)	25	0
>3 cm (n=9)	4/9 (44.4)	25	0.019*
Lower pouch mobilization (n=15)	7/15 (46.6)	25	0.024*
Tension at anastomosis (n=18)	9/18 (50)	25	0.002**
Post-operative ventilation (n=29)	9/29 (31)	25	0.233

*Significant, **Highly significant



Figure 1: Radiograph showing hemivertebra associated with Esophageal atresia and tracheoesophageal fistula

Age at Presentation and Sex

In this series, patients who presented on the 1st day of life had better survival as compared to those who presented late. This finding was contrary to the Western reports^{2,10} but consistent with various Indian series.^{11,12} Leak rate was not found significantly different in patients who presented late. Male patients formed the predominant group. The rate of survival in female babies was 66.6%, whereas 80% of the male babies survived. Survival in male patients was better as compared to the female neonates.

Birth Weight

The rate of mortality was 33.3% in patients whose weight was between 2 kg and 2.5 kg. The survival rate in patients with more than 2.5 kg weight was found to be 100%. However, the weight was not found to be significantly affecting the leak rate. In western reports, low birth weight does not seem to affect survival, contrary to the reports of Indian series.^{10,13} In Indian setup Waterston classification is still relevant, and weight is a significant factor in neonatal survival.¹⁴

This reflects delayed and faulty diagnosis, absent neonatal transport facility and lack of sufficient neonatal intensive care infrastructure.

Associated Anomalies

Associated anomalies were found in 37.5% of patients which is quite comparable with other Indian reports.^{4,7,11,12} Survival in patients without associated anomalies was obviously found to be better than in patients with associated anomalies. Most of the anomalies were cardiac (53%).

History of Feeds before Surgery and Antenatal Diagnosis

Babies who were fed before attending the hospital did not have increased mortality. Even if the patients were fed before the presentation to the hospital, leak rate was not found to be significantly different in these patients as compared to those who were not fed, as seen in other published reports also.¹⁴ Antenatal diagnosis was possible in only 5 patients. However, 29 out of 40 were hospital deliveries. Antenatally, the presence of polyhydramnios led to the suspicion of EA being present.

Gap Length, Tension at Anastomosis, Lower Pouch Mobilization and their Relationship to the Leak Rate

Overall leak rate in our series was 25% which is comparable with other Indian series.^{4,11,12} In patients with gap <2 cm, leak rate was 0% whereas in intermediate (2-3 cm) and long gap (>3 cm), overall leak rates were 31% (6 out of 19) and 44% (4 out of 9) respectively. Our results are comparable with report of Brown *et al.* who reported leak rate of 31% in patients of long gap and 25% in intermediate gap.¹⁵ Similar reports were obtained in Indian

series by Sharma *et al.* who reported leak rate of 32% in long gap.⁴ Mortality rate in patients with long gap was higher.

Tension on anastomosis is considered a significant factor in predicting leak rate and has been proven in other series as well.^{3,6} Lower pouch mobilization was done in 15 patients, and leak rate in these patients was 46.6% as compared to overall leak rate of 25%. However, the results were not statistically significant.

Post-operative Ventilation

Mortality rate was higher in patients who required ventilatory support for more than 10 days. The patients who required post-operative ventilatory support (9 out of 29), (31%) had anastomotic leak more often than the patients who were not ventilated postoperatively (1 out of 11), (9%).

Analysis of Risk Factors for Anastomotic Leak

Various risk factors associated with increased incidence of anastomotic leakage such as increased age at presentation, weight at presentation, associated anomalies, gap length, lower pouch mobilization, tension at anastomosis and post-operative ventilation have been described in the literature.^{2,11,14,16-18} and have been implicated to a variable extent. We analyzed the risk of anastomotic leakage associated with each factor and compared the overall leak rate (Table 1).

A total of 40 patients who formed basis of this study were operated by 11 pediatric surgeons in all. Out of 10 patients who had anastomotic leak, 6 were operated by senior residents and 4 by consultants. Although technical expertise is one of the factors affecting outcome in EA and TEF, including anastomotic dehiscence but this factor was difficult to control in our set up. For a more reproducible outcome, an extended study with more number of patients is required.

CONCLUSIONS

Age at presentation and birth weight had an impact on survival but not on anastomotic healing. Lower pouch mobilization and gap length increase the chances of anastomotic dehiscence. Overall leak rate was 25% study series. Overall survival rate was 77.5%. Anastomotic tension is a significant risk factor for dehiscence.

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Changes of Macular and Retinal Nerve Fiber Layer Thickness Measured by Optical Coherence Tomography in Diabetic Patients with and without Diabetic Retinopathy

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Abstract

Introduction: Diabetes mellitus (DM) is one of the leading causes of blindness. The long-term effects of DM on vascular tissues and its consequence on the retina are well-established, and this ranges from milder grades of non-proliferative diabetic retinopathy (NPDR) to advanced grades of proliferative retinopathy with or without clinically significant macular edema.

Materials and Methods: The retinal nerve fiber layer (RNFL) and macular thickness were measured in 100 patients (200 eyes) using spectral domain optical coherence tomography in the prospective observational study. The patients with DM over 40 years of age were included. Patients with a history of recent ocular surgery (1 month), pseudoexfoliation, pigment dispersion syndrome, thyroid dysfunction, long-term steroid users, high myopia, and media opacities such as cataract, other causes for secondary glaucoma, and DR with tractional retinal detachment, and post glaucoma and retinal surgery were excluded. The values of participants with DM were compared to controls. The participants were divided into 4 groups of containing 25 patients in each group: Controls (normal patients without diabetes), diabetics without retinopathy (NDR group), NPDR (NPDR group), and proliferative DR (PDR group).

Results: The average temporal RNFL thickness and average macular thickness are 65.02 μm and 278.46 μm , respectively. It is significant ($P < 0.01$) across the groups.

Conclusion: DR is associated with a decrease in RNFL thickness though this is not statistically significant in our study. However temporal RNFL shows a significant increase in thickness, which worsens with the stage of DR, this is due to the clinical significant macular edema which is associated with the retinopathy.

Key words: Diabetic retinopathy, Glaucoma, Macular thickness, Optical coherence tomography, Retinal nerve fiber layer thickness

INTRODUCTION

Diabetes mellitus (DM) is no longer an epidemic that can be ignored with over 80% of patients being concentrated in low and middle-income countries.¹ Currently, the number of cases of diabetes worldwide is estimated to be

around 387 million.¹ This number is predicted to increase by additional 205 million by 2030. The World Health Organization reports indicate that India is second in the world after China with the largest number of diabetic subjects (65.1 million).²

DM is one of the leading causes of blindness.³ Diabetic retinopathy (DR) is the most common ocular complication of diabetes with 5% of diabetics, progressing to severe visual loss of 5/200 or less.⁴

The long-term effects of DM on vascular tissues and its consequence on the retina are well-established, and this ranges from milder grades of non-proliferative DR

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(NPDR) to advanced grades of proliferative retinopathy with or without clinically significant macular edema.

DR has been described as a type of optic neuropathy, which is different from glaucomatous optic nerve damage by that the cup of the disc was not enlarged in diabetic eyes in spite of discrete signs of retinal nerve fiber layer (RNFL) defects. The reduced visibility of the RNFL, the increased optic disc pallor and the unchanged size of the neuroretinal rim and parapillary atrophy suggest that DM may be associated with non-glaucomatous optic nerve atrophy.⁵

The evolution of newer technologies such as the Heidelberg retina tomography, glaucoma diagnostics - variable corneal compensation, and optical coherence tomography (OCT) has made an evaluation of the optic nerve head (ONH), the peripapillary area, the macula and the RNFL revolutionary. The resolution and reproducibility of these technologies almost give us a near histological evaluation of the tissue or area we study in the retina.⁶

This study is intent to highlight the OCT characteristics of the RNFL in patients with DR. We plan to evaluate the association if any of RNFL thickness with DR and to evaluate the possibility of RNFL thickness (RNFLT) changes being a precursor to diabetic retinal changes. Early detecting of RNFL thinning, which seems to be a common factor in both diabetes and glaucoma, may be a useful tool in the understanding the progression of DR and may explain the probable higher incidence of glaucoma in diabetic patients.⁷⁻¹⁰

MATERIALS AND METHODS

This study was conducted on patients coming to the Department of Ophthalmology, St. John's Medical College Hospital during the period from September 2009 to August 2011. The study was approved by the Ethics Committee of St John's Medical College and adhered to the tenets of the declaration of Helsinki. We prospectively analyzed 100 patients (200 eyes). The study design was a prospective observational study.

Inclusion criteria were patients with DM (DM was diagnosed on the basis of the diabetes diagnostic criteria of the World Health Organization,¹¹ and the patients were under medical treatment by an experienced physician/endocrinologist) and age > 40 years of age.

Exclusion criteria were recent ocular surgery (1 month), patients < 40 years of age, patients with pseudoexfoliation and pigment dispersion syndrome, thyroid dysfunction, long-term steroid users, high myopia, media opacities such as cataract, other causes for secondary glaucoma, post

glaucoma surgery, DR with tractional retinal detachment, and Post retinal surgery patients.

A detailed history which included demographics, information on past medical illness and drug intake (with special reference to DM and hypertension) and their duration was recorded. Ocular disease if any was noted. Family history of diabetic mellitus or glaucoma was recorded.

Ophthalmological examination was recorded in each eye individually which included visual acuity and best corrected visual acuity (BCVA), slit lamp examination, gonioscopy, fundus examination (cup to disc ratio [CDR] was measured with micrometer scale attached to eyepiece of slit lamp), applanation tonometry (with central corneal thickness - CCT correction), visual field testing with Humphrey field analyzer, RNFL analysis using Zeiss Cirrus™ HD-OCT. Blood sugars, glycosylated hemoglobin (HbA1c), serum cholesterol and serum creatinine was routinely done for all patients done.

In this study, the patients were divided into 4 groups: Controls (normal patients without diabetes) - 25 patients (50 eyes), diabetics without retinopathy (NDR group) - 25 patients (50 eyes), NPDR (NPDR group) - 25 patients (50 eyes) and proliferative DR (PDR group) - 25 patients (50 eyes).

Patients with DM were divided into three groups on the basis of the international clinical DR disease severity scale.¹² NDR was defined as the absence of all features of DR in diabetic eyes; NPDR was defined as the presence of micro aneurysms, hard exudates, dot and blot hemorrhages, cotton wool spots, venous beading and intraretinal microvascular abnormalities; and PDR was defined as the presence of neovascularization on optic disc or elsewhere, vitreous or preretinal hemorrhage, and fibrovascular proliferative tissue.

The statistical analysis was done as follows: First, the descriptive statistics were computed. Range, mean and standard deviation (SD) was estimated for quantitative variables and frequency counts with percentages for qualitative variables. Then, inferential statistical analysis was undertaken.

One-way ANOVA was done to evaluate the correlation of the diabetic groups and controls with the variables included in the study, such as nerve fiber layer thickness, macular thickness, BCVA, intraocular pressure (IOP) and CDR. Whenever there was statistical significance across groups, *post hoc* analysis (Bonferroni) was done to study any statistically significant difference between groups.

All tests were done using Statistical package for Social sciences version 10 software. Statistical significance was

considered whenever $P < 0.05$. There may be a fallacy while measuring temporal RNFL thickness, as anatomically the same fibers constitutes the macular nerve fibers also; an increase in macular thickness due to CSME may cause a fallacious increase in temporal RNFLT also. To differentiate an increase in temporal RNFL due to CSME from a true change in temporal RNFLT due to increasing severity of DR the study group was further divided into 3 different groups, i.e., no DM (NDM) group, DM without CSME (no CSME [NCSME]) group and DM with CSME (CSME), and data were analyzed.

OBSERVATIONS AND RESULTS

OCT was done in 100 patients. For analysis purpose, the data were taken as 200 eyes, which contain 50 eyes in the control group and 150 eyes in the DR group.

Demography

Age

The age of the patients in the study ranged from 40 to 77 years with a mean of 54.01 ± 7.94 (SD).

Sex

The study group had 65 males (65%) and 35 females (35%).

Duration of diabetes

It was increasing proportionately according to the severity of the retinopathy.

Family history

About 18 out of 75 (24%) diabetic patients had family history of diabetes in 1st and 2nd degree relatives.

BCVA

Since there was a statistically significant difference across the groups for the BCVA, between groups comparison of BCVA was analyzed.

IOP with CCT correction

1. The mean value is 14.10 ± 2.45 mm of Hg
2. There is no statistically significant of IOP with CCT across the groups.

CDR

The mean value is 0.30 ± 0.10 .

RNFL defect

RNFL defect present in 78 eyes out of 150 (52%) eyes of diabetic group.

RNFLT

Average, Inferior, Superior, and nasal RNFLT were not statistically significant across the groups. Temporal RNFLT

was statistically significant difference across the groups hence, between groups comparison was analyzed.

Macular thickness

Macular thickness was a statistically significant difference across the groups for the hence, between groups comparison was analyzed.

Macular thickness was significantly more ($P < 0.01$) in PDR group when compared to controls group, NPDR group to NDR group and PDR group to NDR group.

Blood Investigations

1. HbA1c was significantly more in PDR group compared to NDR group
2. Serum creatinine was minimally high in PDR group
3. Serum cholesterol is not statistically significant across the groups.

Analysis between NDM Groups, NCSME Group and CSME Group - Group 1

Since there was a statistically significant difference across the groups for the BCVA, temporal RNFLT and macular thickness, between groups comparison of the same were analyzed (Table 6).

BCVA

BCVA was significantly worse ($P < 0.01$) in CSME group when compared to NDM group, CSME to NCSME group.

Temporal RNFL Thickness

Temporal RNFLT was significantly more in CSME group when compared to NDM group and CSME to NCSME groups.

Macular Thickness

Macular thickness was significantly increased ($P < 0.01$) in CSME group when compared to NDM group and CSME group to NCSME group. It was not significant in NDM group versus NCSME group.

DISCUSSION

Demographic and Epidemiological Details

In the present study, most of the patients were in the age group of 40-60 years which accounted for 75% of the patients. Most of the patients were male patients accounting for 65% of the study group.

Duration of Diabetes and HbA1C Levels

As shown in Table 1, the stage of DR worsened with the duration of DM. Uncontrolled sugars trended towards worsening of DR as shown by Table 1 in which the HbA1c levels correlated well with severity of the DR.

BCVA

In our study, BCVA was a statistically significant ($P < 0.001$) across the groups for the (Table 2). Hence inter-group comparison of BCVA (Table 3) was analyzed, in which it was significantly worse ($P < 0.001$) in the NPDR group when compared to controls group, PDR group to controls group, NPDR to NDR group and PDR to NDR group. The BCVA is worse in PDR group. These differences in values may be due to the associated macular edema which often accompanies NPDR and PDR group. Hence to confirm this we divided the groups into three different groups, i.e. NDM group, NCSME, and CSME, and these data were analyzed. BCVA was significantly worse ($P < 0.01$) in CSME group when compared to NDM group, CSME to NCSME group as shown in Table 7.

These results are consistent with the study done by Sa'nchez-Tocino *et al.*,¹³ in which they concluded that the retinal thickness at the foveal center correlated with BCVA in normal and diabetic eyes.

Otani *et al.*¹⁴ reported a correlation between retinal thickness and visual acuity in eyes with diabetic macular edema, with or without cystoid macular edema.

Table 1: Duration of diabetes, RNFL defect, HbA_{1c}, serum cholesterol and serum creatinine across the groups

Parameters	Mean (SD**)		
	NDR [‡]	NPDR [§]	PDR
Duration of diabetes (in months)	73.04 (79.10)	136.24 (71.57)	140.64 (70.10)
RNFL* defect (%)	21/50 (42)	31/50 (62)	26/50 (52)
HbA _{1c} [†] (in %)	7.68 (1.65)	9.47 (1.60)	10.62 (1.09)
Serum cholesterol (in mg/dl)	192.32 (46.33)	191.04 (33.08)	182.96 (43.00)
Serum creatinine (in mg/dl)	1.22 (1.21)	1.34 (0.84)	1.58 (0.98)

*RNFL: Retinal nerve fiber layer, †HbA_{1c}: glycosylated hemoglobin, ‡NDR: No diabetic retinopathy, §NPDR: Non-proliferative diabetic retinopathy, ||PDR: Proliferative diabetic retinopathy, **SD: Standard deviation

IOP with CCT

The mean value of IOP with CCT of 200 eyes is 14.10 ± 2.45 . There is no statistically significant variation of IOP across the groups (Table 2). Our study suggests that there is no association between increased IOP and diabetes.

Dielemans *et al.*⁷ (The Rotterdam study) concluded that the newly diagnosed DM and high levels of blood glucose are associated with elevated IOP and high-tension glaucoma. Klein *et al.*⁸ (The beaver dam eye study) concluded that the presence of open-angle glaucoma is increased in people with older-onset diabetes.

Tielsch *et al.* (the baltimore eye survey)⁹ concluded that, there is no evidence from this population-based investigation that supports an association between diabetes and POAG. Ellis *et al.*¹⁰ concluded that, their study failed to confirm an association between DM and primary open angle glaucoma and ocular hypertension.

CDR

The mean value in 200 eyes is 0.30 ± 0.10 .

CDR showed statistical significance ($P = 0.036$) across the groups. CDR was increased ($P = 0.06$) in PDR group when compared to controls group though this was not statistically significant. Similarly, CDR was increased ($P = 0.08$) in PDR group when compared to NDR group, which was again not statistically significant (Table 2).

Klein *et al.*¹⁵ analyzed change in optic disc cupping was evaluated in a 4 years follow-up of a well-defined cohort of people with DM. People who developed proliferative retinopathy by the follow-up examination were not more likely to have such an increase in the ratio at the follow-up. They concluded that clinically significant increases in CDR cannot be consistently predicted in people with diabetes from the risk factors evaluated with the grading system used in this study.

Table 2: BCVA, CDR, IOP, retinal nerve fiber layer and macular thickness across groups

Parameters	Mean (SD)				F value	Significance (P value)
	Controls	NDR	NPDR	PDR		
BCVA	0.84 (0.21)	0.83 (0.24)	0.62 (0.29)	0.48 (0.29)	22.474	<0.001
CDR	0.28 (0.12)	0.29 (0.15)	0.30 (0.11)	0.34 (0.13)	2.89	0.036
IOP	13.67 (2.14)	14.03 (2.77)	14.47 (2.63)	14.20 (2.20)	0.96	0.42
Average RNFLT* (µm)	93.26 (8.77)	91.80 (9.80)	94.24 (19.65)	96.36 (12.89)	1.54	0.205
Inferior RNFLT* (µm)	120.36 (13.38)	118.78 (14.16)	121.50 (22.03)	119.16 (21.26)	0.231	0.88
Superior RNFLT* (µm)	113.44 (13.79)	117.48 (16.01)	120.02 (16.9)	117.06 (21.56)	1.23	0.30
Nasal RNFLT* (µm)	71.38 (9.18)	69.46 (10.6)	72.66 (12.74)	73.96 (12.66)	1.41	0.24
Temporal RNFLT* (µm)	61.48 (8.33)	62.08 (9.67)	61.78 (10.84)	74.74 (21.43)	11.45	<0.001
Macular thickness (µm)	267.86 (17.39)	249.76 (28.94)	290.24 (42.69)	305.96 (40.49)	26.70	<0.001

*RNFLT: Retinal nerve fiber layer thickness, BCVA: Best corrected visual acuity, CDR: Cup disc ratio, IOP: Intraocular pressure

RNFL Defect

RNFL defect was detected by red free indirect ophthalmoscopy or red free slit lamp biomicroscopy and confirmed by OCT. In our study, RNFL defect (Table 1) was present in 78 eyes out of 150 (52%) eyes of the diabetic group. RNFL defect was present in 21/50 (42%) of NDR group, 31/50 (62%) of NPDR group and 26/50 (52%) of PDR group. RNFL defect was not found in any controls group.

Table 3: Between groups comparison of best corrected visual acuity

Groups	Comparison between the groups	Mean difference	P value
Control	NDR	1.3	1.00
	NPDR	0.22	<0.001
	PDR	0.36	<0.001
NDR	NPDR	0.21	<0.001
	PDR	0.35	<0.001
NPDR	PDR	0.13	0.05

NDR: No diabetic retinopathy, NPDR: Non-proliferative diabetic retinopathy, PDR: Proliferative diabetic retinopathy

Table 4: Between groups comparison of temporal retinal nerve fiber layer thickness

Groups	Comparison between the groups	Mean difference	P value
Controls	NDR	0.6	1.00
	NPDR	0.3	1.00
	PDR	13.26	<0.001
NDR	NPDR	0.3	1.00
	PDR	12.6	<0.001
NPDR	PDR	12.96	<0.001

NDR: No diabetic retinopathy, NPDR: Non-proliferative diabetic retinopathy, PDR: Proliferative diabetic retinopathy

Table 5: Between groups comparison of macular thickness

Groups	Comparison between the groups	Mean difference	P value
Controls	NDR	18.1	0.048
	NPDR	22.38	0.07
	PDR	38.10	<0.001
NDR	NPDR	40.48	<0.001
	PDR	56.20	<0.001
NPDR	PDR	15.72	0.127

NDR: No diabetic retinopathy, NPDR: Non-proliferative diabetic retinopathy, PDR: Proliferative diabetic retinopathy

Table 6: BCVA, temporal RNFLT and macular thickness across the Group 1

Parameter	Mean (SD)			F value	Significance (P value)
	NDM*	NCSME†	CSME‡		
BCVA	0.85 (0.20)	0.76 (0.28)	0.45 (0.25)	37.34	<0.001
Temporal RNFLT	61.48 (8.33)	63.32 (15.22)	71.48 (16.16)	7.83	0.001
Macular thickness	267.86 (17.39)	262.61 (30.82)	317.45 (43.63)	53.14	<0.001

*NDM: No diabetes mellitus, †NCSME: No clinically significant macular edema, ‡CSME: Clinically significant macular edema, BCVA: Best corrected visual acuity

This is inconsistent with the study done by Chihara *et al.*¹⁶ They photographed the RNFL of the right eye of 137 patients with diabetes and 144 healthy control subjects. The level of DR¹⁷ ranged from levels 1 (no microaneurysm) to 4 (eyes with localized intra-retinal microvascular abnormalities or venous beading). Defects of the RNFL were found in 6/30 (20%) eyes with level 1 retinopathy, 8/14 (57%) eyes with level 2 retinopathy, 24/47 (51%) eyes with level 3 retinopathy, and 36/46 (78%) eyes with level 4 retinopathy. These findings suggest that the RNFL abnormalities are common in patients with early DR. But in our study, nerve fiber layer defect was present more in NPDR group than PDR group.

RNFL

In our study inferior RNFLT is thickest and temporal is thinnest in controls and NDR groups. The superior and inferior areas were thicker because of the superior and inferior arcuate bundling of nerve fibers. In our study The average, inferior, superior and nasal RNFLT in the study are 93.92 µm, 119.95 µm, 117.0 µm and 71.87 µm, respectively, and were not significant across the groups (Table 2). The average, nasal and inferior RNFL thicknesses were decreased in NDR group when compared to controls group, but it is not statistically significant.

The average temporal RNFLT in the study is 65.02 µm and it is significant ($P < 0.01$) across the groups (Table 2). Temporal RNFLT was significantly more ($P < 0.01$) in PDR group when compared with the controls group, PDR group versus NDR group and in PDR group versus NPDR group. Temporal RNFLT is increased in PDR group (74.74 ± 21.33) when compared to other groups (Table 4). This is due to associated CSME. The paired comparison of temporal RNFLT in NDM group and CSME group was statistically significant ($P < 0.001$), i.e. temporal RNFLT is increased in CSME group than in NDM group. Similarly, it was statistically significant ($P < 0.001$) between NCSME group and CSME group (Table 8).

Macular Thickness

The average macular thickness is 278.46 µm and it is statistically significant across the groups (Table 2). The paired comparison of macular thickness in controls group and PDR group was statistically significant ($P < 0.001$),

i.e. the macular thickness is increased in PDR group compared to NDM group. Similarly, it was statistically significant ($P < 0.001$) between NDR group and NPDR group, NDR group and PDR group (Table 5). The macular thickness is increased in both PDR group ($305.96 \pm 40.49 \mu\text{m}$) and NPDR group ($290.24 \pm 2.69 \mu\text{m}$). The increase in thickness is due to associated CSME. The paired comparison of macular thickness NDM group and CSME group was statistically significant ($P < 0.001$), i.e. the macular thickness is increased in CSME group than in NDM group. Similarly, it was statistically significant ($P < 0.001$) between NCSME group and CSME group (Table 9).

The increase in macular thickness corresponds to increase in temporal RNFLT in PDR group but not in NPDR group. This is again due to increased association of CSME with PDR group.

This result is consistent with the study done by Kim *et al.*,¹⁸ in which RNFLT and ONH in diabetic patients with normal tension were analyzed using OCT. There was an increase in the temporal average thickness of RNFL in the PDR group. Diabetic changes should be considered when diabetes patients are diagnosed with glaucoma or glaucoma

progression. However, in subjects with very early glaucoma or in glaucoma suspects, the discriminating power of OCT might have been decreased because of thicker RNFL measurements affected by increased vascular permeability and changes in blood flow in DR.¹⁹

Since the association of glaucoma and DM is quite common, this issue should be taken into account while assessing RNFL in diabetic glaucomatous patients. When a decrease in RNFLT is detected in a diabetic glaucoma patient, one should consider the metabolic state of diabetes and the presence of retinopathy which may cause RNFL loss themselves before considering progression of glaucomatous damage in these patients.²⁰

Sugimoto *et al.*²¹ did a study to detect early diabetic damage in Type 2 DM patients with no DR using OCT and to evaluate OCT as a clinical test. The results of the study state that comparing the normal and NDR eyes, retinal thickness (which involves all the layers of the retina) significantly increased ($P = 0.03$), and RNFLT significantly decreased ($P = 0.02$) in the superior areas. There still remains a contrast with regard to the thickening of the retina that is seen in the macula compared to the thinning that is seen for the RNFL in the surrounding papilla. Because of the macular region has an abundance of Müller cells and it has no vasculature, it is more fragile with regard to diabetic damage than the peripapillary region. They concluded that OCT might be used to detect much earlier signs and structural changes of DR.

The results of our study are consistent with Sa'nchez-Tocino *et al.*,¹³ study. They did a study to quantitatively assess retinal thickness by OCT in normal subjects and patients with diabetes. This study was intended to determine which retinal thickness value measured with OCT best discriminates between diabetic eyes, with and without macular edema. In this study, there were statistically significant differences in foveal thickness between control eyes and all the other eye groups ($P < 0.001$). Eyes with NPDR or PDR had a greater macular thickness in all regions than that in normal eyes. However, differences were not statistically significant in any of the areas. There were no significant differences in average thickness in any area between NPDR and PDR without CSME.

Hee *et al.*,²² have reported similar results, finding differences in central foveal thickness between normal eyes and eyes with DR and no significant differences in average thickness between eyes with NPDR and PDR. Diabetic eyes with CSME had a statistically significant greater thickness in each of the areas compared with the other groups.

Table 7: Between Group 1 comparison of BCVA

Groups	Comparison between the groups	Mean difference	P value
NDM	NCSME	8.72	0.15
	CSME	0.40	<0.001
NCSME	CSME	0.32	<0.001

BCVA: Best corrected visual acuity, NCSME: No clinically significant macular edema, CSME: Clinically significant macular edema

Table 8: Between Group 1 comparison of temporal retinal nerve fiber layer thickness

Groups	Comparison between the groups	Mean difference	P value
NDM	NCSME	1.83	1.00
	CSME	9.99	0.001
NCSME	CSME	8.16	0.003

NCSME: No clinically significant macular edema, CSME: Clinically significant macular edema

Table 9: Between Group 1 comparison of macular thickness

Groups	Comparison between the groups	Mean difference	P value
NDM	NCSME	5.26	1.00
	CSME	49.60	<0.001
NCSME	CSME	54.85	<0.001

NCSME: No clinically significant macular edema, CSME: Clinically significant macular edema

CONCLUSION

DR is associated with a decrease in RNFL thickness though this is not statistically significant in our study. However temporal RNFL shows a significant increase in thickness, which worsens with the stage of DR, this is due to the CSME which is associated with the retinopathy.

As temporal RNFL shows a significant increase in thickness in some stages of DR, an early increase in this thickness could be an indicator of impending CSME. Similarly, while assessing a patient with glaucoma with diabetes, special care must be taken to evaluate the temporal RNFLT independently as this may be increased and should be excluded from analysis, as these values could in reality due to the diabetic changes in the retina and may skew the averages of the RNFLT while evaluating glaucoma.

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Evaluation of the Mode of Failure of Glass Fiber Posts: An *In Vitro* Study

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Abstract

Introduction: It is the era of increased esthetic demands. Post and core systems used for restoration of the mutilated endodontically treated tooth are no exception. Post and core system used for supporting translucent all-ceramic restoration had to be looked for. The glass fiber posts were introduced in 1992 with this aim. Although fiber-reinforced post systems are becoming very popular, they are not foolproof and failures of restorations have been reported.

Purpose: The purpose of the present study is to evaluate the mode of failure of glass fiber post.

Materials and Methods: 20 extracted single-rooted teeth were endodontically treated and restored with glass fiber posts. They were then loaded using Universal testing Machine until catastrophic failure occurred. Then, the mode of failure of each sample was determined and categorized as (a) root fracture, (b) core fracture, (c) post fracture, and (d) post debonding.

Results: 11 samples showed post debonding as a mode of failure. In 05 samples, there was core fracture and post fractured in the remaining 04 samples.

Conclusion: The mode of failure for prefabricated glass fiber post is predominantly post debonding followed by core fracture and post fracture.

Key words: Core fracture, Glass fiber post, Mode of failure, Post debonding, Post fracture

INTRODUCTION

A tooth though a small part of the human body serves many functions such as mastication, improving phonetics, enhancing esthetics, and providing self-confidence to one's personality. However, the presence of a healthy tooth is usually taken for granted unless they are affected by caries or damaged by trauma. Centuries ago the only treatment of choice for such conditions was extraction. However, with the advent and improvement in the field of endodontics, the dental treatment and techniques have evolved from

“removing the infected tooth” to “treating the infected tooth.”¹

With proper endodontic therapy, pulpless mutilated teeth have proved to be the useful members of the dental arch.² However, badly broken-down pulpless tooth has few features such as: (1) They are brittle; (2) they possess little or no coronal tooth structure; and (3) they have lower resistance to decay. These features make them far more vulnerable than vital tooth. So, to become useful members of the chewing apparatus and function effectively, such mutilated teeth require special reinforcement provided either intracoronally by post and core or extracoronally by crown restoration or both.³

Various methods of restoring these pulpless teeth have been reported in the past 200 years. The available post and core systems can be classified into two types. (a) Metal post and the core cast as a single unit. (b) 2 - element design

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comprising of prefabricated posts to which core have been subsequently attached.

The traditional custom-cast dowel core provides a better geometric adaptation to excessively flared or elliptical or irregular canals, they almost always require minimum tooth structure removal and can be used in roots with minimal remaining coronal tooth structure. But, there are some drawbacks such as root fractures, post separation, and failures.⁴ Furthermore, on esthetic consideration, the cast metallic post can result in discoloration and shadowing of the gingiva and the cervical aspect of the tooth. Moreover, they require two appointments with added laboratory fee.⁵

The use of prefabricated posts and composite resin core was introduced in the 1966.⁶ Since then prefabricated post systems have become more popular because they provide acceptable results, better esthetics, and function while saving clinical time and reducing cost of treatment.⁷

In earlier days, prefabricated posts were made of metal alloys such as stainless steel, titanium, and its alloys, and gold plated brass. Stainless steel has been used for a long time in prefabricated posts.⁸ Although successful they do have certain disadvantages such as high elastic modulus, unesthetic appearance, corrosion, and catastrophic root fracture.⁹

In 1990, Bernard Duret and M. Reynaud introduced a non-metallic material for fabrication of post.¹⁰ These posts were based on carbon fiber reinforcement principle (Composipost, RTD). These posts had high tensile strength and modulus of elasticity similar to that of dentin. However, this post system had a major disadvantage of being unesthetic due to the unsightly black of the carbon.

With the increasing demand for esthetics in today's era post and core system used for supporting translucent all-ceramic restoration had to be looked for. The glass fiber posts were introduced in 1992 with this aim.¹¹ Glass fiber posts provide increased light transmission through the root, giving more life-like appearance to the prosthesis. The modulus of elasticity of glass fiber post is comparable with that of dentin which reduces chances of root fracture due to stress concentration. Glass fiber posts also eliminate the problem of corrosion and hypersensitivity that occurs with metal posts.⁶ With its many advantages, the fiber-reinforced post is becoming a paramount restorative option for endodontically treated tooth. Although fiber-reinforced post systems are becoming very popular, they are not foolproof and failures of restorations have been reported.

Hence, the purpose of this *in-vitro* study is to evaluate the mode of failure of endodontically treated tooth restored with glass fiber posts.

MATERIALS AND METHODS

Step 1: Collection of extracted maxillary anterior tooth.

20 freshly extracted maxillary anterior teeth were collected.

Inclusion Criteria

- a. All samples were caries free
- b. All samples were fracture free
- c. All Selected samples were devoid of debris and calculus
- d. All samples had complete root formation.

Exclusion Criteria

- a. Tooth with two or more canals
- b. Roots with aberrant anatomy
- c. Roots with open apices.

All samples were cleaned, disinfected, and stored as per the recommendations, and the guidelines laid down by the Center for Disease control and Prevention.

Teeth were stored in phosphate buffer saline solution. During all stages of the study, dehydration of the specimens was avoided.

Step 2: Sectioning of the sample.

- a. All the collected samples were marked and decoronated 2 mm above the cemento-enamel junction with diamond rotary bur mounted on high-speed handpiece
- b. Exposed surface of the dentine was made flat and perpendicular to the long axis of the tooth.

Step 3: Root canal treatment.

- a. The root canal was prepared using the sequential endodontic file from No.10 to size of No. 35
- b. 17% ethylenediaminetetraacetic acid for 30 s was used as lubricant with intermittent irrigation of 3% sodium hypochlorite for 1 min followed by final irrigation with saline for 1 min
- c. Canals were dried with absorbent paper points
- d. Obturation was done using gutta-percha and endodontic sealer.

Step 4: Post space preparation.

- a. Gutta-percha was removed using the heated plugger
- b. DT light post drill size no: 1 (red) was marked at a length of 10 mm and post space was prepared.

Step 5: post cementation.

- a. The prepared canal walls were etched with 37% phosphoric acid for 15 sec, water rinsed for 1 min, and gently air dried. Excess water from the post space was removed using absorbent paper points.
- b. 20 DT light fiber post of size 1.5 mm were marked at the length of 14 mm and cut with double sided

- diamond disk mounted on a micromotor handpiece.
- c. Next calibra dual cure composite resin base and catalyst paste were mixed for 20 s, applied on the post surface. Then, the post was placed into the root canal under constant finger pressure for 10 min. Excess luting material was removed light activation was done through a cervical portion of the root for 40 s on buccal and lingual surfaces, totalizing 80 s of light exposure.

- Step 6: Mounting of tooth sample in acrylic resin block.
- a. The root part of each prepared sample was marked and encircled with a thin single sheet of spacer wax (0.3 mm thickness) 2 mm below the cement-enamel junction.
 - b. A custom made two-piece stainless steel mold was used for the fabrication of standardized resin blocks in which the specimen were mounted.

Each tooth specimen with cemented post was attached to mandrel on surveying arm of the dental surveyor. The custom made stainless steel mold was lubricated with petroleum jelly and placed on the horizontal table of the surveyor.

- a. The surveyor was adjusted to stabilize the tooth specimen at the center of the mold such that 1 mm of the root structure lies above the mold.
- b. After confirming proper positioning of specimen and mold on surveyor, auto polymerizing acrylic resin powder and liquid was mixed in thin consistency and poured around tooth specimen to fill the mold completely.
- c. The tooth was removed from acrylic resin block after the first signs of polymerization to eliminate the effect of heat of polymerization.
- d. Then, the spacer wax was removed, and the space created in the block was filled with light body vinyl polysiloxane impression material.
- e. Then, the tooth was again placed back in the block; excess impression material was removed. Moreover, the entire block was removed from the mold.

- Step 8: Testing of samples.
- a. The specimens were positioned in a customized jig so that the longitudinal axis will be perpendicular to the load direction.
 - b. The teeth were then loaded from buccal surface of the core at 90° to the long axis and 3 mm from tooth core interface.
 - c. A universal testing machine with 1 mm diameter rounded loading plunger was used to load the specimens at a crosshead speed of 0.5 mm/min.
 - d. The specimens were loaded until catastrophic failure occurred.
 - e. The ultimate failure load was recorded.

- Step 9: Identification of mode of failure.
- a) All samples were subjected to radiographic evaluation.
 - b) The mode of failure was recorded as:
 - Root fracture
 - Core fracture (Figure 1)
 - Post fracture (Figure 2)
 - Post debonding (Figure 3).

RESULTS AND OBSERVATIONS (TABLE 1 AND GRAPH 1)

Discussion

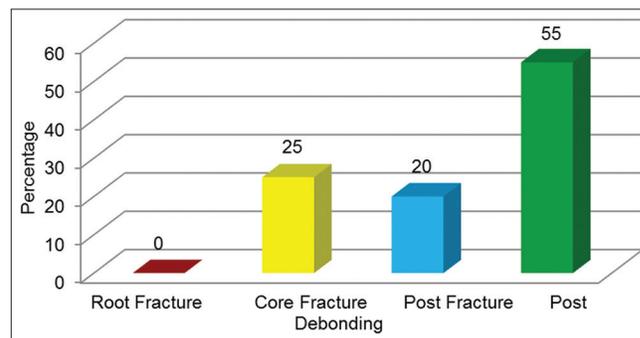
After endodontic treatment, the dentist is still faced with the problem of restoring the crown and reinstating the tooth as a permanent, functional, and esthetic member of masticatory apparatus. Endodontic treatment dose saves the tooth, but they become weaker as compared to a normal vital tooth. These affected physical properties of pulpless teeth are often attributed to loss of moisture, loss of structural integrity due to endodontic access preparation and changes in collagen cross-linking.¹²

Reinforcement of endodontically treated tooth was suggested by many authors as a viable option to regain lost strength. Such reinforcement can be in form of intracoronary reinforcement (post and core) and extracoronary reinforcement (crown) or both.^{2,3}

With the advanced technology of today, we, as clinicians, have at our disposal a wide range of dental materials of ever-increasing quality. In addition, the field of intraradicular posts is no exception. We have an increasing extent of

Table 1: Mode of failure of glass fiber post (Group II)

Glass fiber post	Type of failure	No. of samples
Group II	Root fracture	00
	Core fracture	05
	Post fracture	04
	Post debonding	11



Graph 1: Mode of failure of restoration in glass fiber post system

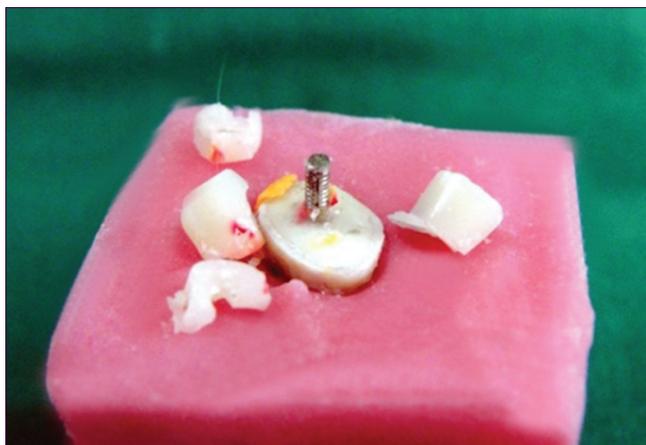


Figure 1: The core fracture in the sample.



Figure 2: Post debonding in the sample

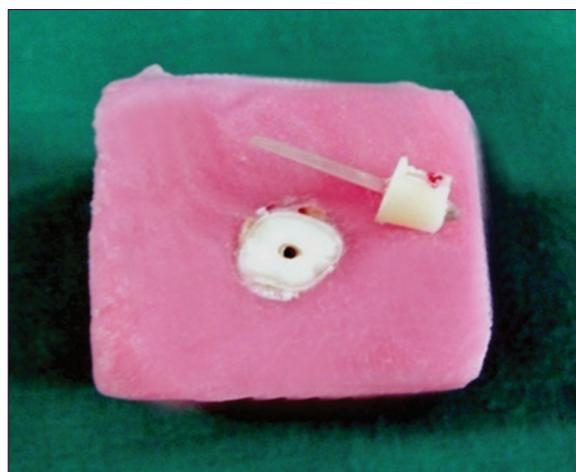


Figure 3: The post debonding in the sample

materials at our disposal. The materials used for posts and core can be divided into cast posts and prefabricated posts.

The cast metal post and core have been the traditional and time-honored method of restoring endodontically treated

teeth. However, there are some disadvantages associated with the conventional post and core systems such as poor retention of the post, greater incidence of root fracture, and risk of corrosion when different metals are used in the system. Fabrication of cast metal post and cores can be time-consuming and involves additional laboratory cost. The laboratory procedure itself may introduce errors within casting and thus increase the risk of failures. Application of a cast post often contributes to further loss of tooth structure that may interfere with the mechanical resistance of the teeth, increasing the risk of damage to residual tooth structure.

At around 1966, the prefabricate posts and composite resin core came into use. This system in which the prefabricated posts is cemented in root canal and the core is built up using composite resins was devised for forming a dowel and core which provides strength and serviceability comparable to, and often exceeding, that of cast dowels.^{6,7}

According to material composition, the posts are classified as:

- a. Metal posts: Titanium and stainless steel
- b. Ceramic and zirconium posts
- c. Fiber posts: Carbon fiber posts, quartz fiber, glass fiber, and silicon fiber post.¹³

Pre-fabricated metal posts were used successfully for restoring endodontically treated tooth for many years. However, they were not the ideal materials. Their high elastic modulus, corrosion or esthetic problems have led to the development of other type of post systems such as zirconia posts and fiber-reinforced post.

Duret and his co-investigators in 1990 introduced carbon fiber-reinforced posts. After that, many other fiber-reinforced materials have been made available to the dental profession and are now seen as an alternative to cast and prefabricated metal posts.¹⁰

The fiber-reinforced composite posts are made of carbon, quartz, glass, and polyethylene fiber embedded in a matrix of epoxy or methacrylate resin.^{7,14} The fibers are oriented parallel to the post longitudinal axis, and their diameter ranges from 6 to 15 μm . Fiber density, i.e. the number of fibers per mm^2 of post cross-sectional surface, varies between 25 and 35, depending on the post type. Therefore, in a transverse section of the post, 30-50% of the area is occupied by fibers.¹⁵ The adhesion between quartz or glass fibers and resin matrix is enhanced by fiber salinization before embedding. A strong interfacial bond enables load transfer from the matrix to the fibers and is essential for an effective use of the reinforcement properties.¹⁶

Fiber-reinforced posts have various desirable properties. Among all the available post systems, the modulus of elasticity of fiber-reinforced post (13-40 GPa) is very close to dentin (18 GPa).¹⁷ Fiber posts also have many other advantages such as biocompatibility, provide increased light transmission through root, giving more life-like appearance to prosthesis, and they are easy to remove when endodontic retreatment is required.⁶

Thus, so far various post and core systems have evolved from the cast post to prefabricated metal post to the newer glass fiber posts. Although the glass fiber post seems to be better than the previous systems yet their clinical success is yet to be proved. Moreover, further research in this aspect is warranted. Hence, this study was undertaken to evaluate the mode of fiber post.

Post length of 10 mm was selected which was in accordance with the study by Giovani, Vansan, Neto, and Paulino which concluded that a post length of 10 mm significantly increased the fracture resistance.¹⁸

Post diameter of 1.5 mm is recommended for maxillary anterior tooth,¹⁹ size: 1 of DT light post was used as these size corresponds to post diameter of 1.5 mm.

To simulate the movement of the periodontal ligament, each root was embedded in an acrylic resin socket lined with a polyvinyl siloxane impression material.²⁰ Although no measurements of actual mobility were made. Specimens were removed from the resin blocks after the first signs of the polymerization to eliminate the effect of heat of polymerization on dentin. The heat generated leads to decreased moisture content, crazing, and weakening of the sample, which indirectly affects the fracture resistance value. The loading angle of 135° from palatal to labial was selected on the basis that it simulates the average angle of contact between maxillary and mandibular incisors in Class I occlusion and is a test of function. A crosshead speed of 1.5 mm/min was selected to allow time for distribution of the force from the point of application, i.e. from the core to throughout the post.²¹ The samples were loaded until the failure occurred. The fracture resistance was recorded. The mode of failure was then determined by observation of the samples. Then, confirmation of the failure mode was done by evaluating each sample radiographically using the digital radiographs.

The type of failures was classified into:

- a. Root fracture
- b. Post deboning
- c. Core fracture
- d. Post fracture.

The mode of failure for each sample was evaluated; collective data were tabulated category wise.

Post Debonding

Most of the failure associated with the fiber posts are due to the debonding. The debonding between post-cement interface rather than cement-dentin or intracemental fracture (cohesive failure of cement). This debonding is often attributed to various causes like Most of the fiber post are made of highly cross-linked epoxy resin which makes it difficult to bond with methacrylate based resin cement.²² Other reasons might be change in physical properties such as flexural strength and modulus of elasticity due to water sorption during prolonged storage (leading to expansion), changes in temperature (difference in coefficient of thermal expansion of fiber post, dentin, and core material), and dynamic functional loading.^{12,22-25}

Core Fracture

When considering fiber post and composite core, it was suggested that resin fiber posts are industrially cured, with a high level of polymerization and concomitant relatively small quantities of free resin available to interact with the reactive chemical constituents present in resin lutes or composite resin cores.

Post Fracture

20% of the fiber post fractured this could be attributed to less rigidity of fiber post as compared to that of the metal post. Three-point bending tests of fiber based post compared with metal post are in accordance with these results.^{10,26,27}

Zhi-Yue and Yu-Xing (2003) proposed a classification of failure modes as:

- a. Resin core or post fracture
- b. Cervical root fracture
- c. Mid root fracture
- d. Apical root fracture
- e. Vertical root fracture.

The resin core/post fracture was considered as the favorable mode of fracture; whereas, all other fracture modes involving root were considered as unfavorable.²⁸

In the present study, all the failures of the fiber post are favorable.

Research is also going on to increase the retention of glass fiber posts through various surface treatments. The effects of these treatments on the failure mode of the post can be verified in further studies.

In this study, a continually increasing static load was applied on the samples which are not the kind of loads in the

oral cavity. A study under cyclic loading would provide a better understanding for the findings observed in the present study.

Furthermore, this was an *in vitro* study. The performance of the materials might be different in clinical situations. A long-term clinical evaluation of success of these materials in restoring the tooth to its natural strength will help in their comparison.

The purpose of this study was to provide useful information and help dental professionals in choosing the most appropriate post system. As on today, extensive research has been carried out in this field, and a lot will be done in the future. It is understandable that each system has its own advantages and disadvantages and no system can be considered the gold standard for restoring the endodontically treated tooth. Until a single system is considered to be adequate, research in this aspect to find new systems and improve the old ones will be conducted.

CONCLUSION

The mode of failure of the restoration of endodontically treated tooth restored with glass fiber post was evaluated and within the limitations of this study, following conclusion was drawn. Prefabricated fiber post mostly shows debonding as a mode of failure which is favorable and amenable to retreatment.

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Surgical Fibrolysis and Skin Grafts in the Management of Oral Submucous Fibrosis

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Abstract

Introduction: Oral submucous fibrosis (OSMF) is a chronic, insidious, irreversible disease characterized mainly by two symptoms, burning sensation in the mouth while eating spicy hot food in early stages of the disease and trismus in the late stages of the disease.

Materials and Methods: This is retrospective hospital-based study of 25 patients, selected from 170 patients of OSMF, who attended OPD of Oral and Maxillofacial Surgical Hospital, Rajkot, Gujarat, India. Patients were selected for surgery based on their inter-incisal distance (IID) (Between 0.00 cm [Complete Trismus] and 2.5 cm). Patients having IID >2.5 cm were not subjected to surgical treatment. Complete records of the patients were maintained, and patients were followed postoperatively for the period of at least 3 Years.

Results: An average pre-operative IID of 25 patients who underwent surgery was found to be 1.49 cm, intra-operative IID was 2.86 cm while immediate post-operative IID was found to be 3.40 cm. All patients were recalled for check-up after 6 months, 1, 2, and 3 years in the post-operative period. The average IIDs recorded at the time of post-operative check-up were found to be as 6 months = 3.51 cm, 1-year IID = 3.45 cm, 2 years IID = 3.43 cm and 3 years IID was 3.44 cm. Thus, improvement in IID at pre-operative period (1.49 cm) was recorded to be (3.44 cm) at the end of 3-year period.

Conclusions: Surgical excision of fibrous bands followed by application of split skin graft covering the raw area in buccal mucosa gives good long-term results without any complications and satisfactory long-term results.

Key words: Oral submucous fibrosis, Skin grafts, Surgery, Trismus

INTRODUCTION

Oral submucous fibrosis (OSMF) is a chronic, progressive, irreversible or incurable, scarring disease, that predominantly affects the people of South-East Asian origin. This condition was described first by Schwartz (1952)¹ while examining five Indian women from Kenya, to which he ascribed the descriptive term “atrophiaidiopathica (tropica) mucosae oris.” Later in 1953, Joshi² from Mumbai, redesignated the condition as OSMF, implying predominantly its histological nature. The WHO definition for an oral precancerous

condition – “a generalized pathological state of the oral mucosa associated with a significantly increased risk of cancer,” accords well with the characteristics of OSMF.³

Described for the first time in detail in the year 1966 by Pindborg and Sirsat,⁴ OSMF is now definitely being recognized as a disease of Indian subcontinent occurring more commonly in countries such as India, Pakistan, Sri Lanka, Nepal, China and few countries where Indians have migrated like Europe and North America.

Patients present themselves to the clinician treating OSMF with two major complaints: Burning sensation in the mouth, particularly while eating spicy food and progressive inability to open mouth fully (Trismus). The clinical examination invariably reveals multiple oral ulcerations, white blanched oral mucosa, particularly mucosa of cheek and palate, partial or complete trismus and submucosal fibrous bands running in either vertical directions in cheek

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mucosa or horizontally across in palatal mucosa. Diagnosis of OSMF is mainly clinical, however, biopsy of the oral mucosa is mandatory to rule out malignant changes. The fibrosis observed during the clinical examination in oral mucosa involves the lamina propria and the submucosa and may often extend into the underlying musculature resulting in the deposition of dense fibrous bands giving rise to the limited mouth opening which is a hallmark of this disorder.

OSMF is associated with significant morbidity, with restricted mouth opening causing eating difficulties so a range of surgical modalities has been attempted, from moderate to significantly invasive. The most common initial surgical intervention includes the release of intraoral fibrous bands, coronoidotomies, muscle of mastication myotomies, and soft-tissue reconstruction with split thickness skin graft or allograft.⁵ Aggressive physical therapy post-surgery is essential: Without physical therapy compliance, the risk of recurrent trismus is possible. Patients should be made aware that, although the trismus has resolved post-surgery, their OSMF has not been cured. As such, continued physical therapy for the rest of their life is the best way to prevent recurrence of trismus. In addition, cessation of betel nut and tobacco use is essential to minimize disease progression. Finally, oral cancer surveillance is necessary for the rest of the patient's life.

For cases in which initial surgical intervention is unsuccessful (recurrent trismus; usually secondary to lack of compliance with physical therapy), the more aggressive surgical therapy is indicated. Again, excision of any fibrous bands intraorally and repeat masticatory muscle myotomy is required. Often, in this situation, a larger soft tissue buccal defect is created, needing large soft tissue reconstruction. This can include a temporalis pedicled flap, pedicled superficial temporalis fascial flap or a radial forearm free flap combined with split thickness skin graft coverage.⁶

The various local or distant tissues used for covering raw areas after surgical excision of the fibrous bands are either extra-oral tissue flaps or intraoral tissue flaps and include split skin grafts, nasolabial grafts, forehead flaps, palatal flaps, buccal fat pad tissue, lateral tongue flaps, absorbable collagen membrane, use of lasers, radial forearm free flaps, anterolateral thigh (ALT) flaps, vascularized temporal myofascial flaps, and collagen/silicone bilayer membrane. Each of these techniques has their own advantages and disadvantages and works best under the hands of those who advocate it (Table 1).

MATERIALS AND METHODS

In this retrospective hospital-based study, 170 patients attending OPD of Oral and Maxillofacial Surgery Hospital,

Table 1: Surgical procedures described in the literature for OSMF

Surgical procedures

Buccal fat pad
Lateral tongue flaps
Palatal flaps
Nasolabial flaps
Forehead flaps
Split skin grafts
Absorbable collagen membrane
Laser surgery
 KTP laser
 CO₂ laser
Radial forearm free flaps
Platysma myocutaneous flap
ADG
Amniotic membrane graft
Fibrin glue and absorbable atelocollagen membrane
Free flap reconstruction
Fibrotomy with coronoidectomy
Vascularised temporal myofascial pedicled flap
ALT thigh flaps
Collagen/silicone bilayer membrane

ADG: Artificial dermis graft, ALT: Anterolateral thigh, OSMF: Oral submucous fibrosis

Rajkot, Gujrat State, India⁷ and who were diagnosed for the presence of OSMF based on pre-determined clinical criteria mainly, burning sensation in the mouth particularly while eating spicy hot food and progressively increasing inability to open mouth (Trismus) were included in this study. Diagnosis of OSMF was confirmed by biopsy. Complete records were maintained including records about areca nut and tobacco chewing habits, and oral hygiene. Inter-incisal distance (IID) (Mouth opening) was measured with calipers. Radiological examinations were carried out whenever found necessary. Whenever possible, considering the presence of trismus, existing dental pathologies such as dental caries and periodontal pathologies like gingivitis were eliminated preoperatively to eliminate source of infection.

Patients exhibiting marked trismus (IID < 2.5 cm) were offered surgical treatment in the form of "Surgical fibrolysis and skin grafts" to relieve them of their trismus. Complete details of surgery were explained to the patients and informed consent was obtained from each patient. A total of 25 patients consented for surgical treatment.

All patients were males and their ages ranged from 21 to 40 years (Groups 3 and 4)⁷ average being 30.5 years. All patients had marked trismus with IID being <2.5 cm.

Inclusion Criteria's

1. Established case of OSMF by clinical and histopathological examination
2. IID < 2.5 cm
3. Patient has fully understood the surgical procedure he is about to undergo and has signed informed consent

4. Patient willing to leave tobacco habit and willing to continue to do so during post-operative period and signs document regarding his cooperation
5. Patients with good general health with no systemic comorbidity like diabetes or hypertension.

Exclusion Criteria's

1. IID > 2.5 cm
2. Patients with chief complaint of burning sensation in the mouth while eating spicy food
3. Patients not fully understanding the surgical procedure and not signing the informed consent
4. Patient expecting high results
5. Patients showing signs of non-cooperation before surgery like not ready to leave tobacco habits or not ready to carry out oral physiotherapy in the post-operative period
6. Patient having poor general health.

Surgical Procedure

Essentially, surgical procedure involved surgical removal of fibrous bands and resurfacing the raw area thus created in the buccal mucosa, bilaterally, by thick split skin graft. All surgeries were performed under general anesthesia. Pre-operative IID is measured and recorded.

A step-wise surgical procedure is described for better understanding of the surgical procedure.

1. Step No. 1 (Induction of anesthesia): General anesthesia was induced by either direct naso-endotracheal intubation or by use of fiber optic bronchoscope. Emergency tracheostomy set was always kept ready.
2. Step No. 2 (Incision): Horizontal incision was taken into both buccal mucosa beginning from a point just behind the oral commissure, going posteriorly to a point just in front of palato-lingual fold, avoiding injury to opening of parotid gland. This incision runs between occlusal surfaces of upper and lower teeth and its depth is limited to oral mucosa only.
3. Step No. 3 (Exposing fibrous bands): After primary incision in both the buccal mucosa, its depth being restricted only to mucosa, mouth is forcefully open, with the help of mouth prop taking care of the teeth. This opens up incisions in both the buccal mucosa in a triangular fashion, with tip positioned posteriorly and exposing underlying fibrous bands and musculature. IID is measured and recorded (intraoperative IID).
4. Step No. 4 (Fibrolysis): After fibrous bands are exposed, they are removed (fibrolysis) by palpating fibrous bands with fingers, till normal tissue without fibrous bands, is felt under palpating fingers. At this stage, surgical myotomies may have to be performed to get desired results. Excessive tissue at the posterior end

of the incision is excised to give raw area a rectangular shape. Bleeding points are checked and bleeding controlled.

5. Step No. 5 (Obtaining skin graft): Thick split skin graft is obtained using suitable skin-grafting knife from hairless areas of the skin. The most suitable area is the medial surface of the forearm. Donor area is covered with dressings. A skin graft is divided into two parts for each buccal mucosa and cut into proper shape. Any fat globules and other tissues attached on the raw area of the graft are excised, and grafts are made ready to place on recipient sites.
6. Step No. 6 (Skin grafting): Skin grafts are placed on the raw areas created in the buccal mucosa bilaterally, their edges matched and skin grafts are sutured into position using absorbable suture material. One end of the suture is kept long so that it can be used to put tie-over bolster dressing on the skin graft. To create pressure on skin grafts and stabilize them, softened dental compound is pressed onto the skin grafts and between teeth on both the sides. IID is measured (immediate post-operative IID).
7. Step No. 7 (End of surgery): After securing grafts in position Ryle's tube is passed through nose and patient is extubated.

Post-operative Course

Patient is kept in the ward for the period of one week. Feeding is carried out through Ryle's tube. On 7th post-operative day, Ryle's tube, intraoral pressure dressings, including tie-over bolster dressings are removed. Excessive suture material is removed. The patient is advised to start post-operative oral physiotherapy until further advice. Patient is recalled after 6 months, 1, 2 and 3 years for post-operative checkup.

For oral physiotherapy, wooden stents of various lengths were provided.

Measurement of IID

IID is measured at regular intervals.

1. Preoperatively
2. Intra-operative after opening the mouth forcefully
3. Postoperatively after surgery is over and pressure dressings are given
4. Postoperatively, after 6 months, 1, 2 and 3 years during recall checkup (Charts 1-10).

Data Analysis

Data were analyzed using two systems:

1. ANOVA Single Factor 6.521E-38 ($P < 0.05$)
2. IBM Watson Analytics: High-quality Results with 93 points. Various IID were compared and recorded (Chart 11).

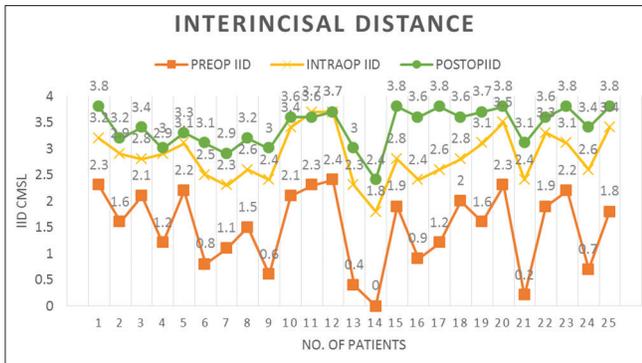


Chart 1: Inter-incisal distance (IID) pre-operative, intra-operative, and immediate post-operative

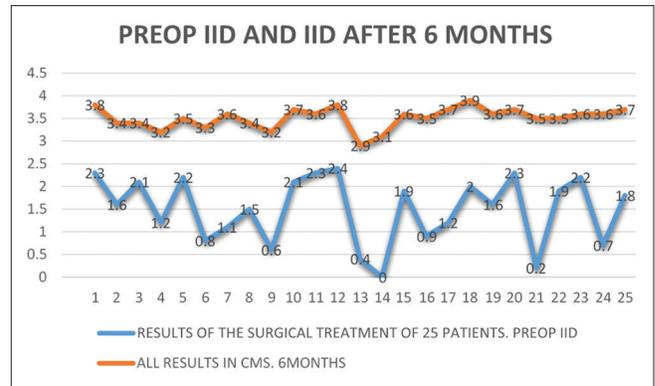


Chart 4: Pre-operative inter-incisal distance (IID) and post-operative IID after 6 months

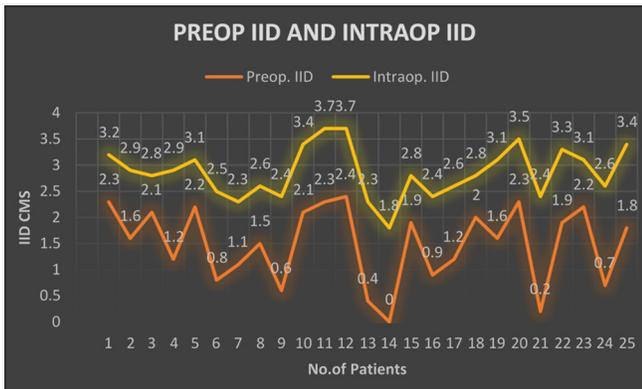


Chart 2: Pre-operative inter-incisal distance (IID) and intra-operative IID

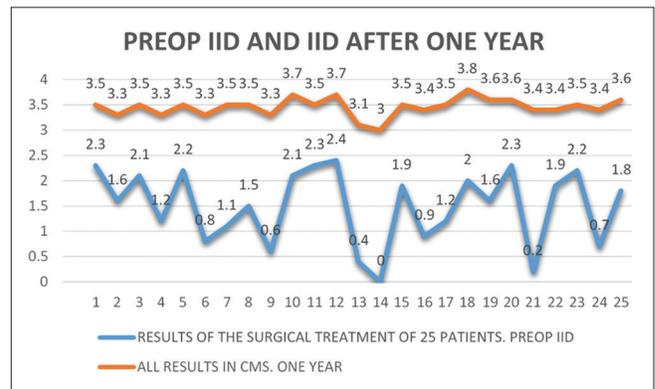


Chart 5: Pre-operative inter-incisal distance (IID) and IID after 1-year

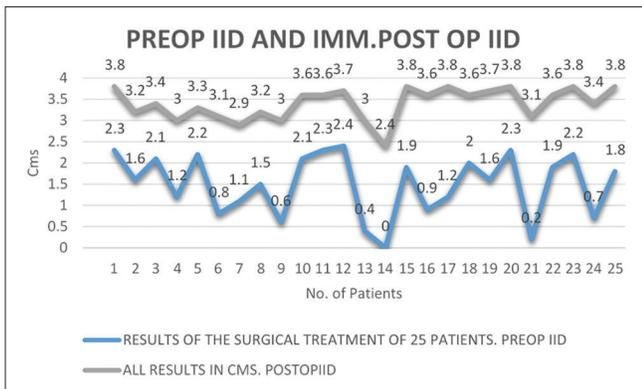


Chart 3: Pre-operative inter-incisal distance (IID) and immediate post-operative IID

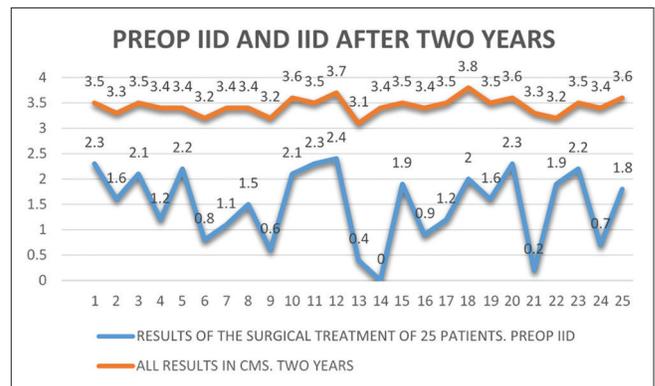


Chart 6: Pre-operative inter-incisal distance (IID) and IID after 2 years

RESULTS

In total, 25 patients underwent surgical fibrolysis followed by skin graft for the treatment of trismus associated with OSMF. Results of IID measured at various stages of treatment protocol was considered as a benchmark for the success of this surgical treatment.

Average pre-operative IID in all patients was found to be 1.49 cm, while Average intraoperative IID was 2.86 cm. Average immediate post-operative IID was 3.4 cm. At the end of 6-month period average post-operative IID in all 25 patients was 3.51 cm, while at the end of 1, 2 and 3 years post-operative periods average IIDs were found to be 3.45, 3.43 and 3.44 cm, respectively. On average pre-operative IID increased from 1.49 cm to 3.44 cm at the end of 3 years post-operative period (Table 2).

Table 2: Results of surgical treatment of 25 patients

Serial number	Pre-operative IID	Intra-operative IID	Post-operative IID	6 Months IID	1 year IID	2 years IID	3 years IID
1	2.3	3.2	3.8	3.8	3.5	3.5	3.4
2	1.6	2.9	3.2	3.4	3.3	3.3	3.3
3	2.1	2.8	3.4	3.4	3.5	3.5	3.5
4	1.2	2.9	3	3.2	3.3	3.4	3.9
5	2.2	3.1	3.3	3.5	3.5	3.4	3.4
6	0.8	2.5	3.1	3.3	3.3	3.2	3.2
7	1.1	2.3	2.9	3.6	3.5	3.4	3.4
8	1.5	2.6	3.2	3.4	3.5	3.4	3.4
9	0.6	2.4	3	3.2	3.3	3.2	3.2
10	2.1	3.4	3.6	3.7	3.7	3.6	3.6
11	2.3	3.7	3.6	3.6	3.5	3.5	3.5
12	2.4	3.7	3.7	3.8	3.7	3.7	3.6
13	0.4	2.3	3	2.9	3.1	3.1	3.1
14	0	1.8	2.4	3.1	3	3.4	3.4
15	1.9	2.8	3.8	3.6	3.5	3.5	3.5
16	0.9	2.4	3.6	3.5	3.4	3.4	3.4
17	1.2	2.6	3.8	3.7	3.5	3.5	3.5
18	2	2.8	3.6	3.9	3.8	3.8	3.8
19	1.6	3.1	3.7	3.6	3.6	3.5	3.5
20	2.3	3.5	3.8	3.7	3.6	3.6	3.6
21	0.2	2.4	3.1	3.5	3.4	3.3	3.2
22	1.9	3.3	3.6	3.5	3.4	3.2	3.2
23	2.2	3.1	3.8	3.6	3.5	3.5	3.5
24	0.7	2.6	3.4	3.6	3.4	3.4	3.4
25	1.8	3.4	3.8	3.7	3.6	3.6	3.6
Averages (cm)	1.49	2.86	3.40	3.51	3.45	3.43	3.44

All results are in cm. IID: Inter-incisal distance

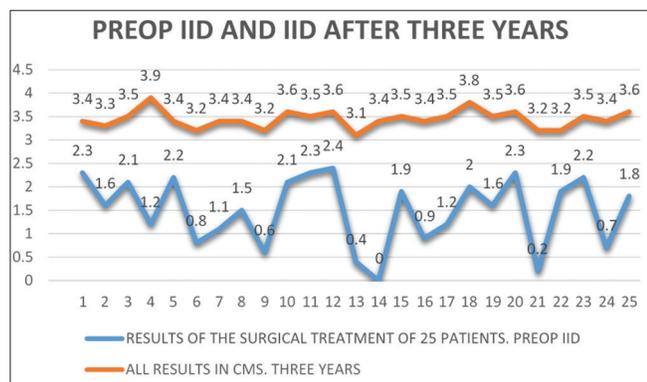


Chart 7: Pre-operative inter-incisal distance (IID) and IID after 3 years

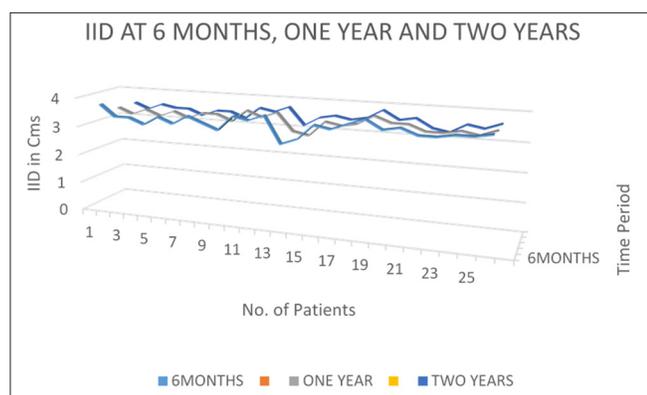


Chart 8: Inter-incisal distance after 6 months, 1 and 2 years

DISCUSSION

Plethora of literature is published on the treatment of OSMF each clinician claiming better success than the other. But in reality, most clinicians attempt to relieve symptoms associated with OSMF, primarily burning sensation in the mouth while eating spicy food in the early stage of the disease when inflammation, ulcerations and vesiculations dominate the clinical picture. At this stage dizzying array of treatment modalities have been administered by various clinicians which are mainly conservative non-invasive treatments. Success has been claimed using intralesional steroids, lycopene, micronutrients, milk from immunized cows, pentoxifylline, interferon gamma, placental extracts, turmeric (curcumin-diferuloylmethane), chymotrypsin, hyaluronidase, dexamethasone, levamisole, vitamin A, and stem cell therapy. The conservative non-invasive treatment of OSMF consists mainly of intraoral submucosal injections of various drugs suggested or it may consists of ingestion of oral medications. Conservative treatment of OSMF is mainly effective during first two stages of disease when chief complaint of the patient is burning sensation in the mouth (Table 3).

When disease advances to late stage of OSMF when trismus predominates the clinical picture, surgical treatment is attempted. Essentially surgical treatment consists of excision of fibrous bands and covering the raw area thus

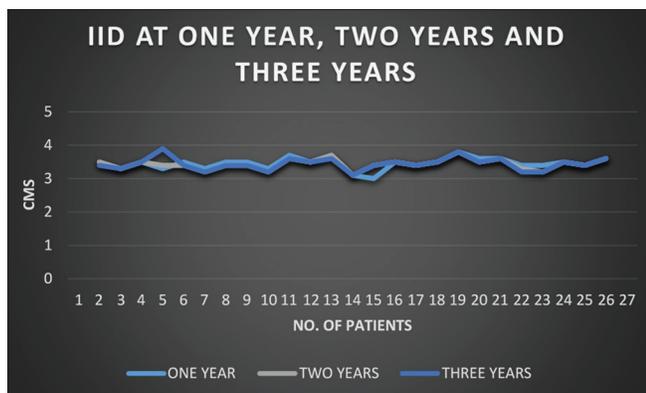


Chart 9: Inter-incisal distance at the end of 1, 2, and 3 years period

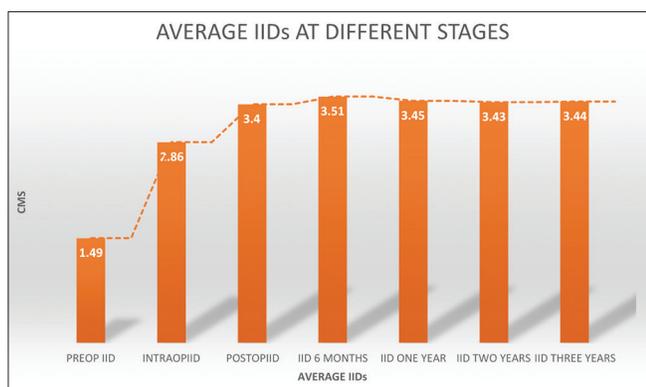


Chart 10: Average inter-incisal distances (IIDs) at different stages

created by various local or distant tissues, and hope for trismus to be relieved. The various local or distant tissues used for covering raw areas after surgical excision of the fibrous bands are split skin grafts, nasolabial pedicled grafts, forehead flaps, palatal island flaps, buccal fat pad tissue, lateral tongue flaps, absorbable collagen membrane, radial forearm free flaps, ALT thigh flaps, vascularized temporal myofascial flaps, and collagen/silicone bilayer membrane^{6,8-26} (Table 1). Lasers have also been advocated by few clinicians.²⁷ Each of these techniques have their own advantages and disadvantages and works best under the hands of those who advocate it.

None of the interventions reported so far, both, conservative non-invasive medical interventions or invasive surgical interventions, have reported any improvement in oral health-related quality of life among patients treated for OSMF. Both, main clinical symptoms, burning sensation in the mouth while eating spicy hot food and progressive inability to open mouth fully (Trismus) can affect oral functions, oro-facial appearance (sunken cheeks), and social interactions (difficulty in speech and deglutition).²⁸

Few reviewers like Ramesh Ram²⁹ are of the opinion that appropriate line of treatment whether conservative

Table 3: Non-invasive treatment for OSMF described in the literature

Non-invasive treatment

- Micronutrients and minerals
- Milk from immunized cows
- Lycopene
- Pentoxifylline
- Interferon gamma
- Steroids
- Placental extracts
- Turmeric
- Chymotrypsin, hyaluronidase, dexamethasone
- Levamisole and vitamin A
- Stem cell therapy

OSMF: Oral submucous fibrosis

or invasive, can be decided only after studying individual mechanisms operating at various stages of OSMF – initial, intermediate and advanced stages of OSMF.

In the year 2015, Kamath³⁰ carried out review of articles published on surgical treatment of OSMF. In total, 56 articles have been published on this subject and 995 surgically treated cases are included in the analysis. According to Kamath³⁰ very few controlled trials are conducted, most being randomized surgical trials on few patients with a short follow-up. The surgical procedure depends on preference of the clinicians and no definite protocols for treatment of OSMF exist. Adequate documentation and follow up need to be established to statistically analyze the results and proclaimed successes of various treatment modalities.

Fedorowicz *et al.*³¹ found no reliable RCT evidence for medical or surgical problems caused by restricted mouth opening and according to him more robust trials are required to identify the most effective treatment approaches to this debilitating condition.

There have been conflicting views about use of skin grafts in the treatment of OSMF, some clinicians favoring its use while others outright rejecting skin grafts. When used for excision of intraoral lesions, small defects are often resurfaced by skin grafts. Use of split skin grafts have certain advantages in covering intraoral mucosal defects like ease of harvest with minimal additional operating time and post-operative hospital stay, an acceptable functional cosmetic result, and the ability to survive post-operative radiation³² when radiation is part of the treatment. Furthermore, the use of split-thickness skin grafts (STSG) increases the practicability of a wider removal of abnormal mucous membranes surrounding the primary lesions.³³

Yen was the first to succeed in covering the buccal defect with a STSG in treating a case of OSMF.³⁴

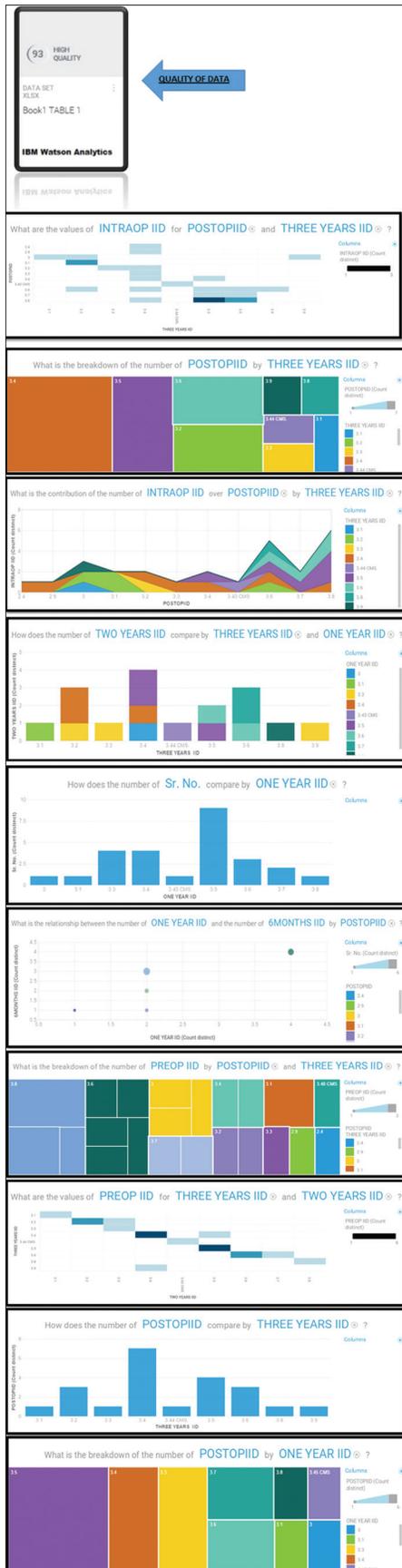


Chart 11: IBM WATSON data analytics

Yeh carried out a surgical procedure of incising the mucosa down to the muscles from the angle of mouth to the anterior tonsillar pillar, taking care to prevent damage to the stoma of the parotid duct, followed by split skin grafting into the defect, with acceptable results.¹¹

Soh and Muthusekhar³⁵ reported in the year 2015 use split skin grafts and polyethylene stent in 15 patients with OSMF. They concluded that fibrotomy followed by split skin graft along with a polyethylene sheet stent and sufficient post-operative physiotherapy is a simple, cost-effective and viable treatment modality for OSMF.

Canniff *et al.*¹² described the procedure of split thickness skin grafting after bilateral temporalis myotomy or coronoidectomy along with daily opening exercise and nocturnal props for a further 4 weeks.

Intraoral skin grafting in the buccal mucosa needs meticulous planning and execution so far as immobilization and adherence of the skin graft to the recipient bed is concerned.

Graft failure can be prevented by immobilizing the graft and closing up any potential dead space that might lead to separation. Multiple approaches for immobilizing skin grafts intraorally have been described in the literature. In 1975, Goshgarian and Miller³⁶ described a parachute stent technique that secures intraoral skin grafts via transcutaneous sutures. In 1981, Friedlander and Miller³⁷ described a technique using eye patches and a denture soft liner, securing the STSG to the cheek using transbuccal bolster sutures. Since then, many materials have been used, including foam, gauze, sutures, silicone, foam rubber pads, and eye patches, in addition to a myriad of different bolstering techniques.³⁸

The traditional tie over bolster technique described by Schramm and Myers involves fixation of the skin graft to the raw area, followed by placement of non-absorbable silk sutures from the adjacent mucosa, which are then tied over the bolster. However, the placement of this tie over sutures requires adjacent normal mucosa for anchorage, which may not be sufficient especially in the gingivobuccal sulcus. Although external fixation of the stents to the cheek has been described, this results in ugly scarring of the cheek.³²

In our surgical technique, these problems were overcome by giving proper rectangular shape to the recipient site with adequate tissue surrounding it, using multiple interrupted absorbable sutures, tie-over bolster dressings and using softened dental compound on the graft between teeth so that adequate pressure is created on the graft and oral movements are restricted.

Improved oral opening is an important objective of OSMF treatment. The treatment of severe trismus requires a combination of surgical release and post-surgical physiotherapy; the latter is essential for preventing a relapse due to post-operative inactivity and scarring.^{14,39-44} Mouth exercising is the well-established method to improve mouth opening and also to prevent post-surgical relapse. Various devices that help patients improve the mouth opening have been described in the literature. A majority of the appliances are tooth-borne, where opening force can be applied with the help of the devices or stents placed between the maxillary and mandibular arches or teeth. Previous literature described many mouth opening devices.⁴¹⁻⁴³ Cox and Zoellner⁴¹ tested the hypothesis that physiotherapy alone can modify tissue remodeling in OSMF to increase oral opening. Mouth-opening devices for this purpose are fixed to the teeth to keep the dental arches apart.^{41,42} Partially or totally edentulous arches, decayed teeth, or periodontitis, do not allow for the use of such devices, and often patients suffering from severe trismus present with these conditions. A non-tooth-borne mouth-opening device applying force to two intraoral screws placed in the vestibule of the maxillary and mandibular bones is described in such a situation. Patient noncompliance prevents surgical intervention for placement of the screws and limits the use of such devices. Patil and Patil⁴⁴ describe the fabrication and use of a new mouth-exercising device that helps patients to squeeze or stretch the cheek, resulting in local tissue remodeling to increase the elasticity of the mucosa for improvement in mouth opening.

In spite of tremendous advances in the oral physiotherapy devices,⁴⁴ a simple and cost effective device which even patient himself can fabricate at home is a wooden stent. We gave patients wooden oral stents (Props) of increasing lengths like 2.5, 2.8 and 3.00 cm and more, and advised them to insert them between their teeth as long as possible till it falls off and does not stay between their teeth because of increased mouth opening. Patient will then start using longer stent till he reaches longest possible stent.

In general, IID are considered as parameters of success in the surgical treatment of trismus associated with OSMF. Accordingly, we measured IID at the end of 6 months period and 1, 2, and 3 years periods. All patients were recalled accordingly, IID measured and clinical examination carried out to notice any change. Patients were encouraged to continue with oral physiotherapy.

A study of first two charts reveal the fact that forceful opening of the mouth improves the IID considerably, however, surgical fibrolysis and myotomies are necessary to achieve desired and further acceptable mouth opening.

Average Preop IID improved from 1.49 to 2.86 cm after forcefully opening the mouth while after fibrolysis and myotomies the average IID showed significant improvement from 2.86 cm to 3.40 cm.

Intraoral split thickness grafts may show some contracture and patients show reduced IID for first 1-year. However at the end of 1-year period, most grafts do not show any further contraction and remains stable as evident by stability in IID measured and compared at the end of 1, 2, and 3 years period (Charts 1-10).

Though use of skin grafts in the management of trismus associated with OSMF has not given expected, or satisfactory results to some clinicians and as a matter of fact few clinicians have outright rejected skin grafts as a suitable replacement tissue for large buccal defects created after fibrous band excision, we believe with proper surgical technique and meticulous follow-up of the patients for long periods gives good results, as it has given in our patients. When split-skin grafts are used for treatment of OSMF patients undergo three phases of healing:

1. Phase of Expansion (Increased in IID): In this phase, patient experiences increased mouth opening postoperatively because of surgical fibrolysis and myotomies followed by intense oral physiotherapy by patient. This phase last from immediate post-operative period until 6 months postoperatively.
2. Phase of Contractility (Reduction in IID): In this phase, patient shows reduction in mouth opening due to normal contracture of the wound and skin graft during healing phase. Another possibility is of non-cooperation of the patient regarding tobacco-habits or oral physiotherapy. This phase lasts from 6 months to 1-year of post-operative period.
3. Phase of Stability (Stable IID): This is final phase in which the wound and skin grafts stabilizes without further contracture. IID remains constant and patient shows signs of cooperation. This period usually starts after 1-year of post-operative period till final follow-up in our case 3 years.

We were able to get good results by using split skin grafts in OSMF. Statistically results were significant with $P < 0.05$ (ANOVA Single Factor 6.3521E-38). IBM Watson Analytics showed High-quality Results with 93 points (Chart 11).

Most importantly, we believe that choice of surgical interventions while treating trismus in OSMF clinicians should bear in mind necessity of repeat surgery in case of surgical failure or refibrosis and trismus following failure of patient compliance as regards to stoppage of tobacco habit and oral physiotherapy. Unfortunately, most surgeries advocated by various clinicians fail on these both accounts.

Repeat surgeries are not possible using same local or distant tissue flaps, and therefore, more radical surgery needs to be undertaken for which patient may not agree and may not be possible on technical grounds. When re-fibrosis takes place, intraoral local flaps like Palatal island flaps or tongue flaps themselves are known to get fibrosed. Use of skin grafts give opportunity for repeat surgery in case of surgical failure or re-fibrosis.

How split skin graft prevents or minimizes re-fibrosis is a question of debate.

Wound healing and scar formation is highly complex process and involves Actin and myosin and tethering movements of fibroblasts and myofibroblasts.

Based on above theory of scar contracture as suggested by Zhang Q, Qian YL, Cui L.⁴⁵ we propose a hypothesis that skin graft, prevents or minimizes re-fibrosis by following three mechanisms:

1. Reduction of levels of Actin and Myosin in myofibrils.
2. Reduction in the levels of Propyl Hydroxylase.
3. Mechanical interference by skin graft.

However, further studies are necessary to arrive at any definite conclusions

CONCLUSIONS

Surgical treatment of trismus associated with OSMF is a challenging task and needs meticulous planning and its execution. Proper choice of surgical intervention is necessary considering likelihood of surgical failure or re-fibrosis. Use of Intraoral tissue flaps may not be possible because of the presence of fibrosis preoperatively or these flaps themselves may get fibrosed in the event of non-compliance by the patient and make their re-use obsolete. Extra-oral tissue flaps are technically difficult, may need additional training or skilled surgeons and leaves behind large facial or extra-facial tissue scars which may not be acceptable to the patient and again in the event of re-fibrosis their use becomes obsolete.

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Burr Hole Irrigation of Hematoma Cavity with and without Drainage in the Treatment of Chronic Subdural Hematoma: A Comparative Study

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Abstract

Background: A chronic subdural hematoma (CSDH) is an old collection of blood and blood breakdown products between the surface of the brain and its outermost covering the dura. The chronic phase of a subdural hematoma begins several weeks after the first bleeding. It has long been recognized that the elderly are more likely to develop a subdural hematoma, particularly from minor trauma. CSDH s have been evacuated by craniotomies, burr holes, and twist-drill craniotomies.

Aim: To investigate the effect of drains, used in burr hole irrigations, on recurrence rates of CSDH and its clinical outcomes.

Results and Observation: 60 patients of CSDH were included in the study out of which 32 underwent burr hole with closed system drainage and 28 were underwent burr hole without closed system drainage and both were nominated by Groups A and B, respectively. 14 (23%) had shown recurrence of CSDH. Out of 14 patients, 8 belongs to Group B (28%) and 6 belongs to Group A (18%) with *P* value of 0.369.

Conclusion: Thus, it can be concluded that Group A, i.e., group where patients underwent burr hole with drain, has comparatively low recurrence rate than Group B, i.e., where patients underwent burr hole without drain.

Key words: Burr hole, Drainage, Subdural hematoma

INTRODUCTION

Chronic subdural hematoma (CSDH) is one of the most common entities encountered in daily neurosurgical practice.¹ Most commonly occur in elderly (average age 63 years) population. Its incidence is 5/100,000 per year in general population; because the proportion of the people aged 65 years or older is expected to be double worldwide until 2030 a large rise in incidence.²

CSDH is a collection of old blood and its breakdown products between the surface of the brain parenchyma and the outermost layer called the dura.³

CSDH classically occurs in the elderly and burr hole drainage is effective in >85% of patients.⁴ The complications of burr hole evacuation include recollection, inadequate drainage, underlying intracerebral hemorrhage, and contralateral hematoma.⁵⁻⁷

CSDH is formed gradually by the hemorrhage from parasagittal veins following a head trauma.⁸ In complicated cases, such as patients with chronic alcoholism, epilepsy, hematological disorders, cerebral atrophy, and under anticoagulant therapy, a minor head trauma may cause CSDH.⁹

The major symptoms of CSDH are a headache, unconsciousness, confusion, and neurological deficits (contralateral motor deficits). It may also present with mild symptoms mimicking dementia such as disorientation several weeks after a minor traumatic injury.¹⁰

Burr hole irrigations can be done with or without closed system drainage. Several comparative studies are going

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on this topic (burr hole drain or without drain) but no conclusive results has come. Debate is going on whether post-operative drainage should be used with burr hole craniostomy or not. As emerging evidence suggest that it lowers the recurrence rate, but most surgeons remained unconvinced about the role of the drain as per their personal experiences. In this study, efforts were made to investigate the effect of drains on recurrence rates of CSDH and its clinical outcomes.

MATERIALS AND METHODS

All patients of CSDH who were operated in the Department of Neurosurgery, Gauhati Medical College and Hospital, Guwahati, Assam, India during the period from January 2013 to June 2014 were enrolled for the study. The study was approved by the Institutional Ethics Committee.

Total of 60 cases of either sex of any age group were randomly selected and divided into two groups depending on the treatment procedure:

- Burr hole irrigation of hematoma cavity with closed system drainage (Group A).
- Burr hole irrigation of hematoma cavity without closed system drainage (Group B).

32 and 28 patients were included in Groups A and B, respectively.

All patients were analyzed by evaluating their hospital clinical and radiological data from computerized patient record system and picture archiving and communication system.

Patients with CSDH with thickness >10 mm, or a midline shift >5 mm on computed tomography (CT) scan were sorted and included in the study, irrespective of age, gender, co-morbidities such as diabetes, hypertension, head injury, on anticoagulants, etc.

Recurrence rate, change in hematoma size, etc., during post-operative hospitalization were compared between these two Groups (A and B). Consent had taken from all subjects and witness with medical, surgical, and drug history.

We followed our patients at 1, 3, 6 months post-operatively. A follow-up evaluation done for patients with assistance from a family member; asked about their activity of daily living and mobility status.

In the present study, CT scan had chosen as a diagnostic modality in follow-up to see the recurrence because it is less expensive compared to magnetic resonance imaging, time saving, easy availability and high sensitivity, and specificity to diagnose the recurrence.

RESULTS AND OBSERVATIONS

A randomized, prospective, comparative study was done on 60 cases of CSDH to compare the recurrence rate between two surgical techniques during the period from January 2013 to June 2014.

Among 60 cases, 32 cases were randomly selected and burr hole with closed system drainage done (Figure 1) and 28 were underwent burr hole without closed system drainage both were nominated by Groups A and B, respectively.

Males outnumbered females (male 49 and female 11). Age of the patients ranged from 15 years to 90 years with mean age of 53 ± 15 years.

The headache was the most common presentation (68%) followed by gait disturbances (53%) and limb weakness (35%).

73% of the patients had a history of minor head injury in recent past (within 3 months), whereas 23% and 8% were on antiplatelet and anticoagulant, respectively.

On evaluating the level of consciousness by Glasgow coma score (GCS), it was found that 55% patients having GCS between 14 and 15, and 36% patients having GCS between 9 and 13.

Radiological findings of CSDH based on non-contrast CT scan of head study.

Burr hole with drain was done in 32 cases and without drain was done in 28 cases of CSDH.

In the present study, a repeat CT scan was done on the 4th post-operative day to see the residual hematoma in each

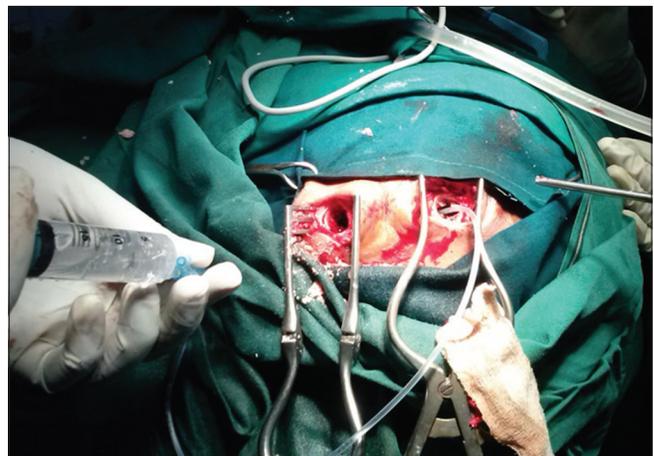


Figure 1: Irrigation through burr hole using feeding tube in the treatment of chronic subdural hematoma

patient. 3% patients of Group A (i.e., 1 in 32 patients) developed residual hematoma with size <10 mm. Whereas, in case of Group B, 17% patients (i.e., 5 in 28 patients) and 3% patients (i.e., 1 in 28 patients) developed residual hematoma <10 mm and >10 mm, respectively.

Follow-up was done for all the patients at 1, 3, and 6 months, and CT scan was done only in those patients who developed symptoms, such as headache, vomiting, altered sensorium, gait disturbance, seizures, and memory disturbance, to minimize the radiation exposure for our study population. Among total of 60 patients, 18 patients presented with symptoms most commonly with the headache and out of those 18 patients, 14 (23%) had shown recurrence of CSDH on CT scan (Figure 2). Out of 14 patients, 8 belongs to Group B (28%) and 6 belongs to Group A (18%) with p value of 0.369.

DISCUSSION

Weigel *et al.*¹¹ stated in an evidence-based review of contemporary surgical techniques for the treatment of CSDH, identified twist-drill craniostomy and burr hole craniostomy as the safest methods. Burr hole craniostomy has the best cure to complication ratio and is superior to twist-drill craniostomy in the treatment of recurrences. Craniotomy and burr hole craniostomy have the lowest recurrence rates. The use of closed system drainage reduces the risk of recurrence without additional risk of complications.¹¹

In the present study, it was found that more number of patients were between sixth and seventh decades (Table 1). Fogelholm and Waltimo¹² estimated an incidence of 1.72/100,000 per year; the incidence increased steeply with advancing age up to 7.35/100,000 per year in the

age group 70-79. Karibe *et al.*¹³ did study on Japanese population shown overall incidence was 20.6/100,000 per year, with 76.5 in the age group of 70-79 and 127.1 in over 80 years of age group. He concluded that not only population aging but also current medical trends (such as elderly patients who receive hemodialysis, anticoagulant, and/or antiplatelet therapy) might influence the increase of CSDH incidence. Sousa *et al.*¹⁴ stated that CSDH occurrence ranges from 3.4/100,000 in patients younger than 65 years of age to 58/100,000 in those older than 65 years.

In the present study, male outnumber females with male:female ratio of 4.45:1 (male 49 and female 11), whereas McKissock *et al.*¹⁵ found 2 or 3:1 ratio and Ahmed *et al.*² found male:female ratio 15:2.

In the present study, the headache is the most common symptom with 68% of patients of CSDH presented with headache. According to Huang *et al.*,¹⁶ headaches in 30-90% of patients of CSDH and Luxon and Harrison¹⁷ shown headaches in 64% patients as an initial symptom and 77% patients as a later symptom. According to Liliang *et al.*,¹⁸ young adults with CSDH usually have headaches and vomiting, whereas elderly have higher frequency or mental changes or motor dysfunction.

Ahmed *et al.*² found 76% of his study population had head injury, 11% on the antiplatelet drug, 5% on anticoagulant, and 37% were alcoholic. Santarius *et al.*¹⁹ shown 19% of study population on anticoagulant drug and 14% on antiplatelet drugs. In the present study, 73% of the study population had a history of head injury in the past.

According to Park *et al.*,²⁰ CT remains the preferred diagnostic method for the CSDH. In the present study, 73% hypodense, 16% isodense, and only 10% mixed hematoma were found in CT (Table 2 and Figures 3-5), whereas Singh *et al.*²¹ found 68.5% homogenous collection and 31.5% of mixed density. Ahmed *et al.*² found 79% hypodense, 9% isodense, and 12% mixed hematoma. They also found

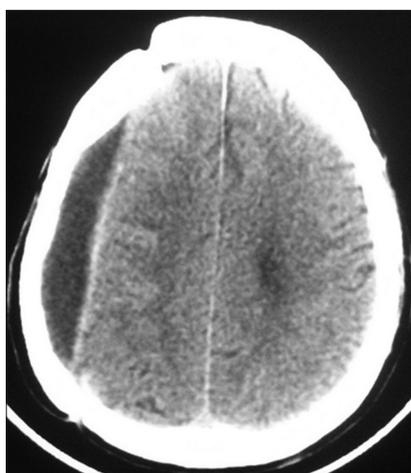


Figure 2: Non-contrast computed tomography of head showing recurrence of chronic subdural hematoma

Table 1: Distributions of number and percentage of cases of CSDH in different age groups

Age group (years)	n (%)
0-20	1 (1)
21-30	4 (6)
31-40	6 (10)
41-50	13 (21)
51-60	15 (25)
61-70	14 (23)
71-80	5 (8)
>81	2 (3)

CSDH: Chronic subdural hematoma



Figure 3: Non-contrast computed tomography of head showing hypodense chronic subdural hematoma

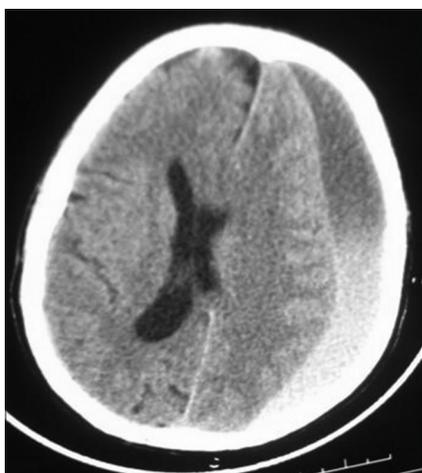


Figure 4: Non-contrast computed tomography of head showing mixed dense chronic subdural hematoma

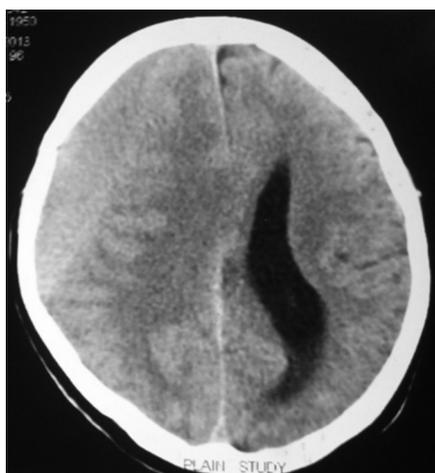


Figure 5: Non-contrast computed tomography of head showing isodense chronic subdural hematoma

bilateral hematoma 14%, 35% left, and on the right side 51%. In the present study, it was found 15% bilateral, 45%

Table 2: Number and percentage of cases of CSDH with findings of CT scan study of head

Imaging	n (%)
Site of hematoma	
Left	24 (40)
Right	27 (45)
Bilateral	9 (15)
Density of hematoma	
Hypodense (Figure 3)	44 (73)
Isodense (Figure 4)	10 (16)
Mixed (Figure 5)	6 (10)
Hematoma size (mm)	
10-13	49 (81)
13-15	9 (15)
>15	2 (3)
Midline shift (mm)	
5-7	42 (70)
7-10	17 (28)
>10	1 (1)

CT: Computed tomography, CSDH: Chronic subdural hematoma

right, 40% left, and 70% of patients with 5-7 mm midline shift, only 1% has >10 mm midline shift on CT scan.

Santarius *et al.*¹⁹ found recurrence of 9.3% with drain and 24% without drain which is statistically significant difference; he also compared mortality and morbidity in these two techniques which he found low morbidity and low mortality in drain group in 6 months follow-up. Singh *et al.*²¹ studied 200 patients out of that 9% recurrence rate in drain group and 26% without drain group, which is also statistically significant. Okada *et al.*²² also found 5% recurrence in drainage group and 25% in irrigation group; he also found post-operative hospital stay was shorter with drainage group. Kiyamaz *et al.*²³ also found continuous drainage for CSDH is superior to one-time drainage due to shorter hospital stay and reduced rate of recurrence. The meta-analysis by Alcalá-Cerra *et al.*²⁴ demonstrates that the insertion of a subdural drain was associated with a statistically significant reduction in the risk of symptomatic recurrence and the requirement for the further surgical intervention of CSDH after surgical evacuation (Table 3 and Figure 2).

In the present study, electrolyte imbalance is one of the most common complication in post-operative period with 10% in Group B and 5% in Group A. It is more compared to Ahmed *et al.*² who found 5% and 7%, respectively. They found more incidence of limb weakness in post-operative period 37-41% compared with us we found only 1-3% more with drain group (Table 4).

CONCLUSION

It can be concluded that with the use of burr hole with drain, i.e., Group A has comparatively low recurrence rate

Table 3: CT findings of the recurrent hematoma

CT findings of recurrent hematoma (n=14)	Group A (n=6) (%)	Group B (n=8) (%)
Hematoma size (mm)		
5-10	4 (66)	3 (37)
10-15	2 (33)	4 (50)
>15	0	1 (12)
Midline shift		
<5	5 (83)	3 (37)
5-7	1 (16)	4 (50)
>7	0	1 (12)

CT: Computed tomography

Table 4: Post-operative complications in Groups A and B cases of CSDH

Post-operative complications	Group A (%)	Group B (%)
Limb weakness	2 (3)	1 (1)
Seizure	1 (1)	3 (5)
Electrolyte imbalance	3 (5)	6 (10)
Wound infection/dehiscence	2 (3)	4 (6)
Post-operative fever	0 (0)	2 (3)
Meningitis	0	0 (0)
Empyema	0	2 (3)

CSDH: Chronic subdural hematoma

of CSDH than Group B, i.e., where patients underwent burr hole without drain, but their difference is statistically not significant.

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Clinical Profile of Conjunctival Lesions: A Prospective Study

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Abstract

Introduction: Conjunctiva unlike the other mucous membranes in the body is partially exposed to sunlight, which may be a factor in the development of some tumors.

Aim: To study the histopathological spectrum of conjunctival lesions.

Materials and Methods: This is a prospective study of 1 year conducted from January 2014 to January 2015. Patients attending the ophthalmology department with conjunctival growth were examined. Conjunctival growth was excised and subjected to histopathological examination.

Results: Present study comprised 144 patients aged between 3 and 88 years. A maximum number of cases were between the age of 51 and 60 years (24%) with least number of cases (0.5%) present between 81 and 90 years. Males (58%) were more commonly affected than females (42%). Bulbar conjunctiva (86%) was more commonly affected. Out of the 144 conjunctival biopsies, 104 (72.2%) cases were purely degenerative lesions, 14 (9.7%) cases were purely epithelial lesions, and 7 (4.9%) cases were purely melanocytic lesions. Degenerative lesions were the most common conjunctival lesions.

Conclusion: Lesions of conjunctiva comprise a large and varied spectrum of conditions. These lesions are to be recognized and treated appropriately to prevent complications.

Key words: Conjunctiva, Inclusion cyst, Ocular surface squamous neoplasia, Pterygium, Pyogenic granuloma, Tumors

INTRODUCTION

The conjunctiva, a mucous membrane composed of epithelium and substantia propria covers the anterior surface of the eye and inner surface of eyelids. It is divided into palpebral portion lining the undersurface of the eyelid, a forniceal portion forming a conjunctival cul-de-sac where it reflects onto the surface of the globe. Bulbar portion covers the exposed part of the eyeball to the cornea, plica semilunaris, and caruncle.¹

The conjunctiva is readily visible, so related lesions that occur in the conjunctiva are generally recognized at a relatively early stage.² Tumors can arise in the conjunctiva from both its epithelial and stromal structures. These are similar clinically and histopathologically to tumors that arise from other mucous membranes in the body.³ The caruncle which has unique composition of both mucous membrane and cutaneous structure can have tumors of both mucous and skin origin.⁴

Lesions of the conjunctiva comprise a large and varied spectrum of conditions.⁵ These tumors are grouped into two major categories of congenital and acquired lesions. The acquired lesions are further subdivided based on the origin of the mass into surface epithelial, melanocytic, vascular, fibrous, neural, histiocytic, myxoid, myogenic, lipomatous, lymphoid, degenerative, leukemic, metastatic,

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and secondary tumors. Melanocytic lesions include nevus, racial melanosis, primary acquired melanosis (PAM), melanoma, and other ocular surface conditions such as ocular melanocytosis and secondary deposition.⁶ In the majority of conjunctival lesions, diagnosis is not difficult due to their clinical features. Sometime difficulty may arise in differentiating granuloma from neoplasms especially when tumor size is small.⁷

MATERIALS AND METHODS

This is a prospective study of 1 year conducted from January 2014 to January 2015. Patients attending the ophthalmology department with conjunctival growth were examined. Conjunctival growth was excised and subjected to histopathological examination. The excised conjunctival specimen was received in 10% formalin. These were grossed, and macroscopic features were noted. After those tissues were processed routinely, paraffin sections cut at 4-5 µm thickness stained with hematoxylin and eosin and were examined microscopically. Special stains and immunohistochemistry were done whenever required.

Exclusion criteria were inadequate biopsies, specimens not sent in formalin, and autolyzed samples.

RESULTS

This study conducted during the period from January 2014 to January 2015 comprised 144 patients. Age of presentation ranged between 3 and 88 years. A maximum number of cases were present between the age of 51 and 60 years (24%) followed by 31-40 years group (22%). Least number of cases was present between 81 and 90 years (0.5%).

Males (58%) were more commonly affected than females (42%). Right eye (54%) was more commonly affected than left eye (46%).

Bulbar conjunctiva (86%) was more commonly affected followed by limbus (9%), caruncle (3%), palpebral (1.8%), and fornices (0.2%), respectively.

Out of the 144 conjunctival biopsies, 104 (72.2%) cases were purely degenerative lesions, 14 (9.7%) cases were purely epithelial lesions, and 7 (4.9%) cases were purely melanocytic lesions. One (0.7%) case of lymphoma, 6 (4.1%) cases were tumor-like congenital lesions, vascular 10 (6.9%), and 2 (1.4%) cases were miscellaneous lesions (Table 1).

Degenerative lesions were the most common conjunctival lesions. Maximum numbers of degenerative lesions were

Table 1: Distribution of conjunctival lesions

Lesions	Number of cases (%)
Degenerative	104 (72.2)
Epithelial	14 (9.2)
Melanocytic	7 (4.9)
Vascular	10 (6.9)
Congenital	6 (4.1)
Lymphoma	1 (0.7)
Miscellaneous	2 (1.2)

seen in age groups ranging from 31 to 60 years. 53% were males, and 47% were females. 99 cases (95%) were seen in the bulbar conjunctiva on the nasal side, and 5 cases were on the temporal side.

Pure pterygium comprised 84 cases (80.7%). Combined pterygium with epithelial lesions comprised 43 cases (8.17%), out of which pterygium with ocular surface squamous neoplasia (OSSN) comprised 28 cases and pterygium with inclusion cyst comprised 11 cases, pterygium with lymphoid hyperplasia 4 cases.

Maximum numbers of epithelial lesions were seen in bulbar conjunctiva with 8 cases (57.1%), followed by limbus 4 cases (28.5%) and palpebral conjunctiva 2 cases (14.2%). Most cases occurred between 35 and 50 years.

Out of 14 epithelial lesions, squamous papillomas accounted for 5 cases, inclusion cysts 6 cases, OSSN 2 cases, and 1 squamous cell carcinoma.

Out of 7 cases of melanocytic lesions, most common lesions were nevus with 5 cases (71.4%), followed by PAM without atypia 1 case (14.2%). PAM with atypia 1 case (14.2%)

Melanocytic lesions were most commonly seen in the bulbar conjunctiva (5 cases) followed by limbus (1 case) and caruncle (1 case).

In the present study, 10 pyogenic granulomas were seen with a maximum incidence between 11 and 20 years. All the cases were seen in bulbar conjunctiva.

Lymphoma was seen in 1 case. Dermoids were seen in 4 cases and Dermolipoma in 2 cases. 2 patients had ophthalmia nodosa.

DISCUSSION

Conjunctiva unlike the other mucous membranes in the body is partially exposed to sunlight, which may be a factor in the development of some tumors.^{8,9} The caruncle,

with its unique composition of both mucous membrane and cutaneous structures, can have tumors found in both mucosa and skin.

In the present study, age distribution of the cases was in the range of 3-88 years which correlated with the studies done by Shields and Shields⁶ (1 month-88 years) and Elshazly⁵ (1.5-77 years).

In the present study, males were more commonly affected than females which correlated with the studies done by Shields and Shields,⁶ Mondal *et al.*,² and Elshazly.⁵

In the present study, bulbar conjunctiva was the most common site which correlated with studies done by Shields and Shields,⁶ Mondal *et al.*,² and Elshazly.⁵

The distribution pattern of conjunctival lesions in the present study was slightly different from other studies. In the present study, degenerative lesions were most common followed by epithelial lesions, vascular lesions, and melanocytic lesions. A study done by Shields and Shields⁶ showed melanocytic lesions were the most common lesions and the least common being tumors such as congenital lesions. A study done by Mondal *et al.*² showed that epithelial lesions were most common, and tumor-like congenital lesions were the least common lesion. In a study by Hans *et al.*,³ pterygium was the most common lesion followed by non-specific inflammation and pyogenic granuloma.

The age distribution with maximum cases of degenerative cases was seen in 41-60 years in the present study, which correlated with the study done by Sanskar *et al.*¹⁰ (31-60 years), but a study done by Chui *et al.*¹¹ showed a wider range of age distribution (21-83 years).

The present study showed a higher incidence in males which correlated with a study done by Chui *et al.* Study done by Shields and Shields showed equal incidence in males and females. In the present study, there was no incidence of pterygium with nevi and pterygium with PAM without atypia.

In the present study, the most common epithelial lesion was inclusion cyst followed by squamous papilloma, OSSN, and squamous cell carcinoma. Most common epithelial lesion in the study done by Mondal *et al.*² was OSSN. Most common epithelial lesion was squamous cell carcinoma in the studies done by Shields and Shields⁶ and Amoli and Heidari¹² Age distribution in present study ranged from 20 to 80 years which correlated with other studies by Elshazly⁵ and Waddell *et al.*¹³

In the present study, conjunctival nevus was the most common melanocytic lesion which was similar to the studies done by Shields and Shields,⁶ Mondal *et al.*,² Amoli *et al.*,¹¹ and Elshazly.⁵ Malignant melanoma was not found in our series.

In the present study, all the 10 vascular lesions were pyogenic granuloma with no cases of hemangioma and lymphangioma. In the study done by Mondal *et al.*² and Elshazly,⁵ pyogenic granuloma was the most common lesion, whereas in Shields and Shields⁶ study, hemangiomas were more common.

In the present study, dermoid was more common than dermolipoma which contradicted with the studies done by Shields and Shields¹⁴ and Elshazly,⁵ where dermolipoma was the most common lesion.

CONCLUSION

A large spectrum of lesions can occur in the conjunctiva. Lesions are recognized by the patient in an early stage. Excised lesions of conjunctiva include a wide spectrum of condition ranging from benign lesions such as pterygium, pyogenic granuloma, dermoid nevus, papilloma, hemangioma to precancerous lesions such as OSSN and infiltrating malignancies such as malignant melanoma, squamous cell carcinoma, and lymphoma. It is important to diagnose correctly so that the treatment can be initiated early.

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Malaria Positive Cases with Reference to Liver Function Test among Patients Attending in Teerthanker Mahaveer Medical College and Research Centre, Moradabad, Uttar Pradesh, India

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Abstract

Introduction: Malaria is also an important infectious vector-borne disease caused by a *Plasmodium* species. According to the World Health Organization, involvement of liver in *Plasmodium Falciparum* malaria is not an uncommon presentation and presence of jaundice (bilirubin ≥ 3 mg/dl) is one of the signs of malaria. In severe and complicated malaria, a term “malarial hepatitis” is commonly used to describe hepatocytic dysfunction; however, actual inflammation is almost never seen in the liver parenchyma. An increased level of serum bilirubin along with increased level of serum glutamate pyruvate transaminase (SGPT) to more than three times the upper limit of normal, is main characteristics of malarial hepatitis.

Materials and Methods: This study was performed on 80 peripheral blood smear (PBS) confirmed cases of malaria. A collection of blood sample was done by venepuncture under aseptic conditions in the ethylenediaminetetraacetic acid tube for the diagnosis of malaria and in a plane vial to perform liver function test (LFT). Diagnosis of malaria was done by the microscopy of PBS and rapid malarial antigen test. The LFT was performed using autoanalyzer and Erba biodiagnostic kit, according to manufacturer instructions.

Results: Out of total 80 malaria positive patients, 60 patients (75%) had got deranged LFT in which 35 (70%) were males and 25 (83.33%) were females. According to serum bilirubin levels, patients were classified into three Groups A (59 patients, serum bilirubin < 3 mg/dl), B (21 patients, serum bilirubin 3-10 mg/dl), and C (no patient, serum bilirubin > 10 mg/dl). Total malaria positive patients had total bilirubin, direct bilirubin, indirect bilirubin, serum glutamic oxaloacetic transaminase, SGPT, and alkaline phosphatase levels in the range of 2.17 ± 1.78 mg/dl, 0.88 ± 0.77 mg/dl, 1.29 ± 1.12 mg/dl, 45.88 ± 28.99 IU/L, 41.04 ± 26.45 IU/L, and 104.48 ± 67.51 U/L, respectively.

Conclusion: Liver dysfunction in malarial infection ranged from mild elevation of liver enzymes and serum bilirubin (≥ 3 mg/dl) to acute hepatitis. It indicates severe illness with a high frequency of complications and mortality rates.

Key words: Liver function test, Malaria, Malarial hepatitis

INTRODUCTION

Malaria is responsible for infecting 300-500 million people and 1-3 million deaths annually in tropical areas.¹ Malaria is

also an important infectious vector-borne disease caused by a *Plasmodium* species. Malaria is caused by *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium ovale*, *Plasmodium malariae*, and rarely *Plasmodium knowlesi* in human.² 90% of the deaths from malaria is caused by *P. falciparum* because *P. falciparum* is the most common cause of malarial infection.³

According to the World Health Organization, involvement of liver in *P. falciparum* malaria is not an uncommon presentation and presence of jaundice (bilirubin ≥ 3 mg/dl) is one of the signs of malaria.⁴ As highlighted in the

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world malaria report 2010, *P. vivax* malaria is a major public health problem, in which puts billions of the world's population at risk of infection.⁵ The transmission of malaria parasite to the human host occurs by sporozoites infection to the liver.⁶

Anemia, thrombocytopenia, and disseminated intravascular are the hematological alterations that are associated with malaria infection.⁷⁻¹⁰ After the bite of female Anopheles mosquitoes, the malarial sporozoites, once reaches in blood, are attached to hepatocytes through receptor for thrombospondin and properdin.¹¹ Then, these sporozoites become mature to form tissue schizonts or become dormant hypnozoites. The amplification of infection by tissue schizonts due to the production of large number of merozoites (10,000-30,000). Each merozoite, which is released from the liver, is capable to enter inside a human red blood cell (RBC) and performing the asexual cycle of replication in that RBC and release of 24-32 merozoites after 48-72 h of asexual cycle.¹²

In severe and complicated malaria, a term “malarial hepatitis” is commonly used to describe hepatocytic dysfunction; however, actual inflammation is almost never seen in the liver parenchyma.¹³ An increased level of serum bilirubin along with increased level of serum glutamate pyruvate transaminase (SGPT) to more than three times the upper limit of normal, is main characteristics of malarial hepatitis.¹⁴

Hepatic involvement in malaria has largely associated with severe infection of *P. falciparum*. Occasionally mixed infection with *Plasmodium vivax*¹⁵ and hepatitis E¹⁶ has been shown. The multiple factors leading to severe anemia in malaria are hemolysis, bone marrow dysfunction, etc., and are proportional to the level of parasitemia.¹⁷ A common feature of falciparum malaria is mainly unconjugated hyperbilirubinemia, and it is attributed to hemolysis of both parasitized and non-parasitized RBCs and partly due to liver damage.¹⁸

The observation of the presence of jaundice and renal failure is found more commonly in recent years in patients infected by *P. falciparum* in Thailand and Vietnam.¹⁹ The most common sign of hepatic dysfunction is jaundice in falciparum malaria, although the most common clinical finding in these patients is tender hepatomegaly. The resultant hemolysis and severe infestation of the RBCs by *P. falciparum* lead to rise in bilirubin level. Clogging of the capillaries in the important organ is caused by sequestration of the parasite - infested RBCs in the capillaries, which results ischemia and can lead to dysfunctioning of the organ system. When the same happens in the liver, it is called hepatic dysfunction.

The symptomatic stage of the infection begins, when the parasites reach densities of about 50/ μ l of blood. These symptoms are characterized by a headache, fatigue, abdominal discomfort, muscle pain, and fever.²⁰ Malaria results to systemic manifestations by affecting major organs such as kidneys and liver.^{21,22} Malarial infection also leads to pulmonary complications.²³ Hyperbilirubinemia often seen in association with other manifestations such as cerebral malaria or renal failure,²⁴ although it has linked with increased mortality related to malaria.²⁵

MATERIALS AND METHODS

This prospective study was conducted at the Department of Microbiology, Teerthanker Mahaveer Medical College Hospital and Research Centre, Moradabad, Uttar Pradesh over a period from March 2015 to January 2016.

Subject Selection

A total 80 samples were taken, after confirming by microscopic examination and rapid malarial antigen test. Patients of all age group with the history of fever, headache, vomiting, gastric, jaundice, chills, and malaise were included in this study. Those patients who were taking hepatotoxic drugs or any anti-malarial drugs were excluded from the study.

Collection of Sample

A volume of 5 ml of blood was collected from each patient under aseptic conditions by venepuncture in ethylenediaminetetraacetic acid vacutainer tube (2.5 ml) for the diagnosis of malaria and plain tube (2.5 ml) for liver function test (LFT). A thick and thin smear was prepared. Thick smears were dehemoglobinized and stained with Leishman's stain and examined under $\times 100$ oil emersion lens.

Methodology

Diagnosis of malaria was done by microscopy of peripheral blood smear (PBS) examination and rapid malarial antigen test. PBS remains gold standard for conformation to the diagnosis of malaria. Thick and thin blood smears were prepared and both are stained with Leishman's stain. Then, the smears were examined to the different stages of malaria parasites under oil immersion lens. Rapid malarial antigen test is performed by following the procedure given by the production company.

Diagnosis of liver function by the semi autoanalyzer of Siemens Company by the use of commercially prepared reagent of liver function (bilirubin, SGPT, serum glutamic oxaloacetic transaminase [SGOT], and alkaline phosphatase [ALP]) using Erba biodiagnostic kit, according to manufacturer instructions.

Statistical Analysis

Mean and standard deviation were calculated for quantitative variables, and Chi-square was used to calculate *P* value. *P* < 0.05 was considered as significant.

RESULTS

The present study was conducted to observe the impact of malaria on LFT. In this study, biochemical parameters (total bilirubin, direct bilirubin, indirect bilirubin, SGOT, SGPT, and ALP) were included. In our study, total 80 patients were taken which were confirmed as malaria positive, 50 patients (62.5%) were males and 30 patients (37.5%) were females (Table 1 and Figure 1). Out of total malaria positive patients, 60 patients (75%) had got deranged LFT (DLFT) in which 35 (70%) were males and 25 (83.33%) were females (Table 2 and Figure 2). In this study, the patients of age group more than 60 years have had major DLFT (100%) followed by the age group of 31-40 years (88.89%) and 21-30 (85%) (Table 3 and Figure 3).

In our study, out of 30 female positive patients, total bilirubin (TBIL), SGPT, SGOT, and ALP were out of

normal range in 18 (54%), 9 (30%), 16 (53.33%), and 16 (53.33%), respectively, while in 50 males TBIL, SGPT, SGOT, and ALP were 27 (54%), 18 (36%), 11 (22%), and 10 (20%), respectively (Table 4 and Figure 4). In our study, according to serum bilirubin levels, patients were classified in three Groups A (59 patients, serum bilirubin <3 mg/dl), B (21 patients, serum bilirubin 3-10 mg/dl), and C (no patient, serum bilirubin >10 mg/dl) (Table 5).

Total malaria positive patients had total bilirubin, direct bilirubin, indirect bilirubin, SGOT, SGPT, and ALP levels

Table 1: Sex wise distribution of total malaria positive patients

Sex	Number of malaria positive patients	Percentage
Male	50	62.50
Female	30	37.50
Total	80	100

Table 2: Sex wise distribution of total malaria positive patients with abnormal and NLFT

Sex	Malaria positive	Percentage (n=80)	DLFT	Percentage	NLFT	Percentage
Male	50	62.5	35	70	15	30
Female	30	37.5	25	83.33	5	16.67
Total	80	100	60	75	20	25

DLFT: Deranged liver function test, NLFT: Normal liver function test

Table 3: Age wise distribution of all malaria positive patients with abnormal and normal liver function test

Age	Malaria positive	% (n=80)	DLFT	%	NLFT	Percentage
1-10	8	10	4	50	4	50
11-20	29	36.25	22	75.87	7	25.13
21-30	20	25	17	85	3	15
31-40	9	11.25	8	88.89	1	11.11
41-50	6	7.5	3	50	3	50
51-60	6	7.5	4	66.67	2	33.33
>60	2	2.5	2	100	0	00
Total	80	100	60	75	20	25

DLFT: Deranged liver function test, NLFT: Normal liver function test

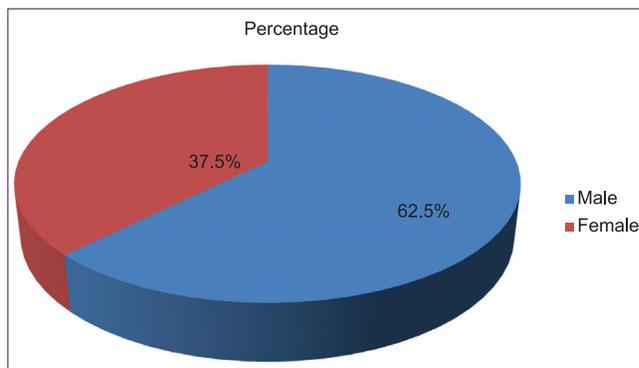


Figure 1: Sex wise distribution of total malaria positive patients

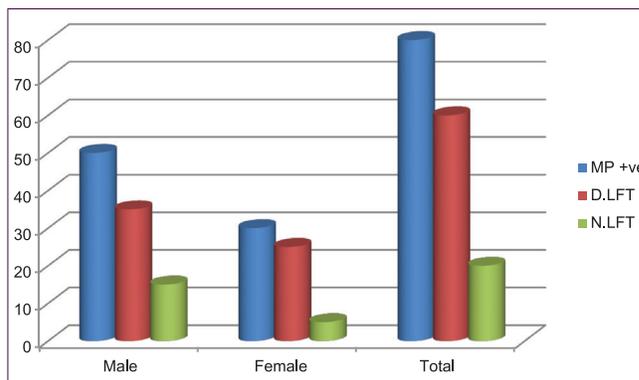


Figure 2: Sex wise distribution of malaria positive patients with abnormal and normal liver function test

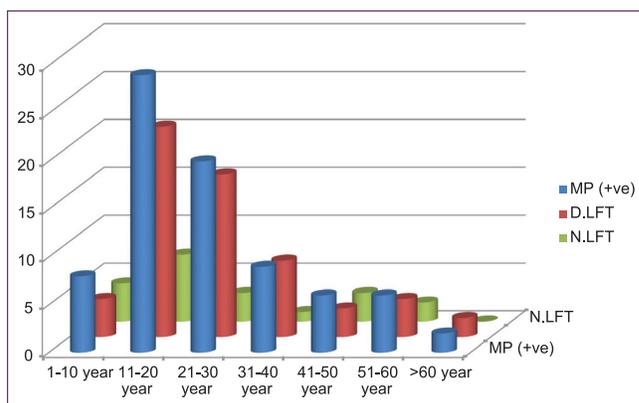


Figure 3: The age wise distribution of malaria positive patients with deranged and normal liver function test

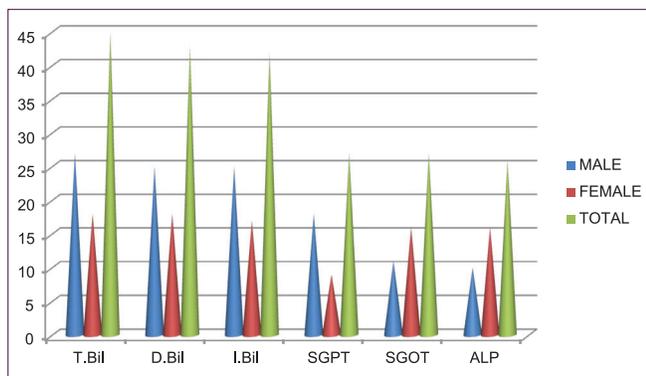


Figure 4: Sex wise distribution of malaria positive patients with increased level of liver function test markers

in the range of 2.17 ± 1.78 mg/dl, 0.88 ± 0.77 mg/dl, 1.29 ± 1.12 mg/dl, 45.88 ± 28.99 IU/L, 41.04 ± 26.45 IU/L, and 104.48 ± 67.51 U/L, respectively (Table 6).

DISCUSSION

In tropical areas, malaria is a major public health problem responsible for infecting 300-500 million people and 1-3 million deaths annually. Malaria involves liver where hepatocytes are invaded by sporozoites and multiply. In erythrocytic stage, the destruction of infected RBCs caused by merozoites. Molyneux *et al.* suggested that hemolysis is the most common cause of moderate elevation of hepatic enzymes than hepatic damage, which causes jaundice.²⁶

This study was performed to observe the impact of malarial infection on LFT. In our study, males 50 (62.5%) are more prone to malarial infection than females 30 (37.5%) out of total 80 positive patients. Our study is similar to the study of Abro *et al.*,²⁷ in which males 94 (91.5%) were more prone than female 9 (8.5%).

In our study, most of the malaria positive patients were in the age group of 11-20 years 29 (36.25%) followed by 21-30 years 20 (25%) and 1-10 years 8 (10%) while in the study of Rathod *et al.*²⁸ the age group 21-30 years 246 (32%) patients were more prone to malarial infection.

In our study, serum alanine aminotransferase (ALT or SGPT) level was above the reference range in 37.75% patients and serum bilirubin level above the reference range in 56.25% patients while in the study of Abro *et al.*²⁷ 67.6% patients had had ALT level above the reference range and in 81% patients serum bilirubin level was found to be higher than the normal level.

In this study, we observed <3 mg/dl serum bilirubin levels in 59 patients out of 80 patients while 20 patients out of

Table 4: Sex wise distribution of malaria positive patients with increased level of LFT markers

LFT parameters	n (%)		
	Male (n=50)	Female (n=30)	Total (n=80)
Total bilirubin	27 (54)	18 (60)	45 (56.25)
DBIL	25 (50)	18 (60)	43 (53.75)
IBIL	25 (50)	17 (56.66)	42 (52.5)
SGPT	18 (36)	9 (30)	27 (37.75)
SGOT	11 (22)	16 (53.33)	27 (37.75)
ALP	10 (20)	16 (53.33)	26 (32.5)

LFT: liver function test, SGPT: Serum glutamate pyruvate transaminase, ALP: Alkaline phosphatase, SGOT: Serum glutamic oxaloacetic transaminase, DBIL: Direct bilirubin, IBIL: Indirect bilirubin

Table 5: Classification of serum enzymes in patients as A, B, and C according to serum TBIL levels (n=80)

Groups	A	B	C
Serum bilirubin (mg/dl)	<3	3-10	>10
Number of patients	59	21	0
SGOT level (IU/L)			
<40	41	4	0
40-100	16	16	0
>100	2	1	0
χ^2 A with B=16.407, P<0.05			
SGPT level (IU/L)			
<40	40	9	0
40-100	19	11	0
>100	0	1	0
χ^2 A with B=6.064, P<0.05			

SGOT: Serum glutamic oxaloacetic transaminase, SGPT: Serum glutamate pyruvate transaminase, TBIL: Total bilirubin

Table 6: The mean value and standard deviation of measured LFT markers in both male and female malaria positive patients separately

LFT parameters	Normal range	Mean±SD (n=80)
TBIL	0.2-1.0 mg/dl	2.17±1.78 mg/dl
DBIL	0.0-0.4 mg/dl	0.88±0.77 mg/dl
IBIL	0.0-0.7 mg/dl	1.29±1.12 mg/dl
SGOT	5-40 IU/L	45.88±28.99 IU/L
SGPT	5-40 IU/L	41.04±26.45 IU/L
ALP	50-126 U/L	104.48±67.51 U/L

SD: Standard deviation, LFT: Liver function test, TBIL: Total bilirubin, DBIL: Direct bilirubin, IBIL: Indirect bilirubin, SGOT: Serum glutamic oxaloacetic transaminase, SGPT: Serum glutamate pyruvate transaminase, ALP: Alkaline phosphatase

50 patients were having 3-10 mg/dl serum bilirubin level, in the study of Kochar *et al.*, 2003.²⁹

CONCLUSION

The results of our study provide valuable information and association between hepatic biochemical derangements in malarial patients. This study was conducted on a small sample size, and it provides basic information about patients

infected with the malaria parasite. Therefore, we suggested that same type of study should also be performed on large sample size, and early diagnosis of malarial infection should be performed with LFT to prevent complications and to reduce mortality. In malaria, severe hepatic dysfunction is usually related with the underlying chronic liver disease. The complications are more common in patients with malarial hepatopathy; that's why it should be recognized promptly.

Thus, in our opinion increased levels of bilirubin, SGOT and SGPT are the strong evidence of hepatic dysfunction in patients with malaria.

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Cardiac Complications of Diabetes Mellitus: A Prospective Study

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Abstract

Background: The purpose of this study is to assess the various cardiac manifestations in diabetes mellitus (DM) like coronary artery disease and non-coronary artery disease. To evaluate the associated risk factors in patients with DM and cardiac diseases. Correlation between cardiac disease and duration of DM.

Methods: A total of 100 patients admitted or attending outpatient clinics and fulfilling the inclusion criteria were evaluated clinically. A baseline electrocardiogram (ECG) was taken in all cases irrespective of cardiac involvement. Patients with normal ECG pattern were further evaluated with a stress test for latent coronary artery disease. All the patients were subjected to routine investigations.

Results: The mean age of the study group was 55.54 years. The mean duration of DM was 9 years. 40 out of 100 patients had ischemic heart disease. Out of 18 patients of angina pectoris, only 4 had symptoms correlating with angina and had resting ECG abnormalities. Rest 14 patients (17.94%) had latent coronary artery disease detected by the stress test. Out of 22 patients with myocardial infarction (MI) eight patients (36.36%) had atypical or silent MI, which was detected by routine ECG recording.

Conclusion: With the present study, it can be concluded that there is a high occurrence of coronary artery disease with coronary risk factors in patients with DM. Every patient with DM should be screened for latent coronary artery disease. Furthermore, all patients with prolonged history of DM should be screened clinically with simple tests for the presence of cardiac autonomic neuropathy and managed accordingly.

Key words: Angina pectoris, Blood sugar levels, Cardiomyopathy, Coronary artery disease, Diabetes, Dyslipidemia, Glycosylated hemoglobin, Smoking

INTRODUCTION

Diabetes with cardiac complications is a well-known global problem. The prevalence of diabetes mellitus (DM) in Urban South India (as reported by Ramachandran *et al.*) is 5%. Diabetes is present in 21% of people aged 40 and above. The peak incidence of 41% is in age group 55-64. The incidence, prevalence, and the pattern of occurrence of coronary artery disease are increasing in India and South Asian countries.¹ Coronary artery disease is more

prevalent and more severe and occurs early in diabetics than non-diabetics. The higher incidence of angina pectoris, myocardial infarction (MI) (including silent MI), and congestive cardiac failure has been reported in DM. Early recognition of coronary artery disease in DM patients may, therefore, be important for management and prognostic purpose.²

Objectives of the Study

- I. To study the various cardiac manifestations in DM like: Coronary artery disease: (1) Ischemic heart disease (IHD), (2) Acute MI, and (3) Silent MI
Non-coronary artery disease: (1) Cardiac autonomic neuropathy and (2) Diabetic cardiomyopathy.
- II. To evaluate the associated risk factors in patients with DM and cardiac diseases.
- III. Correlation between cardiac disease and duration of DM.

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MATERIALS AND METHODS

The protocol was approved by the local ethics committee and written informed consent was obtained from each patient. 100 patients admitted or attending outpatient clinics and fulfilling the inclusion criteria (mentioned below) were evaluated clinically. A baseline electrocardiogram (ECG) was taken in all cases irrespective of cardiac involvement. Patients with normal ECG pattern are further evaluated with the stress test for latent coronary artery disease. All the patients subjected to the following investigations.

1. Fasting blood sugar (FBS) level
2. Postprandial blood sugar level
3. Blood urea
4. Serum creatinine
5. Lipid profile
6. Cardiac enzymes (is necessary)
7. Echocardiography (if necessary)
8. Glycosylated hemoglobin.

Inclusion Criteria

- I. Patients above the age of 18 years
- II. Patients with type 1 DM
- III. Patients with type 2 DM.

Exclusion Criteria

- I. Patients with hypertensive heart diseases
- II. Patients with cor pulmonale
- III. Patients with rheumatic heart disease and congenital heart disease
- IV. Patients with gestational diabetes mellitus.

RESULTS AND OBSERVATIONS

About 100 patients of DM type 1 and type 2 attending the outpatient clinics and admitted in ICCU and medical wards that satisfied the inclusion criteria were studied, and the following observations were made (Tables 1-13).

The maximum numbers of patients were found to be in the age group of 41-60 years (73% of patients) (Table 1).

46% of patients had FBS between 120 and 180 mg% (Table 3).

65% of patients had blood sugar level between 200 and 400 mg% (Table 4).

In this study, 40% of patients had evidence of IHD. 36% of patients had cardiac autonomic neuropathy. 10% of patients developed congestive cardiac failure and 4% of patients had dilated cardiomyopathy (Table 6).

Table 1: Sex preponderance

Age (years)	Male	Female	Total (%)
20-40	1	1	2 (2)
41-50	28	15	43 (43)
51-60	17	13	30 (30)
61-70	8	4	12 (12)
71 and above	10	3	13 (13)
Total	64	36	100 (100)

Table 2: Duration of diabetes mellitus

Age (years)	Male	Female
0-5	21	8
5-10	25	18
11-15	12	7
16 and above	16	3
Total	64	36

Table 3: The fasting blood glucose value at the time of presentation

Range (mg%)	Male	Female	Total (%)
<120	4	4	8 (8)
120-180	33	13	46 (46)
181-250	19	11	30 (30)
>250	8	6	14 (14)

Table 4: Post prandial blood sugar level at the time of presentation

Range (mg%)	Male	Female	Total (%)
<200	7	9	16 (16)
200-300	35	9	44 (44)
301-400	12	9	21 (21)
>400	-	2	2 (2)

Table 5: The presenting symptoms of the patients in present study

Symptoms	Male	Female	Total (%)
Chest pain	8	10	18 (18)
Swelling of feet	4	6	10 (10)
Palpitation	10	8	18 (18)
Dizziness	5	3	8 (8)
Breathlessness	6	8	14 (14)
Other symptoms	26	12	38 (38)

Table 6: The varied clinical manifestations in the present study

Patten	Males	Females	Total (%)
Angina	9	9	18 (18)
Myocardial infarction	10	12	22 (22)
Cardiac autonomic neuropathy	20	16	36 (36)
Congestive cardiac failure	4	6	10 (10)
Dilated cardiomyopathy	2	2	4 (4)
Sudden cardiac death	0	0	-

Table 7: Pattern of IHD

Pattern	Males	Female	Total (%)
Angina	9	9	18 (18)
Myocardial infarction	10	12	22 (22)

IHD: Ischemic heart disease

Table 8: Pattern of myocardial infarction

Pattern	Male	Female	Total (%)
Symptomatic MI	6	8	14 (63.63)
Atypical symptoms or silent MI	4	4	8 (36.36)

N=22, male=10, female=12. MI: Myocardial infarction

Table 9: Symptoms associated with atypical manifestations of myocardial infarction

Symptoms	Number of cases
Chest pain	1
Angina	-
Atypical	1
Epigastric pain	2
Dyspnea	1
Only	-
With pulmonary edema	1
With congestive cardiac failure	-

N=8, male=4, female=4

Table 10: The pattern of MI (N=22)

Pattern of infarction	Number of patients (%)
Anterior or anterolateral infarction	12 (55.54)
Inferior wall infarction	4 (18.18)
Inferior wall infarction with right ventricular extension	2 (9.09)
Non-Q wave MI	4 (18.18)

MI: Myocardial infarction

Among 40 patients of IHD 18 patients had angina and 22 patients had MI. Out of 18 patients of angina, only 4 had typical ischemic changes on resting ECG, rest of the 14 patients had latent coronary artery disease, which was detected by stress test (Table 7).

36.36% of patients in this study presented with atypical symptoms or silent MI, which was detected on routine ECG recording (Table 8).

4 patients out of 22 patients presenting with MI had atypical presentations. 4 out of 22 (18.20 %) patients with MI were totally silent detected on routine ECG (Table 9).

Parasympathetic involvement was more common than sympathetic involvement (Table 11).

The most common symptoms of autonomic neuropathy in this study were postural giddiness, impotence, and bowel disturbances (Table 12).²

Table 11: Cardiac autonomic neuropathy in this study

Pattern	Male	Female	Total (%)
Parasympathetic	13	9	22 (61.11)
Sympathetic	7	7	14 (38.88)

N=36, males=20, females=16

Table 12: The symptomatology of autonomic neuropathy

Symptoms	Number of cases (%)
Postural giddiness	8 (22.22)
Impotence	3/20 (15.00)
Constipation	7 (19.45)
Disordered sweating	5 (13.89)
Bladder disturbances	4 (11.12)
Diarrhea	3 (8.34)

N=36, males=20, females=16

Table 13: The mean lipid levels in the study group

Lipid levels	Males (mg%)	Females (mg%)
Total cholesterol	200.4	214.8
LDL-cholesterol	117.7	117.4
Triglycerides	161.2	163.5
HDL-cholesterol	40.9	40.3

LDL: Low-density lipoprotein, HDL: High-density lipoprotein

Congestive Cardiac Failure

In this series of study, 10 patients presented with signs and symptoms of congestive cardiac failure (4 males and 6 females).

Dilated Cardiomyopathy

Four patients (2 males and 2 females) who presented with congestive cardiac failure were evaluated with echocardiography. All four patients had dilated chambers and decreased ejection fraction. Diagnosis of diabetic cardiomyopathy was made excluding other causes of dilated cardiomyopathy.

Lipid Profile

The mean total cholesterol level was higher in females compared to males (214.8 vs. 200.4 mg%). The mean triglyceride level was again higher in females (163.5 mg% vs. 161.5 mg%). High-density lipoprotein (HDL)-cholesterol was less in females compared to males (40.3 mg% vs. 40.9 mg%) (Table 13).

Build table showing the mean body mass index (BMI) in the study:

Males	Females
22.6	23.1

The mean BMI of male patients in this study group was 22.6 and that of females was 23.1. BMI of females was higher. 13 males and 5 females had BMI above 25.

Smoking and Alcoholism

16 males (25%) and one female (2.7%) among the study group were chronic smokers (biddies and or cigarettes). 18 males (28.12%) consumed alcohol; none of the female patients were alcoholics.

DISCUSSION

In the present study, 100 patients of DM were studied and following observations were made.

Age

The mean age of the study group was 55.54 years (males - 55.73 years and females 55.19 years). The mean age group of the study group by Meenu Walia *et al.* was 53.71 ± 8.17 years for males and 52.61 ± 7.05 for females. The age range in this study group is 40-82 years.

Sex

In the present study, group of 100 patients, 64 were male patients, and 36 were female patients. The ratio of male:female is 1.7:1.

Duration of DM

The mean duration of DM in this study was 9.00 years. 9.07 years being in males and 8.86 years for females.

Levels of Hyperglycemia

The mean fasting blood glucose level in this study was 185.9 mg% (males - 184.5 mg% and females - 188.55 mg%). Meenu Walia *et al.* reported an FBS value of 155.67 ± 53.92 mg% in males and 173.61 ± 71.70 mg% in females.³ The values in our study correlate with the above-mentioned study.⁴

The mean post prandial blood sugar level at the time of presentation in the study group was 263.3 mg% (males - 264.15 mg% and females - 261.89 mg%).

IHD

In this study of 100 patients of DM, 40 patients had IHD.

Out of 40 patients of IHD, 18 patients had angina pectoris. Only 4 patients had typical history of chest pain correlating with angina pectoris and resting ECG was showing ischemic changes. Rest of 14 patients (17.94%) had latent coronary artery disease which was detected by thread mill test. Gupta and Pandit have reported in their study a prevalence of 36.3% of latent coronary artery disease. Meenu Walia *et al.* reported the prevalence of coronary artery disease among type 2 diabetes patients to be 15.57%.⁵ The present study

correlates with the above-mentioned studies. Various other studies report widely variable prevalence of coronary heart disease among diabetics in India (6.6-33%).⁶

MI

Among 22 patients with MI in the present study, 10 patients were male and 12 patients were females. Females outnumber males in this study, which correlates with the study reported by Partamian and Bradley in their series.⁷

In this series of 22 patients with MI, 18 patients (36.36%) of patients presented with atypical manifestations or silent infarction, which was detected during routine electrocardiographic recording.

Margolis *et al.* reported 23% of silent infarctions in their study.⁴ Other authors have estimated the occurrence of unrecognized MI between 0 to 60%.

The immediate mortality (within 1 week) in this series of 22 patients was 31.2%. Seven patients died within 1 week of admission. Four died within 24 h of admission. Three died between 24 h to 1 week. Partamian and Bradley have reported immediate mortality in their patients at 38% (immediate mortality was arbitrarily defined as 2 months of attack in their study).⁷

Two patients out of four who died within 24 h presented with cardiogenic shock (systolic blood pressure. less than 90 mm Hg). Two patients who died between 24 h and 1 week had diabetic ketoacidosis and one patient developed fatal ventricular arrhythmias.

Pattern of MI

12 out of 22 patients had evidence of anterior/anterolateral infarction (55.54%). Four patients (18.18%) had evidence of inferior wall MI. Two patients had evidence of inferior wall MI with right ventricular extension. Four patients had subendocardial infarction (18.18%).

Cardiac Autonomic Neuropathy

36 out of 100 patients studied had evidence of cardiac autonomic neuropathy (36%). Tankhiwale *et al.* have reported an incidence of 30% in a study of type 2 DM patients.⁸ The incidence of cardiac autonomic neuropathy in other series varies from 17% to 68%.

In our study, parasympathetic involvement was more common than sympathetic involvement, which correlates with Tankhiwale *et al.* study.

Predominant symptoms of patient with autonomic neuropathy in our series were postural giddiness (22.22%), constipation (19.45%), and impotence (15%). Tankhiwale *et al.* in their series have reported giddiness (14.3%),

nocturnal diarrhea (11.7%), and impotence (11.7%) as predominant symptoms in their study.⁸

Diabetic Cardiomyopathy

In this study, 4 out of 100 patients (2 males and 2 females) had evidence of dilated cardiomyopathy. Echocardiography done on these patients revealed left ventricular dysfunction, dilated chambers, and decreased ejection fraction.⁶ ECG showed non-specific ST-T changes in one patient. All 4 presented with features of congestive cardiac failure.

Sudden Cardiac Death

There were no cases of sudden cardiac death in our series.

Congestive Cardiac Failure

In our study, 10 patients presented with signs and symptoms of congestive cardiac failure. Females outnumber male patients (6 vs. 4).

BMI

The mean BMI in males in this study is 22.6 and females are 23.1. Females are more obese than males. 13 males and 5 females had BMI above 25. Meenu Walia *et al.* in their study group reported a mean BMI in males and females as 21.32 ± 3.64 and 22.22 ± 4.80 , respectively.⁷ Our study correlates with the above study.

Smoking and Alcoholism

About 16 males and one female (25% and 2.7%, respectively) among study group were chronic smokers (biddies and cigarettes). 18 males (28.12%) males consumed alcohol almost regularly; none of the female patients were alcoholics.

Lipid Profile

The mean total cholesterol, low-density lipoprotein (LDL)-cholesterol, triglyceride, and HDL-cholesterol levels were 207.8 mg%, 117.57 m%, 162.35 mg%, and 40.6 mg%, respectively. In our study, 22 (22%) of patients had HDL-cholesterol below 40 mg% and 11 patients (11%) of patients had hypertriglyceridemia (>250 mg%).

The mean HDL-cholesterol in females was less than in males. The mean total cholesterol and triglyceride levels

were higher in females when compared to males. Meenu Walia *et al.* in their study have reported lipid profile levels as follows mean total cholesterol 205.7 ± 55.9 ; HDL-cholesterol 42.78 ± 8.53 , and triglyceride level 175.24 ± 92.75 .⁹ Our study correlates with the above-mentioned study.

CONCLUSION

With the present study, it can be concluded that there is a high occurrence of coronary artery disease with coronary risk factors in patients with DM. Even modifiable risk factors such as smoking are present in a significant proportion of patients. All patients with DM should be screened for latent coronary artery disease (as it has prognostic implications). Furthermore, all patients with prolonged history of DM should be screened clinically with simple tests for the presence of cardiac autonomic neuropathy and managed accordingly. Diabetic dyslipidemia is commonly present in many cases. Hypercholesterolemia, high LDL-cholesterol, hyper-triglyceridemia, and low HDL-cholesterol are all significant predictors of coronary artery disease in DM.

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Serum Fibrinogen Levels and its Relation to Hypertension

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Abstract

Background: Fibrinogen has been identified as major independent risk factor for cardiovascular disease. Fibrinogen levels (FLs) in our hypertensive Kashmiri population have not been studied so far.

Aims and Objectives: To compare serum FL in hypertensive with non-hypertensive patients in Kashmiri ethnic population.

Materials and Methods: It was a prospective, hospital-based, non-randomized study. The study was conducted for a period of 18-month from August 2011 to January 2013. Fibrinogen detection was done as per standard guidelines.

Results: The total number of patients included in our study were 101 in which females were 65 (64.35%) and males were 36 (35.64%). The mean age for males was 57.5 years and females was 54.6 years. Total numbers of hypertensive patients were 64 and non-hypertensive were 37. There was no significant difference in mean serum FLs in patients with and without hypertension (4.465 g/l vs. 4.666 g/l. $P = 0.552$).

Conclusion: There is no association of FLs and hypertension in our population. Further prospective studies with larger sample size are needed to fully elucidate the relationship between FLs and Hypertension in our population.

Key words: Fibrinogen, Hypertension, Risk Factor

INTRODUCTION

Fibrinogen is a recognized risk factor for macrovascular disease and increased levels may exert effects through a variety of mechanisms including increased blood viscosity, increased size of fibrin clots, increased tissue deposition and stimulation of atherosclerosis, and vascular thickening thus involved in the pathogenesis of thrombotic cardiovascular events.¹⁻⁵ Various studies have tried to studied association of fibrinogen with hypertension in which few are showing positive association⁶⁻¹⁵ and few are showing negative association between two.^{2-5,16,17} As in Leigh study, which suggest that fibrinogen levels (FLs) may affect

prognosis in hypertension in which hypertensive patients with plasma fibrinogen above 3.5 g/L had a 12-fold greater coronary risk than those with fibrinogen below 2.9 g/L.¹⁸ These and other clinical and laboratory observations have led to the hypothesis that hypertension per se may confer a hypercoagulable state^{19,20} that might be related to the development of target-organ damage and long-term prognosis.²¹ On other hand, in the biracial atherosclerosis risk in communities study, the prospective association between plasma FL and incident hypertension is still not clear.²² Thus, to investigate further any possible relationship between serum FLs and hypertension, we evaluated serum FL in both hypertensive and non-hypertensive patients in Kashmiri ethnic population.

MATERIALS AND METHODS

This was a prospective, hospital-based, non-randomized study of 101 cases which was conducted at the Department of Ophthalmology, Government Medical College Srinagar,

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Kashmir, India. The study was conducted for a period of 18-month from August 2011 to January 2013. The study was approved by the Institutional Ethics Committee.

Inclusion Criteria

- Known cases of hypertension.

Exclusion Criteria

- Patients taking anticoagulants
- Inherited diseases which cause either hypercoagulability or bleeding tendencies
- Patients with severe liver, cardiac, or renal failure
- Systemic illnesses altering the blood coagulation profile.

Based on the status of hypertension, two groups for comparison were made cases and control:

1. Group 1: Cases with hypertension
2. Group 2: Control without hypertension.

Estimation of Plasma Fibrinogen

Test principle

In presence of excess of thrombin, the clotting time of diluted plasma has a direct bearing on the level of plasma fibrinogen.^{23,24}

Procedure

Specimen collection and treatment was done as per standard guidelines described by us previously.²⁵

Statistical Analysis

Statistical software GraphPad InStat-3 was used for statistical analysis. The statistical method involved included independent student *t*-test for normally distributed continuous variables, the Pearson Chi-square test for categorical variables, and ANOVA was used for comparison of more than two continuous variables. The data were expressed as mean (\pm standard deviation) and percentage values, and $P < 0.05$ was considered statistically significant.

RESULTS

The total number of patients included in our study where 101 in which females were 65 (64.35%) and males were 36 (35.64%). The mean age for males was 57.5 years and females was 54.6 years, 66.33% of cases in our study were between 41 and 60 years of age (Table 1 and Figure 1). Total numbers of hypertensive patients included in the study group were 64 and total number of patients without hypertension which were included in the control group were 37. In our study, mean serum FLs in patients with hypertension were 4.465 g/l and mean serum FLs in patients without hypertension were 4.666 g/l. There was not a statistically significant difference between the mean

serum FLs of patients with and without hypertension $P = 0.552$ (Table 2 and Figure 2). In our study, difference in the mean serum FL of male (4.079) and female (4.794) seems to be significant as $P = 0.033$, but the statistical result was underpowered, thus statistical significance between two groups is questionable and can be due to the fact that female patients outnumbered male patients in our study population. The maximum number of patients attending the OPD for an ophthalmic checkup was urban dwellers 68.31% in comparison to rural 31.68%. The relationship of serum FL was found to be statistically insignificant with the geographical distribution of population $P = 0.754$ (Table 3 and Figure 3).

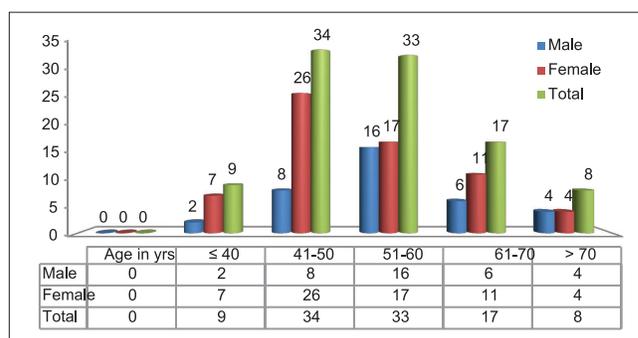


Figure 1: Age and gender distribution

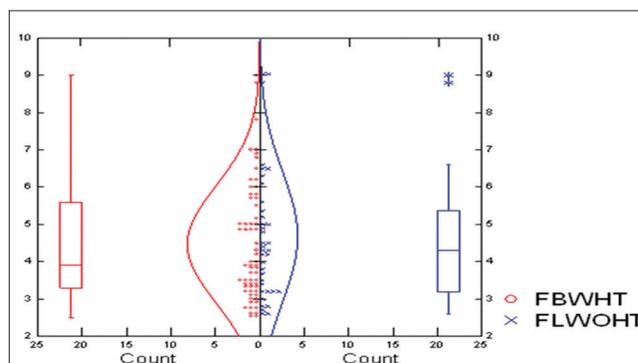


Figure 2: Two-sample t-test

Table 1: Age and gender distribution of the studied subjects

Age in year	n (%)			P value
	Male	Female	Total	
≤40	2 (5.55)	7 (10.76)	9 (8.91)	0.204 (NS)
41-50	8 (22.22)	26 (40.00)	34 (33.66)	
51-60	16 (44.44)	17 (26.15)	33 (32.67)	
61-70	6 (16.66)	11 (16.92)	17 (16.83)	
>70	4 (11.11)	4 (6.15)	8 (7.92)	
Total	36 (35.64)	65 (64.35)	101 (100)	
Mean±SD	57.5±10.8	54.6±11.0	55.6±11.0	
(max, min)	(32, 80)	(35, 80)	(32, 80)	

SD: Standard deviation, NS: Not significant

Table 2: Serum FLs of patients with and without hypertension

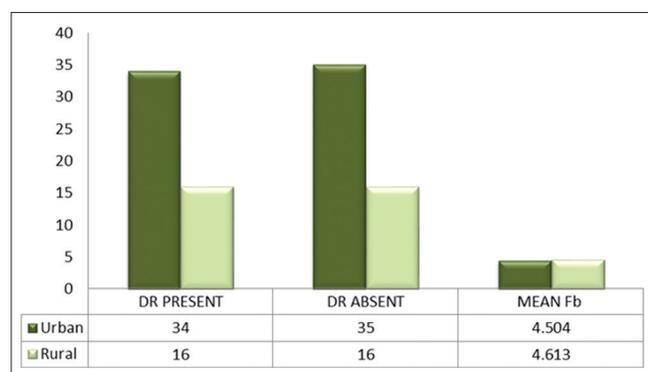
Variable	n	Mean	SD	Mean difference	95% CI		Cal.t	Df	P value
					Lower limit	Upper limit			
Fb with HT	64	4.465	1.563	-0.201	-0.868	0.466	-0.598	99	0.552
Fb without HT	37	4.666	1.736						

t (Cal)=-0.598 with 99° of freedom (P=0.552), SD: Standard deviation, CI: Confidence interval

Table 3: Relationship of FLs with urban and rural population

Dwelling/ geographical status	n (%)			FL (mean±SD)
	DR present	DR absent	Total	
Urban	34 (49.27)	35 (50.72)	69 (68.31)	(4.504±1.431)
Rural	16 (50.00)	16 (50.00)	32 (31.68)	(4.613±1.999)

SD: Standard deviation, DR: Direct Relationship, FL: Fibrinogen level

**Figure 3: Relationship of fibrinogen with geographical distribution**

DISCUSSION

Many studies have compared FLs in normotensive and hypertensive patients.²⁶⁻²⁸ Our study demonstrated that there was no significant difference in FLs in hypertensive as compared to the normotensive population. We also observed that this was true irrespective of gender. Conflicting results in various studies may be explained by the difference in blood pressure values of patients; less sample size included in these studies and interference of antihypertensive treatment on the hemostatic system. Papadakis *et al.*, reported that patients who were on lipid-hostile antihypertensive drugs had significantly higher levels of fibrinogen as compared with those on lipid-neutral antihypertensives or those who were not receiving antihypertensive treatment.

Hypertensive patients have been shown to have increased the degree of platelet and coagulation system activation while as the fibrinolytic system has decreased activity²⁹ which may be explained by the prothrombotic state related to hypertension. However, our study did not show any significant difference between elevated FLs

and blood pressure. Anoop Shankar *et al.*, observed the lack of association between FL and incident hypertension among women in their study although they showed significant association of FLs and development of hypertension in men. These gender-related differences between fibrinogen and other cardiovascular outcomes have been noted in coronary heart disease,⁸ carotid intima-media thickness,³⁰⁻³² and peripheral vascular disease. However, our study failed to show any gender difference. Limitations of our study included a smaller number of sample size. Furthermore, we did not study the relationship between FLs and target end-organ damage in hypertensive patients.

CONCLUSION

There is no association of FLs and hypertension in our population. Further prospective studies with larger sample size are needed to fully elucidate the relationship between FLs and Hypertension in our population.

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Spectrum of Malformation of Cortical Development with Clinico-radiological Correlation

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Abstract

Introduction: Malformations of cortical development (MCD) are one of the recognized causes of childhood epilepsy presenting as epilepsy, development delay, and other neurological manifestations.

Purpose: Purpose of the study was for emphasis on the clinical and radiological spectrum of MCD.

Materials and Methods: We evaluated 14 patients of MCD who were diagnosed on structural neuroimaging. Retrospective and prospective reviewing of magnetic resonance imaging (MRI) and computed tomography (CT) of the brain were done in our department of radiology from January 2013 to July 2015, including outside scan films. Assessment of clinical details was done in coordination with the department of pediatrics and medicine.

Result: Out of 14 patients 8 were male and 6 were female with age ranging from 2.5 months to 22 years with mean age of 7.3 years. Epilepsy and developmental delay were main clinical presentation in most of the cases. On structural neuroimaging, multiple abnormalities were noted in 50% cases. Heterotopias and lissencephaly-pachygyria complex were most common among MCDs, seen overall in 42.8% and 21.4% cases respectively (including cases with multiple abnormalities).

Conclusion: MRI of the brain has a definitive role in the diagnosis of most cases of MCD aided by CT for initial evolution. Most cases of MCD present with a different spectrum of epilepsy or developmental delay.

Key words: Computed tomography, Epilepsy, Malformations of cortical development, Magnetic resonance imaging

INTRODUCTION

Malformation of cortical development (MCD) is structural abnormality of the cortex of brain parenchyma caused by derangement of the normal developmental process due to various underlying factors. It can be genetic mutations, environmental insults¹ seen during antenatal, perinatal, or postnatal period, during corticogenesis or after corticogenesis.²

MCD is classified based on earliest disruption of development,^{2,3} which includes neural stem cell

proliferation, migration, and finally neuronal differentiation. Malformation resulting from abnormalities of cell proliferation is microcephaly, megalencephaly, and cortical dysplasia. Disorders of neuronal migration may cause heterotopia and classical lissencephaly. Disorders of neuronal arrest can result in cobblestone lissencephaly. An abnormal cortical organization may result in schizencephaly and polymicrogyria. Although cortical development has been separated into these stages, there is significant overlap between the stages and many abnormalities may cause dysfunction at more than one level.³ Malformations of the proliferative stage seen from ventricles to the piamater while those resulting from abnormal cellular migration are located in the white matter and/or the cortex, and those caused by abnormal organization are limited to the cortex.⁴⁻⁶

MCD clinically presents as one of the important cause of epilepsy, refractory to treatment and many of previously considered idiopathic or cryptogenic epilepsy has

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developmental malformations of the cortex on imaging.⁷ Structural imaging findings of brain, especially magnetic resonance imaging (MRI) findings are most important noninvasive technique for its diagnosis, which has greatly improved with the progress in contemporary imaging techniques.⁸

Many studies have found underlying MCD in 23-26% cases of refractory epilepsies in children and young adults.^{9,10} So, MCD should be ruled out in every case of epilepsy or developmental delay by neuroimaging.

The objective of this study was an analysis of clinical details along with an emphasis on neuroimaging findings critical for its diagnosis.

Microcephaly is small brain with head circumference below two standard deviations of population mean with correction for age and sex.³

Hemimegalencephaly is characterized by overgrowth of part or all of the cerebral hemisphere. It may be isolated anomaly or seen in association with other syndromes such as epidermal nevus syndrome, Proteus syndrome, unilateral hypomelanosis of Ito, neurofibromatosis Type I, Klippel-Trenaunay syndrome, and tuberous sclerosis. MRI shows variable blurring of gray-white matter differentiation with variable abnormal prolongation of T1 and T2 of the white matter due to underlying heterotopia and astrocytosis. MRI shows associated enlargement and elongation of ipsilateral lateral ventricle with a characteristic shape of the frontal horns that appears straight and pointed anteriorly and superiorly.¹¹⁻¹⁵

Focal cortical dysplasia (FCD) is characterized by the abnormal focal presence of neurons and glial cells within the cerebral cortex. MRI typically shows blurring of gray-white matter differentiation with localized area of cortical thickening and abnormal signal such as subtle T2 hyperintensity within adjacent white matter.¹⁵⁻¹⁷

Heterotopia is the presence of normal neurons in abnormal location. On MRI, they appear isointense to the normal gray matter on all sequences with no enhancement on the post-contrast study. Periventricular heterotopia (PVH) or subependymal heterotopia is gray matter nodules seen along the ventricular wall of the lateral ventricles.^{4,5,18-20}

Subcortical band heterotopia is seen as band of gray matter neurons and is located between the ventricles and the cerebral cortex with contiguity to either cortex or ventricular region.¹⁸⁻²⁰

Classic or Type I lissencephaly patients have either completely smooth brain surface (seen in complete

form) with complete loss of the normal gyri and sulci, or smooth surface with few small gyral formation in the region of inferior frontal and temporal lobes (incomplete form). These are caused by arrest of the migration process.^{21,22}

Type II lissencephaly also known as cobblestone lissencephaly is characterized by nodular surface of the cerebral cortex, ocular anomalies, and congenital muscular disorders caused by over migration of the neuronal cells beyond the external glial limitations into the subarachnoid space.²¹⁻²³

Polymicrogyria refers to an excessive number of small fine gyri separated by shallow sulci not detectable on imaging. On imaging, overall cortical thickness may be normal

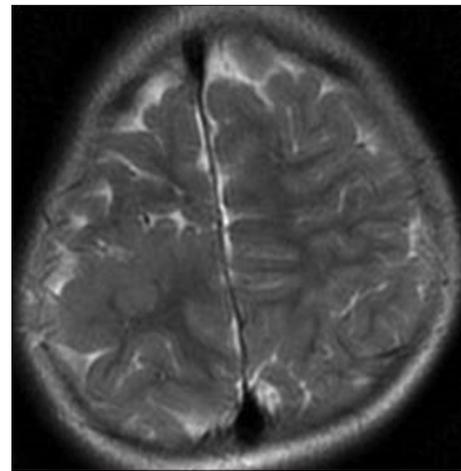


Figure 1: Axial T2-weighted magnetic resonance image of 17-year-old male patient showing localized cortical thickening in right superior frontoparietal region suggesting focal cortical dysplasia

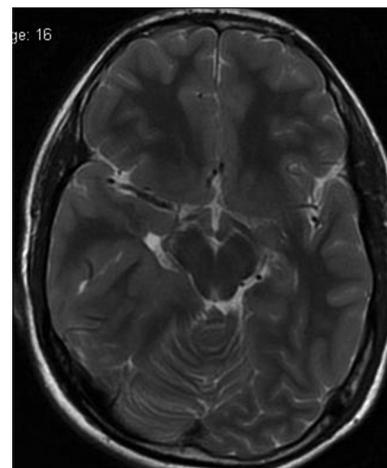


Figure 2: Axial T2-weighted magnetic resonance image of 12-year-old female patient shows subtle cortical thickening in right temporal lobe region with relative enlargement of left cerebral hemisphere suggesting focal cortical dysplasia with hemimegalencephaly

or increased seen in age <12 months and >18 months, respectively. Imaging mostly shows lumpy appearance with thickened cortex (5-7 mm) with an abnormal T2 prolongation of the underlying white matter noted in approximately 25% of cases.^{5,24}

Schizencephaly refers to cerebrospinal fluid (CSF) filled cleft lined by gray matter seen extending from subarachnoid CSF space to the ventricular system. Schizencephaly results from injury involving the entire thickness of the developing hemisphere during cortical organization. Schizencephaly is divided into Type I

(Closed-lip schizencephaly) and Type II (Open-lip schizencephaly) based on visualization of CSF cleft with closed lip schizencephaly showing approximation of gray matter-lined lips.^{25,26}

MATERIALS AND METHODS

Case series was done in those 14 patients who presented to an outer institution with variable neurological abnormalities and were diagnosed to have MCD on structural neuroimaging. Retrospective and prospective analysis of MRI and CT of brain findings were done in our department of radiology from Jan 2013 to July 2015 with the categorization of anomalies. Detailed correlation with clinical history and physical examination (mainly neurological) was done in coordination with the department of pediatrics and medicine.

RESULTS

During the retrospective and prospective study, we came across about 14 cases of MCD.

The mean age of study was 7.3 years with the youngest age of study being 2.5 months and oldest age 22 years (Table 1). There was no significant statistical difference between males and females with 8 (57%) being males and 6 (43%) being female. There was no history of drug intake (other than iron or folic acid) or maternal infection or radiation exposure during the antenatal period. In all cases, delivery was uneventful with delayed cry in one of the case. History of consanguineous marriage was noted in four cases.

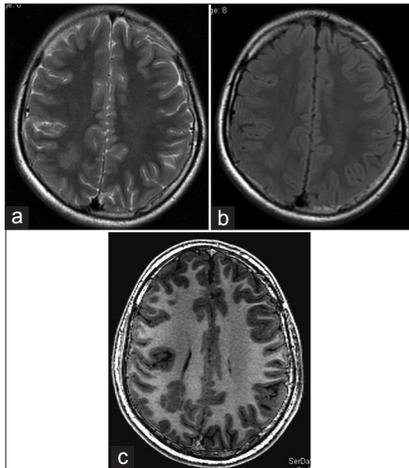


Figure 3: Axial T2 (a), Axial T1 (b) and Axial fluid attenuated inversion recovery (3c) weighted magnetic resonance image of brain of 11-year-old male child shows small nodular lesion in right parietal white matter region with isointense appearance on all sequences suggesting subcortical nodular heterotopia

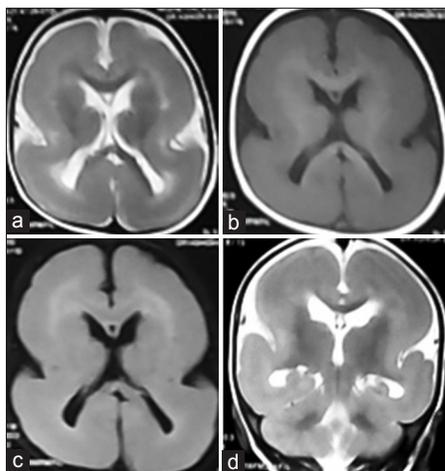


Figure 4: Axial T2 (a), Axial T1 (b) and Axial fluid attenuated inversion recovery (c) and coronal T2 (d) weighted magnetic resonance (MR) images of brain of 7-month-old female infant shows near complete absence of sulcal and gyral pattern with smooth outline with figure of '8' appearance with associated diffuse subcortical heterotopia with isointense appearance on all MR sequences s/o Type I lissencephaly

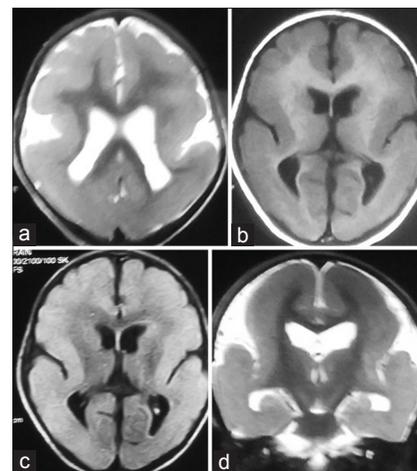


Figure 5: Axial T2 (a), Axial T1 (b) and Axial fluid attenuated inversion recovery (c) and coronal T2 (d) weighted magnetic resonance images of brain of 11-month old male infant shows significant paucity of sulcal spaces and gyral pattern with relatively smooth cortical with figure of '8' appearance with associated diffuse subcortical heterotopias s/o Type I lissencephaly-pachygyria complex (incomplete form)

Epilepsy was chief complaint in 42.8% of cases (Table 2). Overall seizure was noted in 71% of cases. On electroencephalogram, partial seizure (8/14, 57%) was most common seizure followed by generalized seizure (4/14, 28.5%). The complex partial seizure was a most common subtype. Mixed type of seizure was noted in 2 patients. Most patients had refractory type of epilepsy with frequent seizures noted even on medication. Variable delayed milestones were noted in 64% of cases.

Neurological examination was done in all cases. It was normal in four cases, variable motor disturbances in seven cases, microcephaly in two cases, left hemiparesis in one case, and hypotonia in three cases.

Only CT was available in two cases, only MRI scan was available in 5 cases, and both CT and MRI were available in rest of cases and with the establishment of diagnosis in all cases. In one case with only CT, polymicrogyria was suspected with underlying localized cortical thickening. Multiple abnormalities were noted in 7(50%) cases (Table 4) with polymicrogyria or heterotopia being a most common associated anomaly.

4 out of 14 patients (28.5%) had a bilateral or diffuse abnormality of the cortex. MCDs were localized to the right side in 6 patients (42.8%) and rest being localized to left cerebral hemisphere with multiple lobes of the same side was involved in 35.4% of total cases.

Heterotopias and lissencephaly-pachygyria complex were most common among MCDs, seen overall in 42.8% (isolated heterotopias in 28.5% cases) and 21.4% cases (Tables 3 and 4) respectively (including cases with multiple abnormalities).

Table 1: Mean age of presentation in study

Type of MCD	Mean age of presentation
Isolated microcephaly	2.5 month
focal cortical dysplasia	17 year
hemimegalencephaly	2.7 year
heterotopias	10.2 year
Lissencephaly-pachygyria complex	7.5 month
Isolated polymicrogyria	9 year
Schizencephaly	11.5 year

MCD: Malformation of cortical development

Table 2: Chief clinical complaint in studied patients

Chief clinical complaint	Number (%)
Seizure	6 (42.8)
Microcephaly	1 (7.15)
Global developmental delay	4 (28.5)
Hemiparesis	1 (7.15)
Delayed motor development	2 (14.4)

Out of 14 cases two patients (isolated microcephaly in one case) had microcephaly with <3 standard deviation below normal for that age, presented after birth with poor feeding. MRI in one patient showed normal cortical thickness with a minimal paucity of sulcal spaces with normal ventricular size. Other patient had associated agyria suggestive of lissencephaly.

One patient had FCD presented at 17 years of age with recurrent refractory seizures with normal milestones. MRI showed localized thickening of cortex in the right superior fronto parietal region with subtle underlying white matter fluid attenuated inversion recovery hyperintensity suggestive of underlying subtle gliosis (Figure 1).

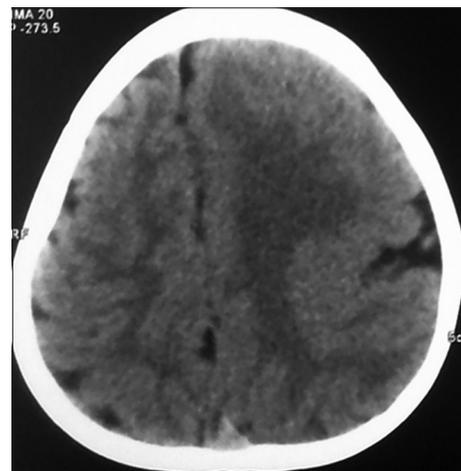


Figure 6: Axial non-contrast computed tomography of brain of 9-year-old child shows thickened cortex in left frontoparietal region with lumpy appearance s/o most likely polymicrogyria complex

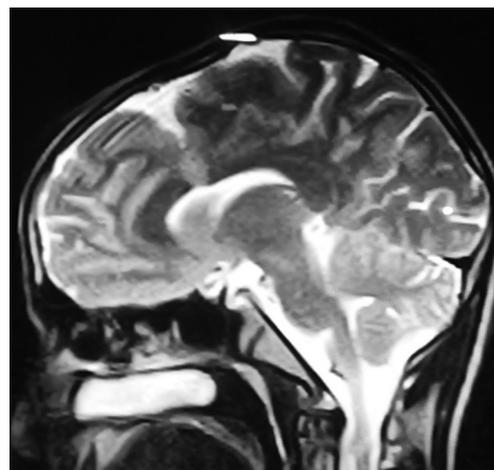


Figure 7: 16-year old male patient on sag T2-weighted magnetic resonance image showing cerebrospinal fluid (CSF) filled cleft in right parasagittal frontal region lined by gray matter seen extending from subarachnoid CSF space to the ventricular system with approximation of gray matter-lined lips towards ventricular end

Table 3: Incidence of various types of MCD with main clinical presentation

Type of MCD	Number (%)	Main clinical presentation
Isolated microcephaly	1 (7.15)	Small head with global developmental delay
Isolated focal cortical dysplasia	1 (7.15)	Convulsion
Hemimegalencephaly	2 (14.4)	Infantile spasm with delayed motor development with hemiparesis
Heterotopias	4 (28.5)	Convulsion
Lissencephaly-pachygyria complex	3 (21.4)	Global developmental delay
Isolated polymicrogyria	1 (7.15)	Convulsion
Closed lip schizencephaly	1 (7.15)	Convulsion
Open lip schizencephaly	1 (7.15)	Delayed milestones with recurrent seizures

MCD: Malformation of cortical development

Table 4: Number of patients with multiple abnormalities

Primary MCD	Associated MCD	Number
Hemimegalencephaly	Polymicrogyria	1
Hemimegalencephaly	Focal cortical dysplasia	1
Schizencephaly	Polymicrogyria	2
Lissencephaly-pachygyria complex	Diffuse band heterotopia	2
Lissencephaly-pachygyria complex	Microcephaly	1

MCD: Malformation of cortical development

Two patients had hemimegalencephaly. Both patients presented with recurrent infantile spasm and delayed milestones with first patient having partial hemiparesis toward the right side. Neck holding was also absent in the second patient.

MRI in one patient with isolated hemimegalencephaly showed mild to moderate enlargement of the left cerebral hemisphere with elongated enlarged left lateral ventricle with relatively thickened cortex with evidence of polymicrogyria complex. Other patient showed moderate enlargement of the left cerebral hemisphere with FCD (Figure 2).

Four patients had isolated gray matter heterotopias. One patient had subependymal nodular heterotopia. Two patients had nodular subcortical heterotopias (Figure 3). One had mixed nodular and band type heterotopias.

All patients with heterotopias had history of recurrent partial seizure refractory to treatment. Associated delayed milestones were noted in two patients with mental retardation seen in one patient.

In the case of subependymal nodular heterotopia, MRI showed oval nodules in the subependymal region of lateral

part of both lateral ventricles with isointense appearance on all MR sequences.

Three patients had lissencephaly with all of them of classical type (Type I). In all patients with Type I, lissencephaly patients had significant hypotonia with poor feeding with significant motor developmental delay. MRI showed complete agyric pattern in one of the patients with rest of the patients showing poor formation sulcal spaces with band heterotopia noted in two patients (Figures 4 and 5).

One patient had an open lip and one had closed lip schizencephaly (Figure 7). Patient with open lip schizencephaly had significantly delayed motor milestones with closed lip type presenting with recurrent seizures. MRI showed gray matter lined cleft in both patients with isointense appearance on all MR sequences.

One patient had isolated polymicrogyria (Figure 6), presenting with recurrent partial seizures.

Six patients (42.8%) patients had multiple abnormalities of which polymicrogyria was most common associated abnormalities seen in two patients of schizencephaly and one patient of hemimegalencephaly. Diffuse band heterotopia was noted in two patients in association with lissencephaly-pachygyria complex.

DISCUSSION

MCD are important causes of developmental delay and epilepsy with variable neurological deficits. Progress in imaging techniques has made the possible initial establishment of diagnosis in most cases of MCD which is very helpful in increasing knowledge about the development of the cerebral cortex and the number and types of malformations reported.

Only CT was available in 2 cases, only MRI scan was available in 5 cases, and both CT and MRI were available in rest of cases and with the establishment of the diagnosis of MCD in all cases.

In present study, isolated heterotopias (28.5%) were most common followed by lissencephaly-pachygyria complex (21.4%) and polymicrogyria (21.4%). Multiple abnormalities were noted in 50 % of the cases. MRI had most important and definitive role in the diagnosis of MCDs.

In Sadek *et al.* study, a maximum number of the patients (42%) had lissencephaly followed by schizencephaly (28%), polymicrogyria (12%), FCDs (10%), and PVH (6%).²⁷ In

Güngör study, polymicrogyria were most common (53.5%) followed by lissencephaly (22.8%), schizencephaly (11.9%), and heterotopia (11.9%).²⁸ In Mathew *et al.* study, multiple abnormality was most common (31%), the most common being a combination of pachygyria and heterotopia.²⁹ In the study by Janszky *et al.*,³⁰ FCD was the most common MCD among cause of intractable focal epilepsy, followed by heterotopia and pachygyria. In the series of Brodtkorb *et al.*,³¹ schizencephaly were the most common abnormality. However, significant differences between different case series are probably due to selection bias rather than true frequencies.

In the present study, recurrent convulsions (42.8%) were the chief complaint followed by global development delay (28.5%) and motor disturbances. The overall seizure was noted in 71% of cases. Multiple symptoms were noted in most of the cases. It was comparable with other studies showing seizure as main clinical complaint. In Sadek *et al.* study, refractory seizures (42%) and global developmental delay were main chief complaint. In this study, overall seizures were noted in 82% of cases. Leventer *et al.*³² found seizures in 75% of patients with MCDs, and Güngör *et al.* found seizures in 71.3%.²⁷

CONCLUSION

MCD are a heterogeneous group of disorders during variable developmental stages of the brain. Recurrent refractory seizures with variable global developmental delay are main complaint with imaging having an important and definitive role (mainly MRI) in its diagnosis. So, it should be mandatory to do initial imaging in all cases of refractory epilepsy and global developmental delay whenever it is feasible. Imaging has also got a role in surgical cases where surgical planning has been done.

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Epidemiology of Secondary Peritonitis: Analysis of 545 Cases

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Abstract

Introduction: Secondary peritonitis is one of the most common emergencies encountered in day to day surgical practice. Very few studies have been done on the epidemiology of this surgical entity in the Indian subcontinent.

Aims and Objectives: This study was done to collect and analyze data from patients with secondary peritonitis at one of the major hospitals in eastern India to throw some light into the related epidemiologic and etiopathologic factors.

Materials and Methods: All the patients who were diagnosed as having secondary peritonitis and who underwent laparotomy for the same were included in our study. Data on different epidemiological parameters, etiological factors, and outcome variables were collected and analyzed.

Results: In a cohort of 545 patients, 48.44% had gastroduodenal (GD) perforation. 84.58% of our patients were males. 36.51% of our patients had wound infection. We had a mortality of 8.4%.

Conclusion: Comparing our results with available world literature, we could figure out few striking differences. Acid peptic GD perforation is the most common cause of secondary peritonitis in this series which is in contrary to appendicular perforation, which tops the list in most of the available international data. The majority of our patients were from younger age group with lesser comorbidities. Wound infection was the most common complication encountered. The overall mortality of our series was 8.4%, which is on the lower side of the range of available data.

Key words: Complication, Epidemiology, Etiopathology, Peritonitis

INTRODUCTION

Secondary peritonitis (henceforth called peritonitis) is one of the most common causes of acute abdomen requiring emergency laparotomy. Despite tremendous advancements in medical care, it still remains a potentially fatal affliction. With a wide range of etiologies, peritonitis declares itself in a variety of ways. Diverse epidemiology and etiopathology are noted among populations of different socioeconomic, geographic, and climatic conditions. Although the

demographic profile of the population in our part of the country is different from the rest of India in several aspects, e.g., dietary habits, the prevalence of infectious disease, etc., any robust study on peritonitis from this part of the country is lacking until date.

Aims and Objectives

World literature is rich with volumes of publications on peritonitis. Few important studies were done in Indian subcontinent also. Most of them have showed important epidemiological and etiopathological differences from their western counterpart. The population in eastern part of India is different in several ways (diet, occupation, and climate) from those in the rest of the country. Certain pathologies and infections are more prevalent in this geographical region while others are less common. The aim of this study was to identify the epidemiological and etiopathological differences in the disease pattern in the

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background of diverse socioeconomic, geographic and climatic conditions.

MATERIALS AND METHODS

This prospective, longitudinal, observational study was done between July 2008 and June 2011 with a minimum follow-up period of 1-year, at a high volume tertiary care teaching hospital located in a densely populated metropolitan city in eastern India. The subjects of this study were all the patients with peritonitis who fulfilled the inclusion/exclusion criteria and who underwent exploratory laparotomy for the same. The patients were admitted under six different general surgical teams of our department who have rigidly followed the hospital protocol in treating these cases. Unit wise data were collected and compiled every fortnightly. Final compilation and statistical analysis were done at the end of study period.

Inclusion Criteria

All patients of peritonitis (≥ 12 years) who underwent laparotomy for the same.

Exclusion Criteria

- i. Cases of primary peritonitis/spontaneous bacterial peritonitis/peritonitis associated with chronic ambulatory peritoneal dialysis;
- ii. Cases of localized peritonitis (e.g., localized collection of bile, managed by percutaneous aspiration and/or stenting, localized collection of pus from acute appendicitis, etc.);
- iii. Laparotomies performed for blunt trauma and subsequently found to have hemoperitoneum from solid organ injury;
- iv. Laparotomies performed on clinical suspicion of peritonitis and subsequently found to have acute pancreatitis;
- v. Pediatric patients and;
- vi. Those died before the operation.

The sample size for this study was 545. Clinical diagnosis of peritonitis was starting point of data collection. All the patients presenting with clinical features of generalized peritonitis underwent clinical, biochemical (sugar, urea, creatinine, amylase, lipase, and electrolyte), and hematological (total leukocyte count, differential leukocyte count, and hemoglobin) evaluation. Straight X-ray lower chest and abdomen (in erect posture or lateral decubitus) was done in all the cases. Ultrasonography and/or contrast-enhanced computed tomography scan were done wherever considered necessary. All the patients had initial resuscitation with intravenous (IV) fluid, analgesia (IV tramadol - 2 mg/kg), and antibiotic (third generation

cephalosporin and metronidazole). Further to initial evaluation and optimization, the patients underwent laparotomy as a definitive measure. Exploratory laparotomy was done following the standard principles. Drains were used in all the cases. Depending on the clinical indications stoma was constructed in some patients. All patients received standard post-operative care in the form of IV fluids, antibiotics (changed if indicated by culture report of peritoneal fluid), analgesics, nasogastric tube aspiration, etc., as per the clinical situation. ITU support was provided wherever indicated. Post-operative complications were noted along with their time of onset since the operation. Patients were discharged when clinically indicated. The collected data were compiled, and statistical analysis was done using Cochran–Mantel–Haenszel Chi-square test.

RESULTS

Spanned over a period of 3-year, we had 545 cases in our series. A clear male predominance was found in our cohort ($n = 461$; 84.58%). Gastroduodenal (GD) perforation due to acid peptic disorder (henceforth called GD perforation) remained the most common cause of peritonitis in our series ($n = 264$; 48.44%). Among 264 cases of GD perforation, 251 (95.07%) were males and only 13 were females (Table 1); clearly showing significant male preponderance ($P < 0.0000001$). Similarly, peritonitis from appendicular perforation, gangrenous intestinal obstruction, abdominal trauma, and typhoid ulcer perforation was also found to be much more common in males. The majority of the trauma patients were also males (89.18%) (Table 1). The age range (Table 1) of our patients was 16-87 years with mean age being 31.9 years. Analysis of month wise incidence of cases failed to reveal any notable seasonal variation.

Apart from peritonitis due to gangrenous changes or perforation of hollow viscus, other causes of peritonitis in our series (grouped as “miscellaneous”) were ruptured liver abscess ($n = 5$), septic abortion with uterine perforation ($n = 8$), anastomotic dehiscence ($n = 8$), and post-cholecystectomy bile leak with generalized peritonitis ($n = 4$). This group was unique in the present series for showing a clear female predominance against the overall trend. The inclusion of peritonitis following septic abortion was the key factor behind this female predominance.

The majority of the traumatic perforations resulted from blunt trauma ($n = 56$, 75.67%) with the remainder from penetrating type (stab, firearm, splinter, and rectal impalement). The range of injuries following penetrating trauma included jejunoileal, gastric, pancreaticoduodenal, colonic, and rectal perforations. 12.16% of the patients with traumatic perforation also had concomitant solid

organ injuries ($n = 09$) and 21.62% had bowel perforations at multiple sites ($n = 16$). We had 2 pancreaticoduodenal injuries among the 56 cases of blunt trauma (3.57%) and 3 such cases among the penetrating trauma group ($n = 18$, 16.66%). In our series, we had only 7 cases of gastric perforation among all the trauma cases (9.45%), all of which were following penetrating trauma.

Typhoid ulcer perforation and peritonitis secondary to gangrenous and/or perforated intestinal obstruction were the fourth and fifth important causes in our series. Among the 34 cases of peritonitis following intestinal obstruction, we had 14 cases of the gangrenous small gut (41.17%) and 13 cases of gangrenous sigmoid volvulus (38.23%). Gangrenous small gut was predominantly due to strangulating obstructions by bands. Sigmoid volvulus is a very common cause of intestinal obstruction in this geographical region.

It was found that 34.86% ($n = 190$) of our patients presented to the hospital within 24 h and 48.44% ($n = 264$) of them presented in between 24 and 72 h of onset of abdominal symptoms (Table 2). It was also observed that there was a trend among trauma patients to present early, whereas intestinal obstruction and typhoid ulcer perforation patients more often presented late.

In patients, wound infection ($n = 199$; 36.51%) and infective chest complication ($n = 183$; 33.57%) were the two major causes of morbidity (Table 3). Wound infection was the most significant complication in cases with appendicular perforations ($P < 0.0001$) and chest complication was the most common complication for cases with GD perforation (Table 3), which was significantly high ($P < 0.01349$).

There was no significant association between the causes of peritonitis and other post-operative morbidities. Unit wise data analysis also showed identical figures without significant difference in wound infection and chest complication rates, range being $36.5 \pm 2.2\%$ for wound infection and $33.5 \pm 1.9\%$ for chest complications.

The majority of the survivors of GD, appendicular, and traumatic perforation could be discharged before 2 weeks, whereas those with strangulated intestinal obstruction and typhoid ulcer perforation stayed longer in the hospital (Table 2). Re-exploration during the same admission was required in 34 (6.23%) patients (21 for burst abdomen with or without residual abscesses and 13 for residual abscesses only). A total of 14 patients (2.56%) required subsequent re-exploration for complications during the follow-up period. At the end of 3 years, 59 patients were lost to follow-up.

The overall mortality in our series was 8.4% ($n = 46$). The maximum number of deaths ($n = 14$, 29.78%) occurred in patients with typhoid ulcer perforations, closely followed by 9 deaths (26.47%) among the 34 patients of peritonitis secondary to intestinal obstruction group. Delayed presentations, infective complications, and multi organ failure were the main contributors to higher mortality in these patients.

DISCUSSION

Generalized peritonitis is one of the most common surgical emergencies encountered across the world. It remains one of the major causes of mortality and morbidity and warrants

Table 1: Distribution of age and sex

Age (years)	Gastroduodenal	Appendicular	Trauma	Ileal (typhoid)	Peritonitis in intestinal obstruction	Miscellaneous	Total
<30	54	48	37	25	9	12	182
30-50	155	36	30	19	11	11	266
>50	55	17	07	03	14	02	97
Total (M/F)	264 (251/13)	101 (76/25)	74 (66/08)	47 (31/16)	34 (28/06)	25 (09/16)	545 (461/84)

Table 2: Pattern of presentation and hospital stay

Pathology (n/%)	After 72 h	24-72 h	Within 24 h	≤7 days	8-14 days	>14 days
GD perforation (264/48.44)	23	131	110	136	106	22
Appendicular perforation (101/18.53)	19	69	13	24	42	35
Traumatic perforation (74/13.57)	03	14	57	23	44	07
Ileal perforation (typhoid) (47/8.62)	20	24	03	09	16	22
Peritonitis with intestinal obstruction (34/6.23)	21	11	02	03	20	11
Miscellaneous (25/4.58)	05	15	05	05	13	07
Total (545/100)	91 (16.69%)	264 (48.44%)	190 (34.86%)	200 (36.69%)	241 (44.22%)	104 (19.08%)
Total deaths	46 (8.44%)					

GD: Gastroduodenal

Table 3: Post-operative complications

Etiology (n/%)	n (%)						
	Wound infection	Chest problems	Wound dehiscence	Residual abscess	MOF	EC fistula	Death
GD perforations (264/48.4)	85 (32.19)	113 (42.80)	07 (2.65)	06 (2.27)	09 (3.40)	01 (0.37)	11 (4.16)
Appendicular perforations (101/18.5)	59 (58.41)	08 (7.92)	05 (4.95)	04 (3.96)	02 (1.98)	01 (0.99)	02 (1.98)
Traumatic perforations (74/13.6)	22 (29.72)	31 (41.89)	02 (02.70)	02 (02.70)	07 (09.45)	00	08 (10.81)
Ileal perforations (47/8.6)	14 (29.78)	08 (17.02)	04 (08.51)	03 (06.38)	14 (29.78)	00	14 (29.78)
Strangulated volvulus - 13	14 (41.17)	16 (47.05)	03 (08.82)	00	08 (23.52)	01 (02.94)	09 (26.47)
Strangulated small gut - 14							
Perforated intestinal obstruction - 7							
Peritonitis following intestinal obstruction (34/6.2%)							
Ruptured liver abscess - 5	05 (20)	07 (28)	02 (08)	02 (08)	02 (08)	00	02 (08)
Septic abortion - 8							
Anastomotic failure - 8							
Post-operative bile leak - 4							
Miscellaneous (25/4.6)							
Total (545/100)	199 (36.51)	183 (33.57)	23 (04.22)	17 (03.11)	42 (07.70)	03 (0.5)	46 (8.4)

EC: Enterocutaneous, MOF: Multiple organ failure

early surgical intervention. Literature search showed a few studies from different parts of our subcontinent but robust data on peritonitis from this part of India is still not available. In our patient cohort, GD perforation was the most common cause of peritonitis (48.44%) and this result corroborated with majority of the available studies from India.¹⁻⁷ However, some series showed different results with small bowel perforation as their most common cause.⁸⁻¹¹ This difference may probably be due to differential disease prevalence rate and/or availability of basic health facilities such as immunization, safe drinking water, safe disposal of excreta, and health awareness among the study population of those series. Studies from Nepal,^{12,13} China,¹⁴ Japan,¹⁵ and Pakistan¹⁶ also revealed GD perforation as the most common cause of peritonitis. However, two other series, one from Pakistan and one from Sri Lanka found small bowel perforation more commonly than GD perforations.¹ According to western experience, acute appendicitis is the most common cause of intra-abdominal infection, and colonic perforation is the second most common cause of peritonitis.¹⁷ Low incidence of infectious diseases, such as tuberculosis and typhoid, and a higher incidence of diverticulitis and inflammatory bowel disease is responsible for this difference.⁸ Again, a study among the African population in northeastern Nigeria reported that 64.6% of the perforative peritonitis cases are small intestinal in origin, most of which were following typhoid ulcers.¹⁸ Among the perforated GD ulcers, most were located in the anterior wall of first part of the duodenum. Duodenal ulcer perforation is by far more common than gastric perforation (peptic or malignancy) all over the world, the ratio ranging from 4:1 to 20:1.⁸ In our series, this ratio is 20:1. As already mentioned, some of the Indian studies found a high incidence of typhoid ulcer perforations. In contrast, only 47 (8.62%) of our patients had peritonitis

from typhoid ulcer perforation. One Chinese series showed 6% of their peritonitis cases were secondary to typhoid ulcer perforation.¹⁴ A very low incidence of typhoid ulcer perforation has also been reported from Thailand.¹⁹

Appendicular perforation is the second most common cause in our series ($n = 101$; 18.53%), and it corroborates with the results from other available studies where the incidences ranged between 5% and 41%. In our series, trauma was the third most common etiology of peritonitis and was responsible for 13.57% of the cases. A more recent study from Northern Indian state of Jammu and Kashmir showed 7% cases of peritonitis resulted from trauma and two other studies from Chandigarh showed the incidences of 21% and 9%, respectively.^{2,3,20} A study by Noon *et al.* from Texas, a state known for high incidence of violence, showed penetrating trauma as the leading cause of peritonitis (210 out of 430; 48.8%), followed by appendicular ($n = 92$; 21.3%) and GD perforation ($n = 68$; 15.8%).²¹ This rising pattern of traumatic injury is related to urbanization and industrialization in developing and developed countries.

In this study, most of the patients were in the age group of 31-50 years (mean age being 31.9 years) which is similar to the observations of most of the authors in this subcontinent. The mean age is one decade higher in western countries which may be accounted for by the fact that colonic perforations secondary to diverticulitis are predominantly seen in the elderly population.^{3,8,16,22} Most of our patients of GD perforation were middle-aged (58.71% in the age group of 31-50 years), and the majority of the patients of appendicular and traumatic perforations were below 30 years in our series which was comparable with the experiences of other studies.^{1,8,23,24} We observed that ileal perforation was most common in second and third decades, and this is comparable to other series.²⁵

Table 4: Pattern of comorbidities

Comorbid conditions	GD perforation	Appendicular perforation	Traumatic perforation	Ileal perforations	Perforations following intestinal obstruction	Miscellaneous	Total (%)
DM	14	04	02	00	03	1	24 (04.40)
HTN	31	10	01	00	13	1	56 (10.27)
COPD	37	05	01	00	06	0	49 (08.99)

GD: Gastroduodenal, DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease

All the leading causes of perforative peritonitis in our series were more common in males, but male predominance was even more prominent in GD perforation. This observation is consistent with results of available literature, although the ratio varies from series to series.^{1-3,8,18} The majority of our patients presented between 24 and 72 h (48.44%) of onset of abdominal symptoms. Most of the trauma patients reached us within 24 h (77.02%). However, intestinal obstruction and typhoid ulcer perforation patients showed a tendency to present late, more often after 72 h (21 of 34 [61.76%] and 20 of 47 [42.55%], respectively). According to the observations by Jhobta *et al.* in Chandigarh and Gupta *et al.* in Jammu and Kashmir, 47% and 60% of their patients presented within 24 h, respectively, which is a better scenario than ours (overall, 34.86% presented within 24 h).³ In Nigeria, where the incidence of typhoid ulcer perforation is very high, the mean time lapse between the onset of symptoms and presentation to hospital is 5.4 ± 3.7 days.¹⁸

The majority of our patients did not have any comorbidity (Table 4), a finding similar to other available literature.^{2,3} Hypertension is the most common comorbidity found in our series, closely followed by respiratory disease (chronic obstructive pulmonary disease) and diabetes mellitus. This finding is contradictory to observations of other series from India and abroad where respiratory disease topped the list of a comorbid condition.^{3,16} In our series, we did not have any patient with concomitant renal disease which, however, is mentioned as the second most common association in some of the world literature.^{3,16}

Wound infection (36.51%) was the most common post-operative complication among our patients, followed by chest complications (33.57%). Chest complication rate was significantly higher in cases of GD perforation, whereas post-operative wound infection was much higher following appendicular perforation. In different kinds of literature, wound infection rate varies from 16% to 42% and chest complication varies from 20% to 26%.^{2,3,8,16,18} A few studies identified higher incidences of abdominal wound dehiscence, accounting for up to 11% of their cases.^{2,3,8,16} Overall mortality in our series was 8.4%, and the highest mortality rate was found among the patients with ileal perforation due to typhoid ulcer (29.78%). In different series, overall mortality rate varied from 6% to

23%.^{1-5,8-11,13,15,16,18,25} Mortality rate among ileal perforation cases varies from 3% to 60% in different series.^{1,8,18,25}

We observed a comparatively lower mortality than many of our Western counterparts in spite of working with limited resources. We assume that this was due to the facts that: (i) Main bulk of our patients was with acid peptic GD perforations and (ii) majority of our patients were of younger age group without many comorbidities.

CONCLUSION

We conducted this study on patients with peritonitis to have epidemiological data from our part of the country since none is available so far. Our patient cohort does not represent the entire population from this region and is mainly from the weaker socioeconomic group, and the data is representative of the adult population. Comparing our results with those observed in other available world literature we found that many of our results are similar to other series. However, we noted a few striking differences as well.

Surgical site infection was the most common complication we encountered, closely followed by chest complications especially among patients of GD perforations. The overall mortality of our series was 8.4%, which is on the lower side of the range of other studies. We observed that majority of our patients were from the younger age group with less number of associated comorbidities in comparison to the western patients. GD perforation was the most common cause of secondary peritonitis in our series which is in contrary to appendicular perforation which tops the list of most of the available international data. It was noted that the patients in our series presented relatively late which contributed to some of the mortalities, although it was observed relatively less morbidity and mortality among the patients.

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Effect of Modifiable Risk Factors on the Prevalence of Type 2 Diabetes in the Tribal Adult Population of Boko Bongaon Block of Kamrup District of Assam

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Abstract

Introduction: The prevalence of chronic non-communicable diseases such as diabetes is showing an upward trend in most countries, and for several reasons this trend is likely to increase. The estimated number of adults with diabetes in 2007 was 246 million of these, 80% live in developing countries, the largest numbers on the Indian subcontinent and in China. Approximately 85-95% of all cases of diabetes are Type 2 diabetes, and the worldwide explosion of this disorder is a major health care burden.

Objective: To assess the effect of various modifiable risk factors on the prevalence of Type 2 diabetes among the tribal adult population of Boko.

Materials and Methods: A community-based cross-sectional study was conducted among 330 tribal adult respondents of Boko. Data were collected by house to house visits, and anthropometric measurements were done along with an estimation of fasting blood sugar using a glucometer.

Results: Increased physical activity was found to significantly decrease the risk of diabetes. Both increased body mass index and waist-hip ratio were found to significantly increase the risk of diabetes.

Conclusion: Physical activity and anthropometric parameters were found to significantly effect the prevalence of diabetes among the tribal adult population of Boko.

Key words: Body mass index, Fasting blood sugar, Waist-hip ratio

INTRODUCTION

Diabetes mellitus is a prototypical chronic health problem. The disease sequel and economic burden of diabetes are extensive owing to its degenerative nature despite the best available treatments. Effective delivery of preventive strategies to delay progression of the disease and its complications are challenging at best, with the persistent need for interventions integrating individual, clinical, and community level approaches. In developing countries like India, it threatens to undermine the family and national

economic progress it substantially impacts the working age population.¹

As we enter the new millennium, diabetes mellitus has reached epidemic proportions worldwide. The World Health Organization has commented there is an apparent epidemic of diabetes which is strongly related to lifestyle and economic change.² The estimates are changing rapidly and showing a rather disturbing state. The total number of people with diabetes were projected to rise from 171 million (2.8%) in 2000 to 366 million (4.4%) in 2030.³ Estimates in 2010 of the total number of people with diabetes was projected to rise from 285 million (6.4%) to 439 million (7.7%) worldwide in 2030.⁴ Nearly 90-95% of diabetics have Type 2 diabetes.⁵

The dramatic rise in the prevalence of Type 2 diabetes and related disorders like obesity hypertension and the metabolic syndrome could be related to the rapid changes

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in lifestyle that has occurred during the last 50 years. From 31.71 million diabetic subjects in the year 2000 to an expected 79.44 million diabetics by the year 2030,³ India is on its march toward having the most number of diabetics worldwide and is aptly called the “diabetic capital” of the world. In 2010, the average age-adjusted prevalence of diabetes in India was 7.8%, higher than that in most European countries.⁶

Urban, rural differences in the prevalence of diabetes have been consistently reported from India. While the ICMR study reported that the prevalence was 2.1% in urban and 1.5% in rural areas,⁷ a later study showed that the prevalence was three times higher among the urban (8.2%) compared to the rural population (2.4%).⁸

As seen a number of studies on diabetes prevalence in rural areas have been carried out in different parts of India but such studies are lacking in the rural areas of Kamrup district of Assam. So, a study was carried out to assess the prevalence of diabetes and the effect of various correlates on it among the adult population of Boko Bongaon Block of Rural Kamrup District of Assam.

Aims and Objectives

To assess the effect of various modifiable risk factors on the prevalence of Type 2 diabetes among the tribal adult population of Boko.

MATERIALS AND METHODS

The present study had been undertaken in the Boko Bongaon Community Development Block, which comes under Kamrup district of Assam. The block was started in 1959. It is situated at a distance of about 85 km from the capital city of Guwahati, Assam and connected by NH-37 highway. The majority of the population are tribal which mainly consists of Rabha, Bodo-kachari, and garo tribes distributed throughout the block.

A community-based cross-sectional study was conducted among the tribal adult population of Boko Bongaon Block of Kamrup District, Assam. A total 330 adult respondents of age 30-60 years who were permanent residents were taken for the study after obtaining their informed consent.

Adults with serious or acute medical illness other than diabetes, pregnant women, adults who were on drugs such as corticosteroids, oral contraceptive pills, and β -blockers, and respondents who were not willing to participate were excluded from the study. The present study was undertaken for a period of 1-year (August 2014 to July 2015). Permission to conduct the study was obtained from the

Institutional Ethics Committee, Gauhati Medical College, Assam before the commencement of the study.

The sample size was calculated by taking the prevalence of diabetes to be 3.23% among the tribal⁹ to evaluate the prevalence of Type 2 diabetes mellitus and anthropological status in tribals and non-tribals of Paschim Medinipur district of West Bengal. The prevalence of diabetes was found to be 3.23% among tribal. Keeping in mind the limited available resources (time, manpower, etc.) and taking an absolute error of 2% with 95% confidence interval and using the formula:

$$N = 4pq/L^2$$

Where, N = Required sample size, p = Prevalence, $q = (100-p)$, and $L = 2\%$ (absolute error), the minimum sample size required for the study was calculated to be 312 which was rounded off to 330.

From the total tribal villages, 10 tribal villages were selected through cluster random sampling using the method of probability proportional to size. From each selected village, 33 households were selected randomly and from each selected household the eldest adult available during home visit irrespective of gender is taken to get the total sample size of 330, i.e., $33 \times 10 = 330$ from the selected tribal. In case, no adult was found in a household or did not fulfill our inclusion and exclusion criteria then the next nearest household was taken. If the required number of sample units was not met in that village, then the adjacent village was taken to get the remaining sample units.

The interviews were conducted by house to house visits. Data were collected using semi-structured schedule by interviewing the eldest adult irrespective of gender present in each selected household during the visit for evaluating the correlates. They were interviewed, and observations were done. Information was collected on a socio-demographic profile such as age, sex, religion, caste, marital status, type of family, family history of diabetes, occupation, education, income, dietary intake, physical activity, alcohol and tobacco consumption, any history of diabetes and hypertension in past and present.

This was followed by anthropometric measurements such as weight, height, waist and hip circumference of each interviewed adult and measurement of blood pressure. All selected adults were tested for fasting blood sugar (FBS) using glucometer before the start of the interview and those having FBS more than or equal to 126 mg/dl were taken as diabetic. Those with blood glucose levels between 100 and <126 mg/dl were taken as impaired or pre-diabetes. Those having FBS below 100 mg/dl were

taken as normal (American Diabetes Association, 2003). Known diabetics on oral hypoglycemic agents were taken as diabetic irrespective of their FBS levels.

RESULTS

The present study was carried out among the adult population of Boko, who were between 30 and 60 years of age. There were 330 tribal respondents of which 145 (43.9%) were males, and 185 (56.1%) were females.

Table 1 shows the socio-demographic profile of the respondents which shows that majority (36.4%) belonged to 40-49 years age group and only 29.7% belonged to 50-60 years group. The majority (71.2%) were Hindus followed by Christians (20%). The majority of respondents (83.3%) were married. Most of them (60%) belonged to the nuclear

family. In education level, 10.6% were illiterate, whereas 44.8% have completed secondary education. A majority of respondents (68%) were agricultural laborers. As per the modified BG Prasad's Classification 2013 (July)¹⁰ on social class 35.2% belonged to lower middle class, 33.9% belonged to upper lower class whereas only 3.6% belonged to upper class. About 54% of respondents had a positive family history of diabetes.

As evident from Tables 2 and 3, there was an increase in the prevalence of diabetes among those who took non-vegetarian diet than among those who took vegetarian diet with a relative risk (RR) of 1.022 which was not significant. Similarly, with factors such as decreased fruit intake, alcohol use, frequency of alcohol use, tobacco use, form of tobacco use, and hypertension, there was no significant increase in the prevalence of diabetes, whereas there was significant decrease in the prevalence of diabetes with increased physical activity with an RR of 0.8809 among

Table 1: Socio-demographic characteristics of the respondents

Variables	Respondents n (%)
Age group	
30-39	112 (33.9)
40-49	120 (36.4)
50-60	98 (29.7)
Gender	
Male	145 (43.9)
Female	185 (56.1)
Religion	
Hindu	235 (71.2)
Muslim	29 (8.8)
Christian	66 (20)
Marital status	
Married	275 (83.3)
Others (unmarried/separated/widow)	55 (16.7)
Type of family	
Nuclear	196 (59.4)
Joint	134 (40.6)
Education level	
Illiterate	35 (10.6)
Primary education	66 (20)
Secondary education	148 (44.8)
Higher education	81 (24.6)
Occupation	
Agricultural laborer	224 (68)
Non-agricultural laborer	39 (11.8)
Homemaker	32 (9.7)
Service	11 (3.3)
Shopkeeper/Business	24 (7.2)
Socio-economic status	
Upper	12 (3.6)
Upper middle	40 (12.1)
Lower middle	116 (35.2)
Upper lower	112 (33.9)
Lower	50 (15.2)
Family history of diabetes	
Present	178 (53.9)
Absent	152 (46.1)

Table 2: Distribution of the diabetes status of the respondents according to the various lifestyle factors

Variables	n (%)			P value
	Total	Non-diabetic	Diabetic	
Diet				1.000
Vegetarian	42 (12.7)	41 (13)	1 (7.1)	
Non-vegetarian	288 (87.3)	275 (87)	13 (92.9)	0.7442
Fruit intake				0.7442
≥1-3 times/week	66 (20)	64 (20.3)	2 (14.3)	
≤1-3 times/month	264 (80)	252 (79.7)	12 (85.7)	0.0475*
Physical activity				0.0475*
Sedentary	22 (6.7)	19 (6)	3 (21.4)	
Moderate	206 (62.4)	197 (62.3)	9 (64.3)	
Heavy	102 (30.9)	100 (31.7)	2 (14.3)	0.7428
Alcohol use				0.7428
User	257 (77.9)	245 (77.5)	12 (85.7)	
Non-user	73 (22.1)	71 (22.5)	2 (14.3)	0.3481
Frequency of alcohol intake				0.3481
1-7 days/week	170 (66.1)	160 (65.3)	10 (83.3)	
1-3 days/2-4 weeks	87 (33.9)	85 (34.7)	2 (16.7)	0.1570
Tobacco use				0.1570
User	123 (37.3)	115 (36.4)	8 (57.1)	
Non-user	207 (62.7)	201 (63.6)	6 (42.9)	0.0852
Form of tobacco use				0.0852
Smokers	39 (31.7)	36 (31.3)	3 (37.5)	
Chewers	67 (54.5)	65 (56.5)	2 (25)	
Mixed variety	17 (13.8)	14 (12.2)	3 (37.5)	0.2051
HTN				0.2051
Present	20 (6.1)	18 (5.7)	2 (14.3)	
Absent	310 (93.9)	298 (94.3)	12 (85.7)	0.0018**
BMI				0.0018**
Normal	294 (89.1)	286 (90.5)	8 (57.1)	
Overweight/obese	36 (10.9)	30 (9.5)	6 (42.9)	0.0013**
WHR				0.0013**
Normal	296 (89.7)	288 (91.1)	8 (57.1)	
Obese	34 (10.3)	28 (8.9)	6 (42.9)	

*P<0.05, **P<0.01, ***P<0.001. WHR: Waist-hip ratio, BMI: Body mass index, HTN: Hypertension

those doing heavy activity than those who were sedentary (RR of 1) which was significant. The prevalence of diabetes was found to be significantly higher among the obese and overweight respondents as measured by body mass index (BMI) and waist-hip ratio (WHR) with RR of 1.167 and 1.181 among the overweight/obese than among the normal (RR of 1) as per BMI and WHR, respectively, which was highly significant.

DISCUSSION

This study was carried among 330 adult tribal respondents of Boko Bongaon Block of rural Kamrup of which majority 69.1% belonged to the lower middle class and upper lower class of the society. Most of them (68%) were agricultural laborers. The majority are Hindus and married with the nuclear type of family. The majority of the respondents are of age 30-49 years.

Among the various modifiable risk factors as evident from Tables 2 and 3, a significant decrease in the prevalence of diabetes had been found with the increase in physical activity of the respondents. Similar studies quoted a significant association between physical activity and diabetes. Rao *et al.*¹¹ in a cross-sectional community-based survey during August 2006 to October 2007 among 1239 individuals of age 30 years and above in the rural field practice area of Kasturba Medical College, Manipal revealed odds of 1.00 in heavy, 2.24 (0.78-6.36) in moderate, 4.54 (1.62-12.71) in light, and 9.10 (3.13-26.47) in sedentary respondents, the difference being very highly significant statistically ($P < 0.001$). Majgi *et al.* (2012),¹² in a cross-sectional study during January 2007 to April 2008 in two villages of Puducherry, studied 1403 subjects of more than 25 years age from two villages and found that prevalence of diabetes was 8.1%, 6.5%, and 3.1% in respondents with low, moderate, and heavy physical activity, showing a significant decrease ($P < 0.05$) in prevalence of diabetes with increase in physical activity.

Furthermore, as shown in Tables 2 and 3, a significant increase in the prevalence of diabetes was seen from normal to overweight/obese respondents as measured by BMI and WHR with RRs of 1.167 and 1.181, respectively. Similar findings were found from following studies. Rao *et al.*,¹¹ in a cross-sectional community-based survey during August 2006 to October 2007 among 1239 individuals of age 30 years and above in the rural field practice area of Kasturba Medical College, Manipal, found significantly higher odds of 1.88 (1.19-2.95) in respondents with BMI 23.0-24.9 and 3.43 (2.44-4.83) in participants with BMI of >25 as compared to respondents with BMI <22.9 and found that participants with central obesity had a

Table 3: Estimates of relative risks and confidence intervals of the various lifestyle factors

Variables	RR	95% CI	P value
Diet			
Vegetarian	1		
Non vegetarian	1.022	0.9691-1.079	1
Fruit Intake			
$\geq 1-3$ times/ week	1		
$\leq 1-3$ times/month	1.016	0.9662-1.068	0.7442
Physical activity			
Sedentary	1		
Moderate	0.9031	0.7630-1.069	0.0968
Heavy	0.8809	0.7444-0.9982	0.0387*
Alcohol use			
User	1		
Non user	0.9802	0.9351-1.027	0.7428
Frequency of alcohol intake			
1-7 days/week	1		
1-3 days/2-4 weeks	0.9633	0.9168-1.012	0.3481
Tobacco use			
User	1		
Non user	0.9629	0.9139-1.014	0.1570
Form of tobacco use			
Smokers	1		
Chewers	0.9515	0.861-1.051	0.3547
Mixed variety	1.121	0.8835-1.422	0.3540
Hypertension			
Present	1		
Absent	0.9362	0.8076-1.085	0.2051
BMI			
Normal	1		
Overweight/ obese	1.167	1.007-1.353	0.0018**
WHR			
Normal	1		
Obese	1.181	1.010-1.382	0.0013**

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, CI: Confidence interval, BMI: Body mass index, RR: Relative risk, WHR: Waist hip ratio, CI: Confidence Interval

significantly higher odds (3.01 [2.12-4.29]) of developing diabetes as compared to participants with no central obesity. Vaz *et al.* (2011),¹³ in a cross-sectional study done in rural area of Mandur, Goa among 1266 participants of >20 years of age, found prevalence of diabetes at 3.3%, 10.3%, 22.2%, and 88.9% among underweight, normal, pre-obese, and obese individuals, respectively, the increase being very highly significant statistically ($P < 0.001$).

CONCLUSION

Among the modifiable risk factors effecting the prevalence of diabetes among the tribal adult population of Boko increased physical activity with normal BMI and WHR played a significant protective role.

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Presumptive Coliform Count in Water Sample Collected from Different Sites of a University, Moradabad, Uttar Pradesh, India

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Abstract

Introduction: Safe water is the most important than any other things for human health on this earth. The World Health Organization (WHO) report approximately 65% of rural and 36% of urban India's were without access to safe drinking water. The aim of our study is to determine presumptive coliform count in water sample collected from different sites of a University, Moradabad, Uttar Pradesh, India.

Materials and Methods: The microbial quality of drinking water sample from different sites was detected using multiple tube fermentation technique test (most probable number/100 ml) for the presence of total coliform count. Bacterial isolate was identified by culture, morphological, and biochemical characterization.

Results: A total 50 water sample were collected from different water cooler located at the different sites of the university. Out of 50 water sample, 22 (44%) positive and 28 (56%) were negative. Out of various positive water samples from various sites, girls and boys hostel had a highest degree of bacterial contamination. It was found were that 10 (45.46%) of water sample are contaminated with a multiple coliform bacteria and 12 (54.54%) of water sample found to be contaminated with a single isolate of coliform bacteria. Out of mix coliform bacteria *Escherichia coli* and *Klebsiella*, we found that out of 22 positive sample, 11 (50%) water sample were satisfactory, 5 (22.72%) were suspicious sample, and 6 (27.28%) were unsatisfactory sample.

Conclusion: Most of the sites met the WHO recommended standard microbiological parameters. However, some sites do not meet the WHO recommended standard. So, we would like to recommend the proper sanitation, regular treatment, supervision of water sources, and regular bacteriological assessment of all water sources for drinking should be planned and conducted.

Key words: *Escherichia coli*, MacConkey broth, Most probable number, Presumptive coliform

INTRODUCTION

One of the most important elements for all forms of life is water. On earth, in the maintenance of life, it is indispensable. For the composition and renewal of cells, it is also essential. Beside this, human being is continuing to contaminate water source and provoking water-related illness.^{1,2}

In general, water is mainly used for drinking especially as domestic purposes. A wide variety of inorganic compound requires to all living organism for growth, repair, maintenance, and reproduction.³

The most important, as well as one of the most abundant of those compounds is water, and it is particularly vital to living organism.⁴

In human life, water plays an essential role. The World Health Organization (WHO) reports approximately 65% of rural and 36% of urban India's were without access to safe drinking water.⁵

Pathogenic microorganisms include bacteria, viruses, and protozoa that are transmitted by water to humans and grow

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in the human intestinal tract most of these microorganisms and are transmitted via feces.⁶

Enteric pathogens such as coliform group of bacteria *Salmonellae*, *Vibrio* and dysentery-causing agents contaminate water. The human fecal material carried in sewage is often dumped in lakes and river. This increases contamination of water. Therefore, for microbial contamination water supply has to be regularly checked. The most reliable indicators of fecal contamination are coliform bacteria. However, strong evidence of fecal pollution is presence of *Streptococci*.⁷

Because of implied public health impacts the microbiological quality of drinking water has attracted great attention worldwide.⁸

In addition, various kinds of disease could be infected in humans by water and has been traced to be one of the ways. Typhoid fever, cholera, and bacillary dysentery are some water born disease. In untreated or poorly treated sewage, usually pathogens are spread by water contamination in water born infection.⁹

Escherichia coli is the most dangerous form enters the water supply and occurs in fecal contaminants in the case of water pollution. Many diseases caused by ingestion of contaminants into the water supply. Examples *Shigella* species, *Salmonella* species, *Vibrio cholera*, and *E. coli*.⁴

The coliform is Gram-negative, non-sporing, motile or non-motile aerobic and facultative anaerobic, rod-shaped bacteria, within 48 h at 35°C that ferment lactose with gas formation. All over the world, indicators organism are coliforms that are used is establish the degree of fecal pollution in water.

Members of coliforms bacteria are *Escherichia*, *Enterobacter*, *Proteus*, *Klebsiella*, *Yersinia*, *Hafnia*, *Serratia*. *E. coli*, and *Enterobacter aerogenes* are most important found as commensals which are abundantly found in the intestinal tract of all humans and are regularly discharged in the feces. *E. coli* and *E. aerogenes* are definitely found in any material which is focally polluted. In the world, we can say that any material with these coliforms indicator fecally polluted.¹⁰

Relationship exists directly among sanitation, water, nutrition, and human well-being health. In India, the major causes of many diseases are by consumption of contaminated drinking water, lack of personal and food hygiene, improper disposal of human excreta, and improper disposal of solid and liquid waste.¹¹

The quality of drinking water may be maintained by protection of water sources, control of treatment

processes, and management of the distribution and handling of water.¹²

By standard water treatment practices, the majority of bacterial pathogen are removed or inactivated. Water treatment in standard drinking water includes sedimentation, coagulation/flocculation, sedimentation, filtration, and disinfection.¹³

MATERIALS AND METHODS

The study was conducted in the Department of Microbiology Teerthanker Mahaveer Medical College and Research Centre.

Study Design and Period

The study was conducted on drinking water source to assess the extent of bacterial contamination from March 2015 to January 2016 in the Teerthanker Mahaveer University Moradabad, Uttar Pradesh.

A total 50 sample were collected from different drinking water cooler located at the different sites of the University, Moradabad, Uttar Pradesh.

Sample Collection Technique

Cotton wool soaked in 70% ethanol was used to sterilize the tip of tap from which sample was collected the tap was allowed to run for 2 min before sterile 250 ml screw capped glass bottle were carefully uncapped and filled with water and recapped.

Collection time, its source, and the name of site were noted on the sample of the bottle.

The water was collected using sterile bottles and transported for testing immediately to the department of medical laboratory science and pathology laboratory by ice cold containers within 50 min of collection.

Determination of Total Coliform

Testing water samples for the presence of coliforms. There will be three principal tests - The presumptive, confirmed, and completed the test.

Presumptive coliform test

Multiple tube fermentation method: Presumptive coliform count-multiple tube test.

The test is called presumptive because the reaction observed may occasionally be due to the presence of some other organisms and the presumption that reaction is due to coliform organisms has to be confirmed.

An estimate of the number of coliform organisms is usually made by adding varying quantities of water (0.1-50 ml) to double strength MacConkey's broth and single strength MacConkey's broth containing bromocresol blue sterilized in bottle/tubes containing Durham's tube (for indication of gas production).

Confirmed test

Confirmed test done by transferring a loopful of culture from a positive tube from the presumptive test into a tube of brilliant green lactose bile broth (oxid) with Durham tubes. The tubes were incubated at 37°C for 24-48 h for total coliforms and 44.5°C for 24-48 h for fecal coliform and observed for gas production.

Completed test

Completed test was carried out in accordance with (WHO, 2012) by streaking a loopful of broth from a positive tube into eosin methylene blue (EMB) agar plate for pure colonies. The plates were incubated at 37°C for 24-48 h. Colonies developed on EMB agar, or MacConkey's agar was further identified as coliforms fecal coliforms (*E. coli*) using culture characteristic, morphology, and biochemical test. For fecal coliforms, colonies with green metallic sheen were Gram-stained, and the IMVIC test was carried out to identify the colony as *E. coli*. The most probable number (MPN) per 100 ml water was determined using the completed test.

Determination of coliforms count

Number of positive test tube with acid (yellow coloration) and gas production were matched with the McCrady's Statistical table, and MPN of coliform present in 100 ml of sample was thus determined.

For the confirmation test, a loopful of cultures from presumptive test inoculated on MacConkey agar, EMB agar, blood agar, nutrient agar, xylose lysine deoxycholate agar, and lysine iron agar. The culture plate will be incubated at 37°C for 24 h.

RESULTS

A total 50 water sample were collected from different water cooler located at the different sites of the university.

Out of 50 water sample, 22 (44%) were positive and 28 (56%) were negative from various sites of the university, which is shown in Table 1 and Figure 1.

Out of various positive water samples from various sites hospital, Medical college, Paramedical college, Girls and boys hostel, Nursing college, Physiotherapy college, College of education and stadium, dental college and dental

outpatient department (OPD), college of computer science and information technology (CCSIT). Girls and boys hostel had the highest degree of bacterial contamination followed by Hospital, Medical college, Nursing college, College of education, CCSIT, which is shown in Table 2 and Figure 2.

In our study, it was found that 10 (45.46%) of water sample are contaminated with a multiple coliform bacteria and 12 (54.54%) of water sample found to be contaminated with a single isolate of coliform bacteria. Out of 12 single coliform bacteria, *E. coli* 8(36.37%) the most common isolate which is followed by *Klebsiella 2* (9.09%), *Enterobacter*, and *Citrobacter 1* (4.54%) which is shown in Table 3 and Figure 3.

Table 1: Percentage of total positive and negative sample

Total sample	50	Percentage
Positive sample	22	44
Negative sample	28	56

Table 2: Site wise distribution of positive and negative sample

Site of sample	Number of positive samples	Number of negative samples	Total number of samples
Hospital	3	2	5
Medical college	2	3	5
Girls and boys hostel	7	12	19
Paramedical college	1	1	2
Nursing college	2	1	3
Physiotherapy college	1	0	1
Engineering college	1	4	5
College of education and stadium	2	2	4
Dental college and dental OPD	1	2	3
CCSIT	2	1	3
Total	22	28	50

OPD: Outpatient department, CCSIT: Computer science and information technology

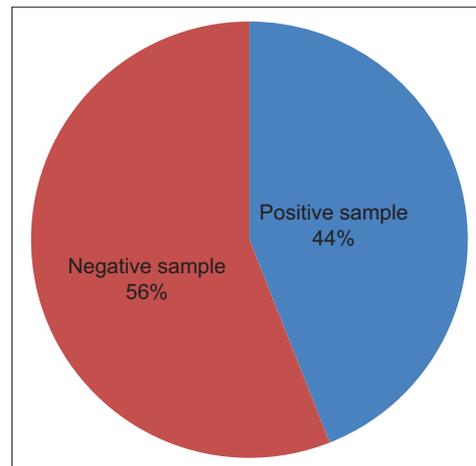


Figure 1: Percentage of total positive and negative sample

Table 3: Frequency of distribution of isolated organism in different sites

Sites of sample	Organism isolated				
	<i>E. coli</i>	<i>K. pneumoniae</i>	<i>E. aerogenes</i>	<i>C. koseri</i>	Mix organism
Hospital	-	-	-	-	3
Medical college	1	-	-	-	1
Girls and boys hostel	2	1	-	1	3
Paramedical college	1	-	-	-	-
Nursing college	1	-	-	-	1
Physiotherapy college	1	-	-	-	-
Engineering college	-	-	-	-	1
College of education and stadium	1	-	1	-	-
Dental college and Dental OPD	1	-	-	-	-
CCSIT	-	1	-	-	1
Total positive sample (%)	8 (36.37)	2 (9.09)	1 (4.54)	1 (4.54)	10 (45.46)

OPD: Outpatient department, CCSIT: Computer science and information technology, *E. coli*: *Escherichia coli*, *K. pneumoniae*: *Klebsiella pneumoniae*, *E. aerogenes*: *Enterobacter aerogenes*, *C. koseri*: *Citrobacter koseri*

Table 4: Distribution of mix isolated organism

Organism	Number of samples
<i>E. coli</i> and <i>Klebsiella</i>	4
<i>E. coli</i> and <i>Klebsiella</i> and <i>Enterobacter</i>	2
<i>Klebsiella</i> and <i>Citrobacter</i>	1
<i>Citrobacter</i> and <i>Enterobacter</i>	1
<i>E. coli</i> and <i>Citrobacter</i>	2
Total	10

E. coli: *Escherichia coli*

In our study, out of mix coliform bacteria, *E. coli* and *Klebsiella* was found to be more followed by *E. coli* and *Klebsiella* and *Enterobacter*, *E. coli* and *Citrobacter*, *Klebsiella* and *Citrobacter*, *Enterobacter* and *Citrobacter*, which are shown in Table 4 and Figure 4.

In our study, we found that out of 22 positive sample, 11 (50%) water sample were satisfactory, 5 (22.72%) were suspicious sample, and 6 (27.28%) were unsatisfactory sample, which is shown in Table 5 and Figure 5.

DISCUSSION

In developing countries, the most common cause of gastroenteritis which affects humanity is due to lack of safe and clean drinking water supply. We expect water to be free from bacterial contaminants and other impurities because it is vital to our life. Even if water appears clear, it may not necessarily be safe and acceptable. The water that is suitable for human consumption must be free of chemical and pathogenic agents, pleasant to taste and usable for domestic purposes. So, potable water is an important source of infectious disease. So, water purification is most important for ensuring public health.

In this study, on the basis of the result obtained the coliform bacteriological quality of different sites of University. Drinking water cooler quality of the paramedical

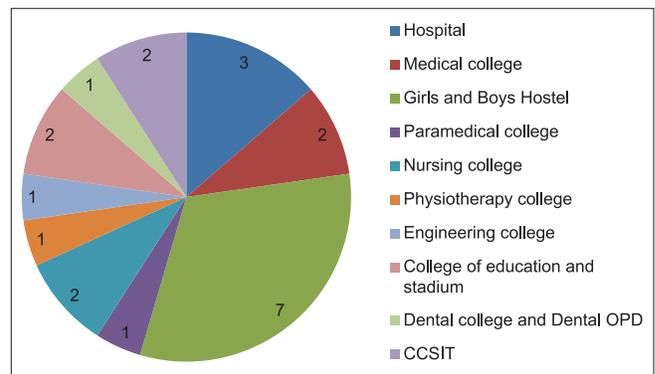


Figure 2: Distribution of site wise positive sample

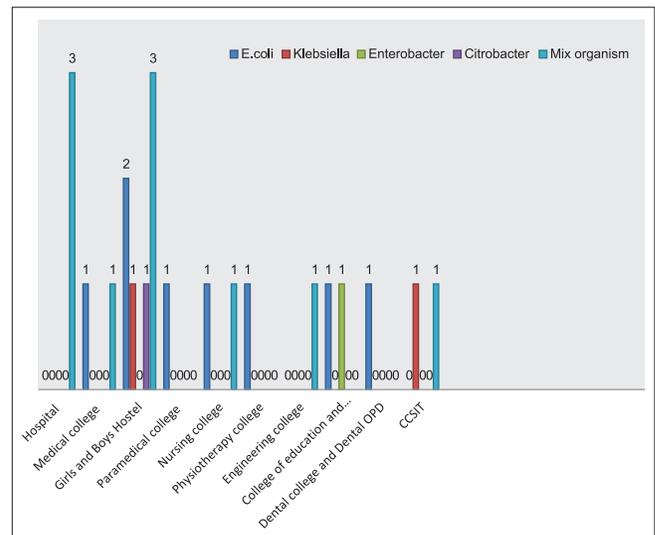


Figure 3: Distribution of organism isolated from different site

college, physiotherapy college, dental college, and OPD were satisfactory as compared to girls and boys hostels.

E. coli were more frequently detected in water cooler sample of girls and boys hostels as compared to hospital and engineering college.

Table 5: Profile of total positive sample (n=22)

Sites of water sample	Number of positive samples	Number of satisfactory samples	Number of suspicious samples	Number of unsatisfactory samples
Hospital	3	2	1	0
Medical college	2	1	0	1
Girls and boys hostel	7	3	1	3
Paramedical college	1	1	0	0
Nursing college	2	0	1	1
Physiotherapy college	1	1	0	0
Engineering college	1	0	1	0
College of education and stadium	2	1	1	0
Dental and college dental OPD	1	1	0	0
CCSIT	2	1	0	1
Total	22	11 (50%)	5 (22.72%)	6 (27.28%)

OPD: Outpatient department, CCSIT: Computer science and information technology

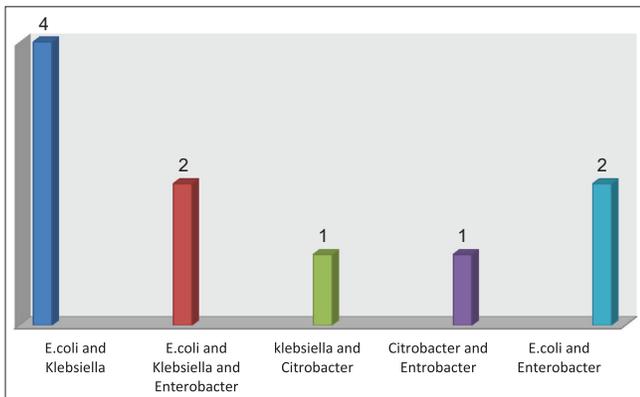


Figure 4: Distribution of mixed isolated organism

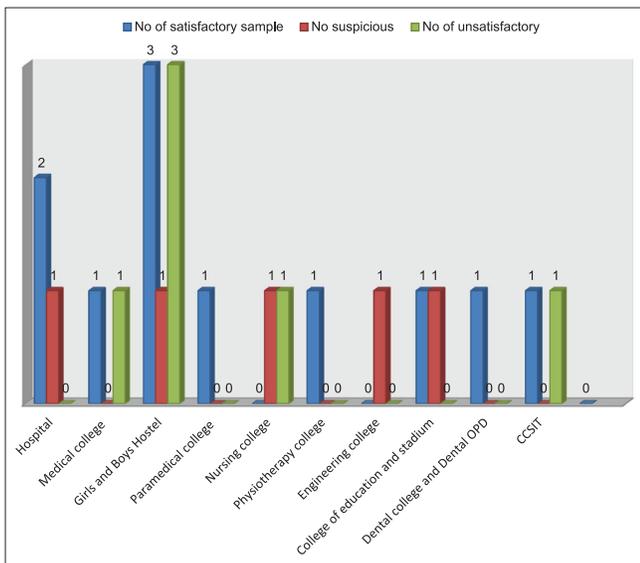


Figure 5: Profile of total positive sample

Mix organisms were more detected in water cooler sample in different sites of TMU as compared to the individual organism.

Hospital, paramedical college, engineering college, college of education and stadium, dental college, physiotherapy

college drinking water cooler is safe as compared to girls and boys hostel, CCSIT, nursing college medical college water cooler. The reasons for the contamination are improper chlorination of water and irregular checking of water.

The water cooler is revealed the high number of *E. coli*; hence, it required the proper maintenance by change the filter and washing the filter time to time as per guidelines.

Our study is comparable with the study of Thakur *et al.* In that study, 17 water sample were collected from different source. Out of those, unsatisfactory 52.94%, satisfactory 11.76%, excellent 29.4%, and suspicious 5.88%. The most common isolates were *E. coli* and *E. aerogenes*. Both the enteric bacteria are considered as water pollution indicator organism¹⁴.

While in the study of Ngwa and Chrysanthus most predominant bacteria was *Klebsiella* species 73.3%, followed by *Salmonella typhi*, 66.7%, *E. coli* 53.3%, *Enterobacter species* 26.7%, and *Proteus mirabilis* 6.7%.¹⁵

E. coli has been used as an indicator of fecal pollution in water for many decades. In the intestinal tract of human and animals bacterium is present in large numbers and is more numerous than disease-causing bacteria and viruses. The advantage of *E. coli* is that, it is not capable of growing and multiplying in water (except warm and food laden waters). Thus, the presence of this bacterium in water is indicators of fecal pollution.¹⁶

CONCLUSION

The result obtained from this study revealed that the microbiological parameters of water sampled from different sites of University were obtained and received. Most of the sites met the WHO recommended standard microbiological parameters. However, some sites do not meet the WHO recommended standard.

Several water born disease and chronic health problem may be caused by consuming unsafe drinking water. Hence, safe drinking water to each and every individual the earth is necessary. That is why proper treatment of water should be employed to avoid health problems.

The bacteriological analysis of drinking water revealed that the some samples of drinking water from different sites were contaminated with coliform and other pathogenic bacteria. The pathogen like *E. coli* and *Klebsiella* were isolated by selective media.

Hence, we would like to recommend the proper sanitation, regular treatment, supervision of water sources, and regular bacteriological assessment of all water sources for drinking should be planned and conducted.

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Surgical Site Infection Following Cesarean Section in a Teaching Hospital

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Abstract

Introduction: Over the last 20 years, the increase in cesarean section (CS) delivery has been substantial in many states in the country. Morbidity after a CS is increased considerably once there is a surgical site infection (SSI) and it may lead on to mortality. Medical science is able to reduce this problem of SSI by adhering to strict aseptic and antiseptic measures. How much we could achieve? What is the current burden of this problem? How we can further reduce it?

Objective: To identify the incidence of SSI after CS and to identify the risk factors of SSI after CS.

Design: Descriptive study.

Setting: Department of Obstetrics and Gynaecology Government MCH Kottayam, Kerala, South India. It is a tertiary care center and a teaching hospital.

Study Subjects: Women who had undergone CS.

Results: 4.1% of subjects had SSI. The significant factors in the final model included were a high body mass index (BMI) (above 25), prolonged pre-operative hospital stay, and hypertensive disorders.

Conclusions: By trying to reduce BMI, limiting the pre-operative hospital stay, and taking stringent measures against HDP (hypertensive disorders of pregnancy), we may be able to reduce SSI further.

Key words: Body mass index, Cesarean section, Hospital Stay, Hypertension, Surgical site infection

INTRODUCTION

A consistent increase has been observed in the rate of cesarean deliveries in most of the developed countries and many developing countries including India over the last few decades and is a matter of concern among the social scientists. In recent years, it is often argued that obstetricians also increasingly prefer for surgical birth than a normal birth. In addition, there is also some evidence from certain countries on increasing preference from women who want to deliver their child through the cesarean section (CS).

There is an argument that medico-legal issues force an institution to go for cesarean at the slightest indication. Interestingly, all the southern states in India recorded CS delivery as high as that of recorded in countries with the highest level of CS in the world.¹⁻⁵ The rates recorded in Kerala, Andhra Pradesh, and Goa are alarming. The data indicate that states with marked demographic transition also records high incidence of CS rate, although, the real cause of such increase would be different. Morbidity after a CS is increased considerably once there is a surgical site infection (SSI) and it may lead on to mortality. Sepsis has become a major cause for maternal mortality in Kerala.²⁷ SSI is a major cause for sepsis after CS. Hence, identifying risk factors of SSI helps to formulate an ideal environment to reduce SSI and thereby sepsis and maternal mortality. This study aimed to determine the incidence of SSI after the CS and to identify risk factors associated with the development of SSI. Medical science is able to reduce this problem of SSI by adhering to strict aseptic and antiseptic

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measures. How much we could achieve? What is the current burden of this problem? How we can further reduce it?^{6,7}

MATERIALS AND METHODS

The Institutional Ethical Committee evaluated the project and granted consent for the same on 23/02/2012. The study period was from March 2012 to May 2013. The data were collected from the post-operative lower segment CS (LSCS) ward on a day-to-day basis. Risk factor profile was analyzed for those who had SSI. Patients with SSI were identified as per the following criteria.

1. Infection occurring in the first post-operative week
2. Involving skin and subcutaneous tissue at surgical site with any one of the following:
 - a. Purulent discharge
 - b. Organisms isolated from fluid/tissues of superficial incision
 - c. At least one sign of inflammation (indurations, erythema, local rise of temperature)
 - d. Wound deliberately opened by the surgeon for drainage
 - e. Surgeon declares that the wound is infected.

Exclusion Criteria

1. Patients requiring obstetric hysterectomy/any other surgical complication
2. Cases operated outside
3. Patients referred from outside centers in active labor and operated later
4. Patients with HIV, hepatitis B, syphilis, or infective hepatitis/leptospirosis/dengue/documentated urinary tract infection.

Variables studied:

1. Body mass index (BMI)
2. Socioeconomic status
3. Hemoglobin level
4. Co-morbidities hypertension/diabetes mellitus/renal disease/bronchial asthma/Thyroid dysfunctions
5. Antibiotic prophylaxis given
6. Presurgery hospital stay
7. Ward used by the patient (general ward/pay ward)
8. Parity
9. Previous surgery
10. Incision transverse/vertical
11. Elective/emergency
12. Anesthesia used (general/spinal/epidural)
13. Surgeon-resident/faculty
14. Soap and water bath before surgery by the subject.

The investigators collected the data from the post-operative ward on the day-to-day basis. BMI was calculated by third

post partum day weight and height. Socioeconomic status was assessed by Kuppaswamy's socioeconomic status scale. Emergency CS was defined as an operation for the compelling reason that had not been planned, and an elective cesarean was defined as an operation planned and done when scheduled.

Sample Size

A total of 1500 subjects were required as per calculation.

Calculated with alpha and beta errors, respectively, as follows.

Alpha (α) error = 0.05

Beta (β) error = 20

Statistical Method

Statistical analysis was performed using SPSS software (version 10.0, SPSS Inc., Chicago, IL). Chi-square test and Fishers exact tests were done where ever necessary. ($P < 0.05$ was considered significant) The significant variables ($P < 0.05$) were entered into a multivariate logistic regression for getting a final model.

RESULTS

About 1500 post LSCS subjects were studied. 62 had post-operative SSI in the first post-operative week. This gave an incidence of 4.1%. After doing Chi-square and Fishers exact tests, 11 variables were found significantly associated with SSI. They are BMI, Socioeconomic status of the patient, anemia, hypertension, diabetes mellitus, renal disease, use of perioperative antibiotics, type of surgery (emergency or elective), pre-operative hospital stay, place of stay in the hospital and the surgeon who did the surgery (Tables 1 and 2).

DISCUSSION

Reported rates of post-cesarean SSI vary greatly, from 0.3% in Turkey⁴ and 11.6% in Brazil⁵ to 18.3% in Saudi Arabia.⁶ The present study included 1500 CS patients, and 62 had infection which accounts for 4.1% and is comparable with rates of different studies.³ A study by Jido *et al.*, in Kano Nigeria, the prevalence of SSI following CS was 9.1%. In India, the infection rate was 24.2% including post discharge surveillance in a study conducted at Lady Hardinge Medical College, New Delhi. Post discharge surveillance was not done and it may have contributed to the low rate of SSI in the present study. Stringent exclusion criteria also might have contributed for a low rate.

Table 1: Risk factor analysis of SSIs following LSCS

Variable	Chi-square	P value	Significance
BMI	11.962	0.008	Yes
Socioeconomic status	11.4782	0.000706	Yes
Anemia	4.115	0.043	Yes
Hypertension	25.695	0.0007	Yes
Diabetes mellitus	21.076	0.00006	Yes
Renal disease	10.6	0.001	Yes
Bronchial asthma	2.276	0.131	No
Hypothyroidism	0.782	0.377	No
Antibiotic use	30.522	0.0001	Yes
Prolonged hospital stay	4.049	0.044	Yes
Place of stay	16.896	0.0005	Yes
Parity	0.1678	0.68	No
Previous surgery	0.1384	0.070	No
Type of incision	0.032	0.858	No
Emergency/elective	4.945	0.026	Yes
Type of anesthesia	0.359	0.549	No
Surgeon (cons/res)	5.482	0.019	Yes
Soap and water bath	0.519	0.475	No

SSI: Surgical site infection, LSCS: Lower segment cesarean section, BMI: Body mass index

Table 2: Multivariate analysis of significant variables

Variable	95% confidence interval for Exp (B)			Significance
	Odds ratio	Lower bound	Upper bound	
BMI >25	1.5047	1.5047	1.5047	0.0008
Anemia	2.287	0.905	5.780	0.080
Hypertension	3.971	2.179	7.237	0.000001
Hospital stay >5	1.977	1.128	3.464	0.017
Emergency surgery	1.905	0.961	3.778	0.065

*: p < 0.05, Hypertension, BMI above 25, and prolonged hospital stay (more than 5 days) are most significant in the given model. BMI: Body mass index

Around 83.3% of study subjects had normal BMI. 13.8% had overweight. This factor needs special attention as obesity is a booming epidemic, especially in the reproductive age group. In the present study, an increased BMI was seen to influence the outcome of surgery in terms of an increased rate of infection. Similar results were found in other studies.⁷⁻¹¹

Socioeconomic status of the majority of the patients was in lower middle class as the setting is a government hospital which caters to the poor and needy section of the society. Compared with patients belonging to upper socioeconomic status, patients of low socioeconomic status had a relatively higher number of high-risk characteristics, increasing their underlying risk for SSI; It was found that there is significantly increased risk of SSI in the low socioeconomic status group. Indian studies analyzing the influence of socioeconomic status of the obstetrics population affecting their surgical outcome are limited.¹²⁻²¹

Patients with anemia were seen to be more prone to SSI. It is generally agreed that anemia diminishes resistance to

infection and is frequently associated with puerperal sepsis. Pre-operative anemia is an important predictor of infection and has been proved by several other studies.^{22,23} In the present study also, anemia was found to be significantly associated with SSI. A study by Awan *et al.*, did not identify anemia as a risk factor of SSI.¹³

Hypertensive disorders were present in 10% of the study population. There is increased surgical intervention for patients with pre-eclampsia. The disease state, inductions, hypoalbuminemia, edema all contribute to the development of SSI. In this study also, patients with hypertensive disorders had significantly increased incidence of SSI.

Patients with pre-existing illnesses, such as diabetes mellitus, renal disease, and hypertensive disorders (pregnancy induced or pre-existing), were seen to be more prone to infection in the present study. Hyperglycemia has several deleterious effects on host immune function, most notably on neutrophil function. Poor control of glucose during surgery and in the perioperative period increases the risk of infection and worsens outcome from sepsis. Hypertension, pre-existing or pregnancy induced, and related co-morbid states have been associated with SSI in several studies.²⁴⁻²⁶ They were all seen to be significant in the present study. Asthma and hypothyroidism predispose to wound infection in general but has shown no significant relation in the present study.

Use of perioperative antibiotics significantly reduces SSI in this study. It may not be corresponding to all published data.

Pre-operative hospital stay has a significant relationship with wound infection. Overcrowding in the wards is a precursor of infection and is also supported by the results that infection was significantly low among patients in pay wards.

Cases done by faculty had more infection as compared to residents. The expertise of the surgeon usually protects against wound infection. Observation was on the contrary. The explanation may be as follows. High risk cases with BMI nearing 30, cases with severe pre-eclampsia, prolonged labor, second stage LSCS are all done by faculty; hence, these factors would have contributed to high rate of infection in these cases. (Cases done by the faculty: Obese cases, cases with anemia or corrected anemia, diabetes mellitus, pre-eclampsia, and renal disease. The majority of emergency cases are being done by one Assistant Professor on duty and not by residents. Cases of prolonged labor and all second stage LSCS are done by the Assistant Professor on duty. Residents are doing cases posted on an elective basis and uncomplicated cases with a faculty assisting them).

Nulliparous women are more prone for infection according to literature.¹⁶ In the present study, no significant relationship was found between SSI and parity. Previous surgery also did not show a significant relationship with SSI.

Type of incision also had no significant relation with the rate of SSI in this study.

Emergency surgery predisposes to infection. Hospitals with a strict policy on reducing primary sections may go for a decision on section after a trial of labor. As a result, emergency surgeries may increase in number. These emergency surgeries have a high chance of SSI.¹ Similar results were obtained in this study also.

Anesthesia also did not show a major difference, although literature shows evidence of general anesthesia being a risk factor for SSI.¹⁶⁻²⁰

Soap and water bath before surgery did not show a significant influence. However, improving personal hygiene helps to prevent SSI. Hence, recommended before all elective surgeries.

Pre-operative hospital stay significantly increased SSI in this study. The stay in the hospital premises increases patient's susceptibility to hospital acquired infections. These infections increase the chances of sepsis and wound infection in these patients. Patients staying in the general ward had more infection than those in pay wards and it was statistically significant. Overcrowding in the general wards may contribute to increased evidence of sepsis (Reasons for prolonged hospital stay in this series were mainly: Diabetes mellitus, pre-eclampsia, anemia, residence is far away and financially not well to spend on taxi fare in case of emergency. Confounding factors are there between high rates of SSI and prolonged hospital stay. However, the SSI rates are low among those who stayed in private rooms. Again relatively better socioeconomic status and better personnel cleanliness of those who are staying in private rooms may be a confounder in the other direction).

CONCLUSION

Three independent risk factors are significantly increasing the chance for SSIs after CS. All the three of them are modifiable to a certain extent. Reduction of BMI should be addressed from the early childhood onwards and unnecessary pre-operative hospital stay, and overcrowding should be discouraged. In public sector Hospitals, this may be a challenge for the caregivers. Another factor worth mentioning is the relationship between hypertensive disorders and prolonged hospital stay (Confounder). Proper guidelines to avoid prolonged stay and proper

management of HDP are the need of the era. Even though the statistical significance was not achieved in the final model, all the modifiable factors attained significance at the individual level also are to be addressed properly to reduce the SSI rates.

Limitation

Follow-up of cases after discharging from the hospital was not done and this might have contributed for a low rate for SSI.

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Incidence of Odontogenic Sinusitis – Experience in a Tertiary Care Centre

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Abstract

Introduction: Chronic sinusitis is a common rhinological problem and odontogenic sinusitis accounts for 10-12%. Odontogenic sinusitis occurs when the Schneiderian membrane is violated by conditions arising from the dentoalveolar unit. Odontogenic sinusitis differs in its pathophysiology, microbiology, diagnostics, and management from sinusitis of other causes hence, failure to identify the dental cause in these patients usually lead to persistent symptomatology and failure of medical and surgical therapies.

Objectives: (1) To identify and evaluate the frequency of odontogenic conditions that may lead to sinusitis, (2) to investigate how clinical features such as sex, age, etiologic factors, and presenting symptoms of odontogenic sinusitis are differentiated from other types of sinusitis.

Materials and Methods: This study was conducted in 100 patients diagnosed with chronic sinusitis between 2013 and 2015. Patients were selected who met the inclusion criteria and detailed ENT and dental examination was done.

Results: In this study, incidence of odontogenic sinusitis was 17%. It was seen commonly seen in males. Maxillary sinus was involved in all the cases of odontogenic sinusitis followed by ethmoid sinus. Most predominant presenting symptoms are a nasal obstruction, facial pain, nasal discharge, headache, and halitosis. Dental caries, periodontitis, and tooth extraction were the most common causes of odontogenic sinusitis.

Conclusion: In this study, odontogenic sinusitis was seen most commonly in the fourth and fifth decade. First molar and second molar teeth were associated with odontogenic sinusitis. Odontogenic sinusitis should be suspected in cases of refractory sinusitis. Medical and surgical treatment should be considered in the treatment of odontogenic sinusitis.

Key words: Dental caries, Molar teeth, Odontogenic sinusitis, Periodontitis

INTRODUCTION

The inflammation of the sinus membrane that covers the paranasal sinus is referred as “sinusitis.” Among the four pair of paranasal sinus, the maxillary sinus is the biggest and most frequently damaged. Possible etiologies of sinusitis comprise local and systemic conditions which can be subdivided into acute, subacute and chronic forms according to their evolution. Chronic sinusitis is an

extremely prevalent disorder that has a significant impact on the quality of life of an affected individual.

About 10-12% of maxillary sinusitis cases have been attributed to odontogenic infections.¹ It occurs when sinus membrane is violated by conditions such as infections of the maxillary posterior teeth, pathologic lesions of the jaws and teeth, maxillary (dental) trauma, or by iatrogenic causes such as dental and implant surgery complications and maxillofacial surgery procedures. Intimate anatomical relation of the upper teeth to the maxillary sinus promotes the development of periapical or periodontal odontogenic infection into the maxillary sinus. The bony wall, separating maxillary sinus from teeth roots varies from full absence, when teeth roots are covered only by mucous membrane, to the wall of 12 mm. Maxillary sinusitis can also develop because of the maxillary osteomyelitis, radicular cysts,

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after mechanical injury of sinus mucosa during root canal treatment, overfilling of root canals with endodontic material, which protrudes into maxillary sinus, incorrectly positioned implants, improperly performed sinus augmentation and oroantral fistulas after tooth extraction.

This disease differs in its pathophysiology, microbiology, diagnostics and management from sinusitis of other causes, although clinical symptoms are not conspicuous. Therefore incorrectly diagnosed, it leads to failure of medical and surgical treatment directed toward sinusitis. This study is done to identify and evaluate the frequency of the different odontogenic conditions that may lead to sinusitis and to investigate how clinical features such as sex, age, etiologic factors, and presenting symptoms of odontogenic sinusitis are differentiated from other types of sinusitis.

MATERIALS AND METHODS

This study was performed from 2013 to 2015. All the patients with symptoms of rhinosinusitis of more than 12 weeks duration are included in the study. Patient's details, symptomatology, clinical presentation, diagnostic nasal endoscopy, dental examination, and radiological findings were recorded from these patients. Diagnostic nasal endoscopy was done using 4 mm Hopkins 0° and 30° angulation scopes, first, second and third pass evaluation of nasal cavity and paranasal sinuses was done after topical anesthesia and decongestion of the nasal cavity of the patients. Radiological evaluation was done using orthopantomogram, X-ray paranasal sinuses using water's view and plain computed tomography scans.

Sample Size

100 patients with chronic sinusitis.

Inclusion Criteria

Patients presenting with two major symptoms persisting for more than 12 symptoms persisting for more than 12 weeks duration are included in the study.

Major factors	Minor factors
Headache	Facial pain/pressure
Nasal obstruction	Halitosis
Nasal discharge/postnasal discharge	Fatigue
Hyposmia/cacosmia	Dental pain
Purulence on nasal examination	Cough, ear pain/pressure/fullness

Exclusion Criteria

1. Children <5 years of age
2. Acute sinusitis
3. Patients suffering from chronic granulomatous diseases of nose.

Statistical methods applied are:

1. Descriptive
2. Chi-square test
3. Frequency
4. Contingency coefficient test.

Descriptive

It displays univariate summary statistics for several variables in a single table and calculates standardized values. Variables can be ordered by the size of their means (in ascending or descending order), alphabetically, or by the order in which the variables are selected.

Frequencies

The frequencies provide statistical and geographical displays that are useful for describing many types of variables.

Chi-square Test

This procedure tabulates a variable into categories and computes a Chi-square statistic. This compares the observed and expected frequencies in each category to test either that all categories contain the same proportion of values or that each category contains a user specified proportion of values.

Contingency Coefficient Test

This procedure forms two-way or multi-way tables and provides a variety of tests and measure the association for two-way tables. The structure of the table and whether categories are ordered determine what test or measure to use.

All the statistical calculations were done through SPSS for windows (version 16.0).

OBSERVATION AND RESULTS

In the present study, it was common in the females (18.6) than males (15.8) (Table 1). There were 6 (35.3) in >51 years age group with dental problem followed by 4 (23.5) in 21-30 years, 4 (23.5) in 31-40 years and 3 (17.6%) in 41-50 years age group. The higher the age group (>51 years), chances of co-existence of dental pain with sinusitis. Furthermore, the mean age group for general sinusitis was 30.2 ± 11.9 and those for odontogenic sinusitis 42.9 ± 14.3 years (Table 2).

About 9 (69.2%) of patients with halitosis had dental problem, which was statistically significant. Around 7 (38.9%) of patients with postnasal discharge, 13 (32.5%) of patients with facial pain, 5 (27.8%) of patients with dental pain, 10 (20.4%) of patients with nasal discharge, 10 (19.2%) of patients with headache, 13 (14.4%) of with nasal obstruction had co-existence of sinusitis (Table 3).

Table 1: Sex distribution

Sex	Tooth disease, n (%)	
	No	Yes
Female	35 (81.4)	8 (18.6)
Male	48 (84.2)	9 (15.8)
Total	83 (83.0)	17 (17.0)

Table 2: Age distribution

Age	Tooth disease, n (%)	
	No	Yes
<20	16 (19.2)	0 (0.0)
21-30	31 (37.3)	4 (23.5)
31-40	21 (25.3)	4 (23.5)
41-50	11 (13.2)	3 (17.6)
>51	4 (4.8)	6 (35.3)
Total	83 (100)	17 (100)

Table 3: Distribution of symptoms

Symptoms	Tooth disease, n (%)	
	No	Yes
Nasal obstruction	77 (85.6)	13 (14.4)
Nasal discharge	39 (79.6)	10 (20.4)
Postnasal discharge	11 (61.1)	7 (38.9)
Headache	42 (80.8)	10 (19.2)
Halitosis	4 (30.8)	9 (69.2)
Sneezing	32 (91.4)	3 (8.6)
Facial pain	27 (67.5)	13 (32.5)
Dental pain	13 (72.2)	5 (27.8)

High co-existence of halitosis, postnasal discharge, and facial pain was statistically significant. In the present study, there were 17 (17%) subjects with some form of dental problem. Exactly, 5 (5%) had dental caries alone, and 2 had dental caries along with generalized periodontal disease, altogether 7 (7%) had dental caries. Similarly, 5 (5%) had generalized periodontal disease alone and 2 had dental caries along with generalized periodontal disease, altogether 7 (7%) had generalized periodontal disease. One subject had localized periodontal disease. About 4 (4%) had history of teeth extraction in last 12 months (Table 4).

Hence 7 (7%) had dental caries, 7 had periodontitis, 4 had teeth extraction, 2 had oroantral fistula.

In the present study, there were 12 involved tooth were seen on examination. Out of these first upper molar was commonly involved 10 (10%), followed by second upper molar 6 (6%), first upper pre-molar 3 (3%) and second upper premolar 2 (2%) (Table 5).

In the present study, 17 maxillary sinusitis was involved and ethmoid sinusitis involved in 6 cases, 4 cases frontal

Table 4: Teeth diseases

Teeth diseases	n (%)
Dental caries	7 (7)
Generalized periodontitis	7 (7)
Tooth caries	4 (4)
Localized periodontal disease	1 (1)
Oroantral fistula	2 (2)

Table 5: Tooth involvement

Teeth examination	n (%)
First upper molar	10 (10)
Second upper molar	6 (6)
First pre-molar	3 (3.0)
Second pre-molar	2 (2.0)

Table 6: Sinus involvement

Sinuses	Dental problem, n (%)
Maxillary sinus	17 (100)
Ethmoid sinus	6 (35.3)
Frontal sinus	4 (23.5)
Sphenoid sinus	2 (11.7)

sinusitis involved and in 2 cases sphenoid sinusitis involved (Table 6).

DISCUSSION

This study was from November 2013 to October 2015. A total of 100 patients were enrolled in the study between 8 and 60-year-old. All the patients presenting with symptoms of rhinosinusitis of more than 12 weeks duration with 2 major and 1 minor or 2 minor symptoms were included in the study.

Frequency of maxillary sinusitis due to odontogenic origin is often underestimated. Proper examination and investigations should be done to rule out dental origin especially in cases of unilateral sinusitis. Normally, the roots of the maxillary premolar and molar teeth are separated from the sinus floor by a dense cortical bone with a variable thickness, but sometimes they are separated only by the mucoperiosteum. Clearly, this anatomical layout can explain the source and development of an inflammatory process. The otolaryngologist should suspect an odontogenic etiology of purulent chronic maxillary sinusitis in patients failing to improve with antibiotics, regardless of a negative dental workup.

In the present study, incidence of odontogenic sinusitis is 17%. Females were more involved than males. The incidence was the highest in the fourth decade.

In a study conducted by Lee and Lee,² in which the male to female ratio was 15:12 with a higher incidence in men.

Most predominant symptoms were nasal obstruction (76%), facial pain (76%), nasal discharge (58%), headache (58%), halitosis (52%), and postnasal discharge (47%). Other symptoms were dental pain (29%) and sneezing ($n = 3$, 17%).

Retrospective chart review of 27 patients diagnosed with odontogenic sinusitis, Lee and Lee² reported that unilateral purulent rhinorrhea was the most common and found in 66.7% of their patients with oral and maxillofacial surgeon, followed by facial pain in one-third of the patients, whereas 26% reported a foul smell or taste.

Longhini and Ferguson³ reports nasal obstruction as the most common and bothersome symptom followed by facial pressure/pain. This case series reported foul smell or rotten taste in 48% and tooth pain in 29% of patients.

Andric *et al.*⁴ showed nasal obstruction in 43% cases, nasal discharge in 43%, and facial pain in 71% cases.

Maxillary sinus was involved in all 17 cases of odontogenic sinusitis; ethmoid sinus was involved in 6 cases, frontal sinus in 4 cases, and sphenoid sinus in 2 cases.

Lechien *et al.*⁵ where maxillary sinus (75%) and frontal sinus (18%) were most commonly involved, ethmoidal or sphenoid sinus being rare.

Lee and Lee² also showed the distribution of paranasal sinus involvement in sinusitis of dental origin, in his study maxillary sinuses were involved 70.4% cases, the maxillary and ethmoid sinuses in 5 cases (18.5%), the maxillary, ethmoid, and frontal sinuses in 2 cases (7.4%), and the maxillary, ethmoid, and sphenoid sinuses in 1 case (3.7%).

Dental caries, periodontitis, iatrogenic causes and oroantral fistula were the most common causes of odontogenic sinusitis. In our study, most of the patients with iatrogenic causes presented within 10 months of dental treatment.

Nimigean *et al.*,⁶ 125 patients suffering from odontogenic chronic maxillary rhinosinusitis (CMRS), the main etiology was periapical chronic periodontitis (79% of patients), followed by complications of endodontic treatment (21% of cases).

In addition, in two prospective studies of Melén *et al.*⁷ and Lindahl *et al.*,⁸ most cases of CMRS were secondary to a dental infectious process such as marginal periodontitis and apical diseases.

In a study conducted by Lee and Lee² showed the interval from the dental procedures to the first visit to the outpatient clinic with symptoms was 1 month in 11 (40.8%), 1-3 months in 5 (18.5%), 3 months to 1 year in 8 (29.6%), and over a year in 3 cases (11.1%).

The time interval between symptoms onset and the causal dental procedure may be highly variable: According to Mehra and Murad,⁹ 41% of patients developed CMRS in the following month, 18% between 1 and 3 months after the procedure, 30% from 3 months to 1 year, and 11% of patients after more than 1 year first upper molar was commonly involved 10 (10%), followed by second upper molar 6 (6%), first upper pre-molar 3 (3%) and second upper premolar 2 (2%).

Melén *et al.*⁷ shows that the most commonly involved teeth are the first (40.6%) and second molars (24.6%). Andric *et al.*⁴ observed similar proportions in their retrospective analysis where first and second molars account for 42% and 35%, respectively. Lindahl *et al.*⁸ reported a higher proportion of the first molar (38%), followed by the second premolar (24%) and second molar (22%).

CONCLUSION

From this study we conclude that:

1. The incidence of odontogenic sinusitis is 17%
2. Mostly seen in males and in elderly people
3. Most common presentation was nasal obstruction, halitosis, postnasal discharge and facial pain
4. Most common causes of odontogenic sinusitis are dental caries, periodontitis and iatrogenic
5. First molar followed by second molar teeth are the most commonly involved in odontogenic sinusitis
6. In all cases of sinusitis, odontogenic cause should be looked both clinically and radiologically
7. Medical treatment should cover Gram-positive organisms and chronic sinusitis should cover mixed organisms
8. Surgical treatment should include dental and sinus surgery.

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Surgical Management of Isolated Tibial Shaft Fractures with Closed Intramedullary Interlocking Nail

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Abstract

Background: Tibial diaphyseal fractures are one of the most common long bone fractures encountered by most of the orthopedic surgeons. The tibial shaft fractures with intact fibula had difficulties in the orthopedic treatment of leg fractures such as reduction of the tibial and an unusually high rate of varus malunion, delayed union, and non-union. Fractures of tibial diaphysis associated with an intact fibula have always interested orthopedic surgeons; there has been debate as to whether the intact fibula was associated with an improved or worse prognosis.

Materials and Methods: A total of 30 patients with isolated tibial diaphyseal fractures (21 closed fractures, 4 Type I open fractures, and 5 Type II open fractures) were operated with closed intramedullary interlocking nailing. This prospective study was done over a period of 2 ½ years with regular follow-up.

Results: Postoperatively following 6 months, excellent functional results were obtained in 70% of cases. Good functional results were obtained in 14%, fair functional results in 3%, and poor functional results in 13%. According to Johner and Wruh's criteria, the percentage of union rate in our study was 87%. The time for union ranged from 4 to 9 months with an average of 5 months, 17 fractures healed before 5 months (20 weeks), 7 fractures healed between 5 and 8 months (20 to 32 weeks), and 4 fractures had gone into non-union.

Conclusion: Intramedullary interlocking nailing is the reliable and effective treatment for undisplaced and minimally displaced closed isolated tibial shaft fractures, also in open Type I tibial shaft fractures. Closed minimal and undisplaced fractures have united well. Displaced, comminuted fractures of tibial shaft with intact fibula are prone to delayed union and non-union. Intramedullary interlocking nailing minimizes the hospital stay and reduces the economic burden and enhances the early return to work.

Key words: Fibula intact, Intramedullary nailing, Tibial shaft fracture

INTRODUCTION

The management of tibial diaphyseal fractures has always held a particular interest for orthopedic surgeons. Not only are they relatively common but also they are often difficult to treat. The subcutaneous location of the anteromedial surface of the tibia means that severe bone and soft tissue

injury are not infrequent, and there is a high incidence of open fractures compared with other long bones.¹

When the fibula remains intact, a tibio fibular length discrepancy develops and causes altered strain patterns in the tibia and fibula. These may lead to delayed union, non-union, or malunion of the tibia with the sequelae of joint disturbances. The lower incidence of complications in patients <20 years old may be due to the greater compliance of their fibulae and soft tissues.² The main difficulties encountered in the orthopedic treatment of leg fractures with intact fibula are reduction of the tibial and an unusually high rate of varus malunion, and non-unions. Nailing is a reliable technique for treatment of tibial shaft fractures with an intact fibula.³ Fractures of

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tibial diaphysis associated with an intact fibula have always interested orthopedic surgeons. There has been debate as to whether the intact fibula was associated with an improved or worse prognosis.^{4,5} Displacement of more than 50% of the width of the tibia at the fracture site was a significant cause of delayed union or non-union. Reduction was difficult to maintain in fractures with more than 50% initial displacement and that comminution delayed fracture healing. Fractures with more than 50% comminution are considered unstable and usually are associated with high-energy trauma. The treatment of displaced isolated fractures of the tibial shaft with closed intramedullary nailing with reaming provides functional results that are superior to those obtained with use of a cast.⁶

Minimally displaced tibial fracture in the presence of an intact fibula has a good prognosis. Initial force may be great enough to break the tibia and tear local soft tissues, the fibula is protected from fracture by its innate flexibility and the significant compliance of its proximal and distal ligaments.⁷⁻⁹ He further stated that roentgenograms often do not reveal the true magnitude of the displacement sustained at the moment of violence and that therefore this fracture pattern can indeed be subject to complications.^{5,10} Isolated tibial shaft fractures with intact fibulae are more prone for complications such as delayed and non-union.¹¹ Intramedullary nailing will remain the treatment of choice for diaphyseal fractures. However, modern plates are become less invasive it is associated with more soft tissue stripping and potential devascularisation.¹²

The aim of this prospective study was to assess the outcome of isolated tibial shaft fractures treated with an intramedullary interlocking nail.

MATERIALS AND METHODS

A total of 30 patients with isolated tibial diaphyseal fractures (closed fractures, Type I open fractures, and Type II open fractures) were operated with closed intramedullary interlocking nailing in the Department of Orthopaedics, R.L.J Hospital attached to Sri Devaraj Urs Medical College and Research Centre, Kolar, Karnataka, during the period from July 2013 to December 2015. This prospective study was done over a period of 2 ½ years with regular follow-up.

Inclusion Criteria

1. Closed tibial fractures with intact fibula
2. Open fractures of tibia with intact fibula, Type I, Type II, and Type IIIA as classified by Gustillo–Anderson grading
3. Tibial fractures in the age group above 18 years.

Exclusion Criteria

1. Open diaphyseal fractures of tibia Type III B, C (Gustillo–Anderson)
2. Tibial fractures with intra articular extensions
3. Pathological fractures.

On admission general condition of the patient was assessed with regards to hypovolemia, associated orthopedic or systemic injuries and resuscitative measures taken accordingly. Patients were selected on the basis of history, clinical examination, radiography, and inclusion criteria. X-ray of full length of tibia antero-posterior and lateral view was taken. All fractures were treated with a closed intramedullary interlocking nail. Follow-up and assessment were performed using Johner and Wruh's criteria at the end of 6 months.

Preoperatively, the length of the nail is calculated by tibial tubercle-medial malleolar distance (TMD). The TMD is determined by measuring the length between the highest (most prominent) points on the medial malleolus and the tibial tubercle. The TMD is an easy, inexpensive, and accurate method of pre-operative determination of correct nail length. The diameter of the nail is assessed by measuring the tibia at its narrowest point, which is best appreciated on lateral radiographs. Accordingly, a stock of interlocking nails 2 cm above and below the measured length and 1 mm above and below the required diameter were kept.

The patient was operated under spinal anesthesia. The patient was placed in supine position over a radiolucent fracture table. The injured leg was positioned freely, with the knee flexed in 90° over the edge of the operating table vertical patellar tendon splitting incision of about 5 cm long was made over the skin extending from center of the inferior pole of the patella to tibial tuberosity. The curved bone awl was used to breach the proximal tibial cortex in a curved manner. After widening the medullary canal of proximal third, a ball tipped guide wire was passed into the medullary canal of proximal fragment and fracture fragment reduced under image intensifier. Its containment within the tibia was confirmed in antero-posterior and lateral view. Medullary canal was reamed starting from 8 mm reamer size to 0.5 to 1 mm larger than the diameter measured using radiographs. Then, ball tipped guide wire was exchanged with smooth guide wire using a medullary tube. This was followed by passing an assembled nail into the medullary canal over the smooth guide wire. Proximal locking was done first followed by distal locking, wound sutured in layers and skin closed with staples; sterile dressing and compression bandage was applied. The patient was started on the active knee, ankle, and toe mobilization after over come from anesthesia. The patient

was allowed non-weight bearing crutch walking/walker on next post-operative day if associated injuries permit, general condition, and tolerance of the patient. Skin sutures were removed on 14 the post-operative day. Partial weight bearing and with crutch walking/walker was commenced immediately, depending on the type of fracture, rigidity of fixation, and associated injuries. Further follow-up was done at 6, 12, 18, and 24 weeks; and each patient was assessed clinically and radiographically according to the Standard Performa.

RESULTS

Data were collected based on detailed patient evaluation with respect to history, clinical examination, and radiological evaluation. The post-operative evaluation was done both clinically and radiologically. All 30 patients were available for follow-up. Period of follow-up was 6-8 months.

Detailed analysis of function results of patients were done at end 6 months on the basis of following criteria by Johner and Wruh's, 21 out 30 patients had excellent results which correspond to around 70%, 4 patients had good results around 14%, 3 patient had fair results around 3%, and 4 patients had poor results around 13%.

The majority of patients are from age group 18 to 39 years (73.3%). The youngest patient was 19-year-old, and oldest patient was 58-year-old. The majority of non-union cases were elderly with open Type II fractures; these patients are also having co-morbidities of diabetes mellitus and hypo-proteinuria. 90% of the patients are males and 10% patients are females.

In our study, right tibial shaft fractures constitute 63% and left are 37%. There was 21 closed fracture out of 30 cases (70%), 4 open Type I fractures (13%), and 5 open Type II fractures (17%). Road traffic accident was the major cause for tibial fracture and it constituted 90% of cases. Second common mode of injury was fall from height and it was 7%, and the third type was an assault which was 3%. Most of the cases are middle one-third fractures (73%). Next common level of fracture in the tibia in our study is lower one-third (20%), and upper one-third is 7%.

In our study, only two had associated injuries of which one had opposite side metatarsal fracture which was fixed with k-wire, another had rib fracture treated conservatively. Rest 28 patients had no associated injuries.

In our study, most of the cases are mobilized (partial weight bearing with crutch walking) on next day after the operation. Majority of the patients, 21 out of 30 (70%) started partial

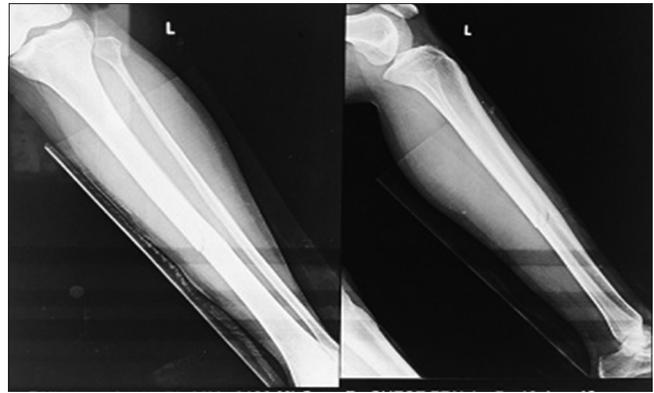


Figure 1: Case 1: Post-operative X-ray with IMIL nail



Figure 2: Case 1: Pre-operative X-ray isolated tibial shaft #



Figure 3: Case 2: Pre-operative X-ray isolated tibial shaft #



Figure 4: Case 2: Post-operative X-ray with IMIL nail

weight bearing with help of walker within 5 days from date of surgery, 5 patients out of 30 (17%) started partial weight bearing between 5 and 10 days because of pain at operated site, 4 patients out of 30 (13%) started partial weight bearing after 10 days because of stability of fracture (comminuted) and patient non-compliance. Most of the patients 27 (90%) in our study commenced protective full weight bearing (FWB) between 8 and 14 weeks. Four patients (10%) commenced FWB after 14 weeks. In these 2 patients, there were no signs of union radiologically and clinically. So, FWB was delayed. Two patients had a deep infection with infected non-union.

Union is defined as the presence of bridging callus on three or more cortices of radiographic views and the ability of the patient to bear full weight on the injured extremity. 26 of 30 fractures had united, so the percentage of union rate in our study was 87%. The time for union ranged from 4 to 9 months with an average of 5 months. 17 fractures healed before 5 months (20 weeks), 7 fractures healed between 5 and 8 months (20-32 weeks). Four fractures failed to unite after 9 months. Delayed union was defined when there was no adequate callus formation even after 20-24 weeks and patients inability or difficulty in partial or FWB. In our study, 7 out of 30 cases went for delayed union which is around 23%. All delayed union were managed successfully with secondary dynamization and bone marrow injection.

Two patients developed a superficial infection. This healed with oral antibiotics; four patients developed deep infection and treated with antibiotics based on pus culture sensitivity. All four fractures had gone into non-union. In our study, 4 patients had poor results. These 4 patients were Type II open fractures treated with primary intramedullary nailing. The open fracture had led to the chance of infection which has gone into non-union and along with fracture pattern.

In our study, 8 out of 30 patients (26%) developed anterior knee pain. In our study cause for knee pain was unclear. However, the probable causes were nail prominence above the proximal tibial cortex, damage to the infrapatellar nerve.

DISCUSSION

Our study highlights the importance of intramedullary nailing for the treatment of isolated tibial shaft fractures in the midst of various other modalities of treatment which include functional cast bracing, external fixation, internal fixation of plates and screws.

In current series, 30 cases of fracture of shaft of the tibia were treated by closed reamed interlocking intramedullary nailing. They were followed up for an average of 6 months. The purpose of this study was to evaluate the end results of

treatment of these patients. These cases were of different age groups, occurred in both sexes; and the fracture was of different types and at different levels. The interlocking nail restores length, alignment, controls rotation, preserves periosteal blood supply, some amount of endosteal blood supply, biological osteosynthesis and reduces the rate of infections and malunion. The advantage of locking screws over conventional methods is that it reduces the rate of malunion, prevents loss of alignment, angulation, and shortening which are commonly found in a plaster cast or functional brace.

The average age of all cases in this series was 34.7 years. The fracture is more common in the age group of 18-39 years. Active young individuals were the major sufferers. Working men with outdoor activities are majority. Road traffic accident is the major cause of injury.

Mid diaphyseal fractures were the most commonly involved site 22 (73.3%) cases out of 30.

The time for union ranged from 4 to 9 months with an average of 5 months. 17 fractures healed before 5 months (20 weeks), 7 out of 30 cases went for delayed union which is around 23%. All delayed union were managed successfully with secondary dynamization and bone marrow injection. In our series, a displaced and comminuted tibial fracture with an intact fibula seems to be a cause for delayed union and non-union. In fact, our study indicates that an intact fibula with comminution of tibial shaft fractures particularly in patients aged more than 20-year-old is frequently associated with delayed tibial union, non-union, and secondary pain.

CONCLUSIONS

Closed intramedullary interlocking nailing is an effective mode of treatment in isolated tibial shaft fractures in closed and open Type I injuries. Isolated tibial shaft fractures with undisplaced or minimal displaced fractures have united well; more displaced fractures have gone into delayed union.

Immediate post-operative partial weight bearing and subsequent FWB helps in fracture union. Open injuries with severe soft tissue injury were the main cause for non-union. The proximal end of nail prominence above cortex is the major cause for anterior knee pain.

Overall functional results are good with closed intramedullary interlocking nailing for tibial diaphyseal fractures. Intramedullary interlocking nails are the current choice of treatment for isolated tibial shaft fractures which are undisplaced or minimally displaced fractures as it shows better union rates and early mobilization.

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Incidence of Enterococcal Urinary Tract Infection and it's Sensitivity Pattern among Patients Attending Teerthanker Mahaveer Medical College and Research Centre, Moradabad, India

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Abstract

Introduction: *Enterococcus* is an opportunistic pathogen which is a major causative agent of nosocomial infection and it is especially in hospitalized patients. It causes urinary tract infection (UTI). The aim of this study is to isolate enterococci from cases of UTI and to know the antibiotic susceptibility pattern of the isolates.

Materials and Methods: Early morning clean catch midstream urine sample was collected into a wide-mouthed sterile screw capped container then transported to the laboratory. Then, culture and antibiotic susceptibility were performed.

Result: Out of 627 bacteriuria patients, 106 *Enterococcus* were isolated and 521 other bacteria (83.09%). Out of 627 patients positive urine culture, the isolation of bacterial species were found as *Escherichia coli* 231 (36.84%), *Staphylococcus aureus* 119 (18.98%), coagulase-negative *Staphylococci* 21 (3.34%), *Enterococcus* 106 (16.91%), *Proteus* 13 (2.07%), *Enterobacter* 26 (4.15%), *Citrobacter* 16 (2.55%), *Pseudomonas* 19 (3.03%), *Acinetobacter* 24 (3.83%), and *Klebsiella pneumoniae* 48 (7.66%). Females 70 (66.04%) were more prone to enterococcal infection as compared to male 36 (33.96%) and high prevalence was seen in the age group of 21-30 years 36 (33.96%) followed by 31-40, 51-60, 41-50, 61-70, 11-20, and <10. *Enterococcus* showed 98.11% sensitivity against vancomycin followed by teicoplanin.

Discussion: The commensal of the intestinal human flora are enterococci. In this study, enterococcal UTI was more prevalent than the other studies. In this study, females were 70 (66.04%) more prone to enterococcal infection as compared to male 36 (33.96%), and the highest prevalence of enterococcal infection was seen in the age group 21-30 36 (33.96%) years and most sensitive to vancomycin (98.11%), linezolid (92.45%).

Conclusion: It is concluded that *Enterococcus* are Gram-positive cocci presenting as a harmless commensals, causes UTI infection and which is highly prevalent among females than males. Early and proper treatment can decrease the antibiotic resistance.

Key words: Coagulase-negative *Staphylococci*, *Escherichia coli*, *Staphylococcus aureus*, Urinary tract infection, Vancomycin resistant *Enterococcus*

INTRODUCTION

In each year, millions of people are affecting by urinary tract infection (UTI), it is a serious health problem. In the

world, all age groups across the lifespan are affected and it is the most cause of mortality and morbidity.¹ The lower urinary tract or both the upper and lower tract is involved.²

Within urinary tract, the most frequent sites of infection are urethra and urinary bladder.³ The risk of infection related to the frequency of sex was found that women were more prone to UTIs than man.⁴ A significant number of microorganism, usually $>10^5$ cells/ml of urine is said to exist by UTI, are detected in properly collected mid-stream "clean catch" urine.^{5,6} The detection and identification of

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the causative pathogen in the urine are the gold standard for diagnosis.⁷

The important opportunistic pathogens and indigenous flora of the intestinal tract, oral cavity and genitourinary tract of human are enterococci especially in hospitalized patients.⁸ The human pathogen capable of causing UTI, intra-abdominal infection, pelvic wound infection biliary tract infection, respiratory infection, neonatal sepsis accompanied by bacteremia or meningitis or both are *Enterococcus faecalis* (80-90%) and *Enterococcus faecium* (5-10%) which are two commonly prevalent species.⁹

Now enterococci are included in the genus *Streptococcus* but originally, it was classified as enteric Gram-positive cocci. Enterococci were classified as Group D streptococci by different biochemical characteristics in the late 1930s. In the late 1930s, it was suggested that for streptococci the term enterococci should be used specifically that grow at pH 9.6, 10 and 45°C both, in the presence of 6.5% NaCl (sodium chloride), hydrolyze esculine and survive at 60°C for 30 min.

Studies were involved during the mid-1980s, that includes fatty acid composition, nucleic acid hybridization and comparative oligonucleotide cataloguing of 16s ribonucleic acid led to the acceptance that enterococci were merited their own genus and sufficiently distinct from other streptococci.

Although approximately a dozen *Enterococcus* species have been recognized, and out of those only two are responsible for the majority of human infections. There are at least 12 species that causes enterococci infection that includes *E. faecalis*, *Enterococcus avium*, *Enterococcus casseliflavus*, *Enterococcus mundtii*, *Enterococcus pseudoavium*, *Enterococcus raffinosus*, *Enterococcus durans*, *Enterococcus gallinarum*, *E. faecium*, *Enterococcus hirae*, *Enterococcus malodoratus*, and *Enterococcus solitarius*. Addition to this list, some additional species have been also proposed such as *Enterococcus columbae*, *Enterococcus cecorum*, *Enterococcus saccharolyticus*, *Enterococcus dispar*, *Enterococcus seriolicida*, *Enterococcus sulfureus*, and *Enterococcus flavescens*. Either *E. faecalis* or *E. faecium* causes infections most clinically. Until recently the predominant enterococcal species are *E. faecalis* and *E. faecium* that accounting for 80-90% and 5-15% of all clinical isolates, respectively.¹⁰

A part of the normal flora of bowel, genital tract anterior urethrae of humans of humans are enterococci¹¹ among hospitalized patients, the organism can cause serious infection like endocarditis UTI, wound infection is enterococci, have been considered of relatively low virulence.¹¹ Symptoms include frequency, dysuria,

suprapubic pain along with loin pain. There may be fever with rigors. UTI due to the enlarged prostate is relatively common cloudy, dark, bloody, or unusual smelling urine.

The most common infection caused by bacteria in the urinary tract is an enterococcal infection but it also causes bacteremia, wound infection, intra-abdominal abscesses, infective endocarditis, and infrequently meningitis.¹² All over the world, particularly in developing countries, UTIs were treated by antibiotics though resistance to antibiotics is highly prevalent in bacterial isolates.¹³ Due to the increasing level of antimicrobial resistance, treatment of UTI has thrown up a lot of challenges in over the years.¹⁴

In UTI, endocarditis, bacteremia, intra-abdominal and intra-pelvic abscesses are the serious relevant infection of nosocomial and among *Enterococcus* genus; the main causative agents are *E. faecium* and *E. faecalis*.¹⁵

The commensal organisms are enterococci. In the bowel, the normal inhabit are enterococci. They become opportunistic pathogens. Human infection caused by enterococcal species includes *E. avium*, *E. gallinarum*, *E. casseliflavus*, *E. durans*, *E. raffinosus* and *E. mundtii*.¹⁶ It increase virulence elements in hospitalized colonize patients of nosocomial enterococci.¹⁷

MATERIALS AND METHODS

The study was conducted in Department of Microbiology, Teerthanker Mahaveer Medical College and Research Centre, Moradabad from February 2015 to January 2016; 106 isolated *Enterococcus* were collected from the urine sample.

Early morning clean catch midstream urine sample was collected into a wide-mouthed sterile screw capped container from clinically suspected patients.

With a calibrated micro loop, 0.001 ml of urine was cultured onto cystine lactose electrolyte lactose deficient agar, blood agar, MacConkey agar, and Muller Hinton Agar Plates. After overnight incubation at 37°C for 24 h, colony counts yielding bacterial growth of $\geq 10^5$ /ml was considered as significant in the urine sample.

Heat tolerance test, i.e., growth for 30 min at 60°C, in the presence of sodium chloride of 6.5% (salt tolerance test), growth occur, *Enterococcus* genus were confirmed by catalase negative and blackening of bile-esculin agar among all the Gram-positive cocci. Sugar fermentation test including, lactose, mannitol, glucose, arabinose, potassium tellurite reduction, motility testing species of *Enterococcus* were further identified.

As per CLSI guidelines, on Mueller Hinton agar, antimicrobial susceptibility testing was performance: Vancomycin (30 µg), penicillin-G (10 µg), ampicillin (10 µg), amoxicillin (20 µg), ampicillin/sulbactam (10/10 µg), norfloxacin (10 µg), co-trimoxazole (25 µg), erythromycin (15 µg), gentamicin (120 µg), chloramphenicol (30 µg), ciprofloxacin (5 µg), clindamycin (2 µg), levofloxacin (5 µg), linezolid (15 µg), tobramycin (10 µg), amikacin (30 µg), pristinomycin (15 µg), teicoplanin (30 µg), tetracycline (30 µg), rifampicin (5 µg), ofloxacin (5 µg), and cefotaxime (30 µg).

RESULT

In this study, 627 patients were showed to be urine culture positive of which there were 106 *Enterococcus* (16.91%) and 521 other bacteria (83.09%) (Figure 1). Out of 627 patients positive urine culture, the isolation of bacterial species were found as *Escherichia coli* 231 (36.84%), *Staphylococcus aureus* 119 (18.98%), coagulase-negative *Staphylococci* 21 (3.34%), *Enterococcus* 106 (16.91%), *Proteus* 13 (2.07%), *Enterobacter* 26 (4.15%), *Citrobacter* 16 (2.55%), *Pseudomonas* 19 (3.03%), *Acinetobacter* 24 (3.83%), and *Klebsiella pneumonia* 48 (7.66%) (Table 1) (Figure 2).

The Gram-positive bacteria and Gram-negative bacteria proportion were 250 (39.87%) and 377 (60.13%), respectively. Female 70 (66.04%) were found to be more prone to enterococcal infection as compared to male 36 (33.96%) (Table 2). The high prevalence of enterococcal infection was seen in the age group 21-30 years 36 (33.96%)

Table 1: Bacterial isolates in positive culture

Bacteria	Frequency (n)	Percentage
<i>Enterococcus</i>	106	16.91
<i>E. coli</i>	231	36.84
<i>Klebsiella</i>	48	7.66
<i>S. aureus</i>	119	18.98
CONS	21	3.34
<i>Streptococcus</i>	4	0.64
<i>Enterobacter</i>	26	4.15
<i>Citrobacter</i>	16	2.55
<i>Pseudomonas</i>	19	3.03
<i>Proteus</i>	13	2.07
<i>Acinetobacter</i>	24	3.83
Total	627	100

E. coli: *Escherichia coli*, *S. aureus*: *Staphylococcus aureus*, CONS: Coagulase-negative *Staphylococci*

Table 2: Distribution of *Enterococcus* according to gender

Gender	Frequency	Percentage
Female	70	66.04
Male	36	33.96

followed by 31-40, 51-60, 41-50, 61-70, 11-20 and <10 age groups (Table 3).

In this study, *Enterococcus* showed that against vancomycin 98.11% sensitivity which is followed by teicoplanin (94.33%) and ampicillin/sulbactam (73.59%), ampicillin (58.49%), amoxicillin (58.49%), rifampicin (58.49%), and cefotaxime (50.94%), among urinary isolates, least sensitivity was observed with clindamycin (11.32%) (Table 4) (Figure 3).

DISCUSSION

The commensal of the intestinal human flora is enterococci. The site such as genitourinary tract, oral cavity and skin especially in the perineal area are less often colonized by these organisms. In the hospitalized patients, the main sites

Table 3: Distribution of *Enterococcus* is according to age and sex

Age	Female n=70 (%)	Male n=36 (%)	Total n=106 (%)
0-10	2 (2.86)	-	2 (1.89)
11-20	14 (20)	4 (11.11)	18 (16.98)
21-30	32 (45.71)	6 (16.67)	38 (35.85)
31-40	14 (20)	8 (22.22)	22 (20.75)
41-50	4 (5.71)	4 (11.11)	8 (7.55)
51-60	-	10 (27.78)	10 (9.43)
61-70	4 (5.71)	4 (11.11)	8 (7.55)
Total	70	36	106

Table 4: Antibiotic sensitivity pattern of *Enterococcus* isolated from urine sample

Antibiotics	Sensitive n (%)
Vancomycin	104 (98.11)
Teicoplanin	100 (94.33)
Linezolid	98 (92.45)
Ampicillin/sulbactam	78 (73.59)
Ampicillin	62 (58.49)
Amoxicillin	62 (58.49)
Rifampicin	62 (58.49)
Cefotaxime	54 (50.94)
Penicillin-G	50 (47.17)
Chloramphenicol	44 (41.50)
Cephalexin	28 (26.41)
Tobramycin	28 (26.41)
Tetracycline	26 (24.52)
Ofloxacin	24 (22.64)
Norfloxacin	22 (20.75)
Pristinomycin	20 (18.87)
Ciprofloxacin	20 (18.87)
Co-trimoxazole	18 (16.98)
Gentamicin	18 (16.98)
Levofloxacin	18 (16.98)
Erythromycin	14 (13.20)
Amikacin	14 (13.20)
Clindamycin	12 (11.32)

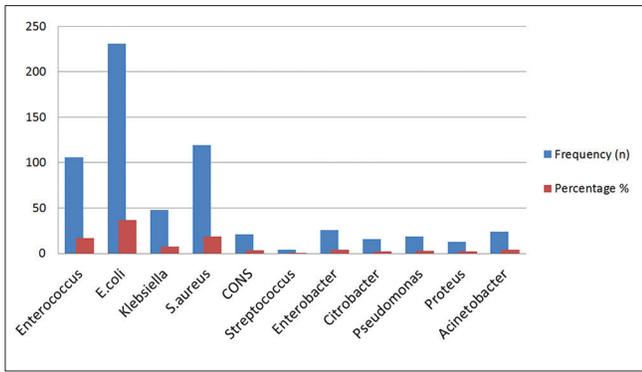


Figure 1: Distribution of different bacteria

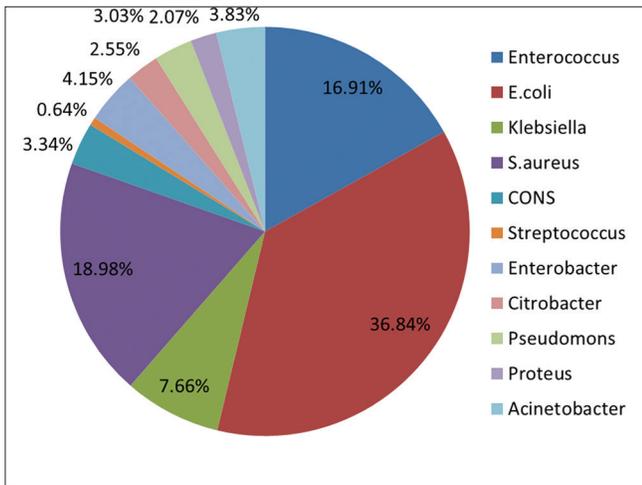


Figure 2: Distribution of different bacterial percentage

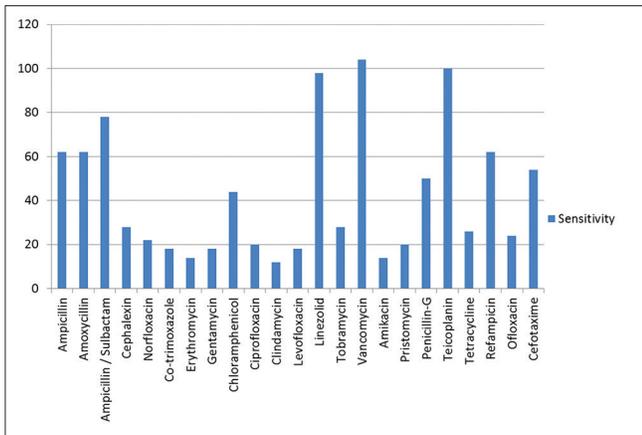


Figure 3: Antibiotic sensitivity pattern of *Enterococcus*

of colonization are ulcers, gastrointestinal tract and soft tissue wounds. In the recent years, important causes which are increasingly of nosocomial infections are enterococci which are regarded as low-grade pathogens traditionally.¹⁰

In the current study, enterococcal UTI was more frequent than has been reported in other studies. In present study 106 (16.91%) *Enterococcus* was isolated from the urine

sample. This study is comparable with the study of Tayebi *et al.*¹⁸ and Jombo *et al.*,¹⁹ in which *Enterococcus* sp. was 8.7% and 12.4%, respectively.

In this study, females were 70 (66.04%) more prone to enterococcal infection as compared to male 36 (33.96%). This is comparable with the study carried out by Shrivastav *et al.* in which the number of females infected with enterococcal infection was more (72%) than number of males.²⁰

In this study, the highest prevalence of enterococcal infection was seen in the age group 21-30 was 36 (33.96%) years. Similar findings of higher infection rate in the age group 21-30 years were reported by Bose *et al.*²¹

In this study, *Enterococcus* isolates from the various clinical samples were sensitive to vancomycin (98.11%) and linezolid (92.45%). This study is comparable with the study carried out by Abdulla and Abdulla,²² in which sensitivity of vancomycin and teicoplanin was 99.1% each.

CONCLUSION

It is concluded that *Enterococcus* are Gram-positive cocci presenting as harmless commensal to multifaceted deadly pathogens. It causes UTI infection, which is highly prevalent among females than males. Thus, in present study *Enterococcus* showed the highest susceptibility to the vancomycin, hence, it is the drug of choice, limiting the use of linezolid only in the case of vancomycin-resistant *Enterococcus*.

The positive urine culture with the antibiotic sensitivity of the isolates is very important to an antimicrobial therapy, as antibiotic resistance is a worldwide problem which causes ineffectiveness of treatment. Early and proper treatment can decrease the antibiotic resistance.

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Risk Factors Associated with Clinically Significant Macular Edema in Patients with Type 2 Diabetes Mellitus

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Abstract

Introduction: Diabetic macular edema (DME) is the major cause of vision loss in diabetic retinopathy (DR). Apart from diabetes, a number of other systemic factors have an important role in occurrence and progression of DME. Control of these factors along with control of blood sugars can prevent or reverse the maculopathy, thereby restore the vision of diabetic patients.

Methodology: Cross-sectional comparative study. Patients with Type 2 diabetes were screened for DR. After thorough examination including fundus examination, patients were divided into two groups (Group 1 - Retinopathy with clinically significant macular edema [CSME] and Group 2 - Retinopathy without CSME). A detailed history of the duration of diabetes, treatment history, hypertension, and hyperlipidemia were taken. The mean values of three consecutive blood pressure (BP) readings were assessed. Following blood investigation, serum lipid profile, glycosylated hemoglobin (HbA1c), urine albumin, renal function test of the concerned patients were done. The significance of the above risk factors was compared in both the groups involved in the study.

Results: In the present study of 170 patients with DR, there was no significant difference in the age and gender distribution among two groups. The mean value of fasting blood sugar, postprandial blood sugar, and HbA1c were higher in the study group than control group. In this study, the mean value of systolic BP and diastolic BP were significantly higher in the study group compared to control group. Serum lipids, serum cholesterol, triglycerides, low-density lipoprotein (LDL), and very LDL levels were significantly higher in patients with CSME. Microalbuminuria and macroalbuminuria showed a correlation with CSME.

Conclusion: Systemic risk factor shows a significant association with CSME in DR. Thus, early detection of these risk factors and their control has a significant role in preventing the development and progression of maculopathy in DR patients thereby preventing severe visual loss.

Key words: Albuminuria, Clinically significant macular edema, Diabetic retinopathy, Glycosylated hemoglobin, Hypertension, Lipid profile

INTRODUCTION

Diabetic retinopathy (DR) is a chronic progressive, potentially sight-threatening disease of the retinal vasculature associated with the prolonged hyperglycemia and other conditions linked to diabetes mellitus (DM) such

as hypertension.¹ It eventually afflicts virtually all patients with diabetes. It is estimated that diabetes affects 4% of the world's population, almost half of whom have some degree of DR at given time.^{2,3} DR occurs in all Type 1 and 75% of Type 2 DM after 15 years of duration of diabetes.^{2,4,5} Visual disability from DM is a significant public health problem. However, this morbidity is largely preventable and treatable.²

Diabetic macular edema (DME) is the most frequent cause of severe vision impairment in diabetic patients.⁶ Diabetic maculopathy can occur at any level of retinopathy and alter the structure of macula, significantly affecting its function. Although treatment of established retinopathy can reduce

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the risk of visual loss by 60%, DR remains the leading cause of blindness among working-aged adults in the world.

The identification of risk factors is important for the evolution of better management strategies for DR. Previous studies have shown possible risk factors for retinopathy included diabetic duration, glycemic control, age of onset diabetic treatment, systemic hypertension, renal function/nephropathy, body mass, sex, human leukocyte antigen status, cigarette smoking, and elevated blood lipids.^{4,5,7-17} Despite the recognized importance of maculopathy as a cause of visual morbidity in diabetes, risk factors for maculopathy have received considerably less attention in the literature. Diabetic duration, age, sex, age of diagnosis, insulin use, higher glycosylated hemoglobin (HbA1C), diuretic use, systemic hypertension, and proteinuria have been associated with DME.^{14,18} Once diabetic maculopathy occurs, there is no satisfactory treatment and the prognosis of visual outcome is poor, so it is always better to prevent its development. Hence, there is a need for a study to find out the risk factors associated with the development of clinically significant macular edema (CSME) in diabetic patients, to control the same and subsequently reduce the incidence of diabetic maculopathy in future.

METHODOLOGY

This is a cross-sectional comparative study conducted in the Department of Ophthalmology from January 2014 to July 2015.

Inclusion Criteria

All patients (outpatients and inpatients) of either sex with Type 2 DM who will be screened for DR at ophthalmology outpatient department and found to have DR with or without CSME.

Exclusion Criteria

(1) Patients who have undergone any intraocular surgery in the past 3 months, (2) patients undergone any intraocular laser treatment or intraocular injection in the past 3 months, (3) patients with history of intake of drugs (corticosteroids, nephrotoxic) in the past 3 months or any non-diabetic renal disease, (4) patients suffering from non-diabetic maculopathy (age-related macular degeneration/macular dystrophy), (5) patients with chronic liver disease, (6) patients with significant media haziness preventing adequate visualization of the fundus, and (7) patients with insulin dependent DM or gestational DM.

All patients presenting with Type 2 DM were subjected to complete ophthalmologic examination by assessing the visual acuity with Snellen chart, slit lamp examination,

intraocular pressure with I care tonometry. Fundus examination was conducted with a direct ophthalmoscope, indirect ophthalmoscope, and slit lamp biomicroscopy using +90D lens.

After fundus examination, only patients having retinopathy in at least one eye were selected for further study and subsequently divided into 2 groups (Group 1 - Retinopathy with CSME and Group 2 - Retinopathy without CSME). Informed consent was taken from the concerned patients. Fundus picture of the patients was taken with DRS and fundus camera. DR was classified according to early treatment DR study criteria. OCT was done in a few patients with CSME to quantify and find out the type of macular edema. FFA was done in a few patients to decide on the treatment plan.

A detailed history of the duration of diabetes, type of treatment, smoking/tobacco use, hyperlipidemia and hypertension were taken from the above-selected patients. The mean value of the three consecutive blood pressure (BP) reading was assessed. Following blood investigations (serum lipid profile, glycosylated Hb, urine albumin, and renal function test) of the concerned patients was done. HbA1c determination is based on the turbidimetric inhibition immunoassay. The significance of the above risk factors was compared in both the groups involved in the study like descriptive.

The data were analyzed using various statistical tests such as descriptive and inferential statistics, mean \pm standard deviation (minimum-maximum), Student's *t*-test (two-tailed independent), and Chi-square or Fischer exact test.

RESULTS

In this comparative study, 85 patients were allotted in each group. The mean age of the patients in the study group (with CSME) was 57.02 ± 9.75 and in the control group (without CSME) mean age was 56.42 ± 9.25 . There was no significant difference in age distribution between the two groups ($P = 0.681$) (Table 1). In the study group, 46 (54.1%) were males and 29 (34.1%) were females. In the control group, 56 (65.9%) were males and 29 (34.1%) were females. There was no significant difference in the gender distribution among the two groups ($P = 0.117$).

In this study, 20% had duration <5 years, 27.1% in between 5 and 10 years, 25.9% in between 11 and 15 years, 16.5% in between 16 and 20 years, and 10.6% >20 years. In the control group, the majority of patients had duration <5 years (44.7%). This shows that the duration of diabetics is more in a study group with $P = 0.003$.

Table 2 shows the distribution of the patients in both the groups on the basis of treatment. In the study group, out of 85 patients, 2 (2.4%) have not received any treatment, whereas in the control group, none of the patients were there without ant treatment. The majority of the patients in both the groups were on treatment with oral hypoglycemic agents (57.7% in the study group and 74.1% in control group). In the study, 40% patients were on treatment with insulin, whereas in control group, 16.4% were on treatment with insulin.

Tables 3 and 4 compare the laboratory investigations between the two groups which are studied such as fasting blood sugars, postprandial blood sugar (PPBS), HbA1c, lipid profile, and urine albumin levels.

Table 5 shows the best corrected visual acuity (BCVA) in patients of both the groups (considering the BCVA of the worst eye). In the study group, out of 85 patients,

Table 1: The distribution of patients as per duration of DM

Duration of DM (years)	n (%)	
	Study group	Control group
<5	17 (20.0)	38 (44.7)
5-10	23 (27.1)	24 (28.2)
11-15	22 (25.9)	14 (16.5)
16-20	14 (16.5)	5 (5.9)
>20	9 (10.6)	4 (4.7)
Total	85 (100)	85 (100)

DM: Diabetes mellitus

Table 2: The distribution of the patients in both the groups on the basis of treatment

Treatment	n (%)	
	Study group (n=85)	Control group (n=85)
No treatment	2 (2.4)	0 (0.0)
OHA	49 (57.7)	63 (74.1)
Insulin	0 (0.0)	1 (1.1)
OHA+Insulin	34 (40)	13 (15.3)

OHA: Oral hypoglycemic agents

Table 3: Comparisons between the mean values of the parameters

Parameters	Study group	Control group	P values
FBS (mean)	151.62±51.54	153.54±53.34	0.812
PPBS (mean)	230.21±62.68	211.84±62.57	0.057
HbA1c (mean)	10.09±1.74	8.90±2.18	<0.001**
Lipid parameters			
Cholesterol	211.15±64.1	173.82±42.28	<0.001**
TGL	199.44±57.02	156.85±62.39	<0.001**
HDL	35.95±11.78	32.67±9.05	0.043
LDL	135.71±46.87	111.54±34.38	<0.001**
VLDL	35.82±12.18	30.28±9.40	0.001**

**p<0.001, FBS: Fasting blood sugars, PPBS: Postprandial blood sugar, HbA1c: Glycosylated hemoglobin, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoprotein, TGL: Triglycerides level

none had BCVA of 6/6, whereas in the control group, 20 patients had BCVA of 6/6. The majority of patients in the study group had moderate visual impairment (51.76%), whereas in the control group, only 24.71% had moderate visual impairment. In the study group, out of 85 patients, 21 (24.71%) had severe visual impairment, whereas in the control group, only 1 patient (1.18%) had severe visual impairment.

Table 6 shows the severity of DR in both the groups (according to the worst eye). The majority of patients in

Table 4: Compares the levels of HbA1c values, lipid parameters, and urine albumin levels

Parameters	n (%)		P values
	Study group (n=85)	Control group (n=85)	
HbA1c			<0.001**
<6.5	0 (0)	10 (11.8)	
6.5-7.0	3 (3.5)	6 (7.1)	
>7.0	82 (96.5)	69 (81.2)	
Total cholesterol			<0.001**
<200	36 (42.4)	58 (68.2)	
200-240	25 (29.4)	21 (24.7)	
>240	24 (28.2)	6 (7.1)	
TGL			<0.001**
<150	19 (22.4)	36 (42.4)	
150-200	23 (27.1)	38 (44.7)	
200-500	43 (50.6)	11 (12.9)	
>500	0 (0.0)	0 (0.0)	
HDL			0.032*
<40	61 (71.8)	61 (71.8)	
40-60	18 (21.2)	24 (28.2)	
>60	6 (7.1)	0 (0.0)	
LDL			0.001**
<100	20 (23.5)	26 (30.6)	
100-130	29 (34.1)	34 (40.0)	
130-160	12 (14.1)	21 (24.7)	
160-190	18 (21.2)	3 (3.5)	
>190	6 (7.1)	1 (1.2)	
VLDL			0.029*
<30	28 (32.9)	42 (49.4)	
≥30	57 (67.1)	43 (50.6)	
Urine albumin			<0.001**
No albuminuria	5 (5.9)	38 (44.7)	
Microalbuminuria	11 (12.9)	2 (2.4)	
Macroalbuminuria	69 (81.2)	45 (52.9)	

***: p<0.001, HbA1c: Glycosylated hemoglobin, TGL: Triglycerides level, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoprotein

Table 5: Comparison of BCVA in the study and control group

BCVA	n (%)	
	Study group (n=85)	Control group (n=85)
6/6	0 (0.0)	20 (23.53)
6/9-6/12	20 (23.53)	43 (50.59)
6/18-6/36	44 (51.76)	21 (24.71)
≤6/60	21 (24.71)	1 (1.18)

BCVA: Best corrected visual acuity

Table 6: Comparison of the severity of DR between the study and control group

Fundus	n (%)	
	Study group (n=85)	Control group (n=85)
Mild NPDR	10 (11.76)	32 (37.65)
Moderate NPDR	33 (38.82)	32 (37.65)
Severe NPDR	23 (27.06)	11 (12.94)
PDR	19 (22.35)	10 (11.76)

DR: Diabetic retinopathy, NPDR: Non-proliferative diabetic retinopathy, PDR: Proliferative diabetic retinopathy

the control group had mild and moderate non-proliferative DR (NPDR) (37.65% each). In the study group, only 11.76% had mild NPDR and 38.82% had moderate NPDR. Severe NPDR was present in 27.06% of patients in the study group, whereas 12.94% of patients in control group. Proliferative DR was present 22.35% in the study group and 11.76% in control group (** $P < 0.001$).

DISCUSSION

DR is the most common microvascular complication in diabetes which can produce a severe visual loss.^{19,20} It is responsible for 4.8% of the 37 million cases of blindness throughout the world.²¹ Severe visual impairment among diabetic patients may be caused by diabetic maculopathy. Since diabetic maculopathy is characterized by increased capillary leakage due to alterations in the microcirculation of the macula.^{22,23} This study was conducted to find out the role of metabolic control and other systemic factors associated with CSME in Type 2 diabetic patients.

Age group of the patients included in the study ranged from 30 to 80 years. There was no significant difference in age and gender between two groups. Both groups were matched in terms of age and gender. In our study, it was found that majority of patients without CSME had duration of DM >5 years (80%). This shows that the duration of DM is significantly associated with CSME. Previous studies such as WESDR data also demonstrated the duration of DM as one of the risk factors for DME.^{19,24}

Raised HbA1c levels have been shown to be a significant risk factor for DME in previous studies.²⁵⁻²⁷ In this study, the mean HbA1c value was significantly higher in patients with CSME. None of the patients with CSME had HbA1c under control, and the majority of patients (96.5%) had suboptimal HbA1c. This correlates well with other studies, Jew *et al.* in their study concluded that HbA1c had a significantly high odds ratio of developing CSME.²⁸ Rema and Pradeepa in CURES study reported that for every 2% elevation of HbA1c, the risk of DR increases by a factor of 1.7. In this study, the mean PPBS value was also higher in CSME group though it was not statistically significant.

In this study, the mean systolic and diastolic BP were significantly higher in patients with CSME.

There has been increasing interest in the link between the serum lipids and maculopathy in view of the evolving medical treatment for hyperlipidemia. In this study, serum cholesterol, triglycerides level (TGL), low-density lipoprotein (LDL), and very LDL levels were significantly higher in patients with CSME. The association between serum lipids and CSME is biologically plausible. Several proposed mechanisms discussed in earlier reports include the direct involvement of serum lipids in endothelial dysfunction²⁹ which subsequently results in the breakdown of the blood-retinal barrier.

In our study, the incidence of microalbuminuria and macroalbuminuria is significantly more associated with CSME. 81.2% patients with CSME had macroalbuminuria and 12.9% patients with CSME had microalbuminuria. This shows that both clinical and subclinical nephropathy has an important role in diabetic maculopathy. Hypoalbuminemia, which may be secondary to renal loss of albumin, has been postulated to be one of the factors involved in the formation of macular edema.

CONCLUSION

In this study, duration of DM, uncontrolled glycemic status, systemic hypertension, albuminuria, serum cholesterol, TGL, LDL, and VLDL showed a significant association with CSME. However, serum high-density lipoprotein has not shown a correlation with CSME.

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Comparative Evaluation of Techniques in Supraclavicular Brachial Plexus Block: Conventional Blind, Nerve Stimulator Guided, and Ultrasound Guided

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Abstract

Introduction: In recent years, real-time ultrasonographic guidance has been introduced for peripheral nerve blocks, which is rapidly evolving and becoming increasingly more useful in the field of regional anesthesia.

Objective: The aim of this study was to compare the three techniques of brachial plexus block. Trial design: This was a prospective, randomized clinical trial.

Materials and Methods: About ninety patients of either sex, aged 18–60 years, ASA physical status I and II, and posted for elective surgery of upper limb were included. Brachial plexus was blocked by conventional blind in Group I (CB), Group II nerve stimulator (NS) technique whereas Group III by ultrasound (US)-guided technique. All the three groups were injected 2% xylocaine with adrenaline 1:200,000 in a dose of 7 mg/kg body weight. The drug solution was diluted with normal saline to make a final concentration of 1.5%.

Results: Comparison of blockade characteristics between the CB, NS, and US-guided groups revealed that the procedural time and number of skin puncture were nonsignificant in all the three groups. The onset of sensory and motor blockade was significantly less in US group compared to other groups. The mean duration of analgesia was significantly higher in both NS and US groups compared to CB group. The incidence of patchy effect and blockade failure requiring general anesthesia was significantly higher in CB group (13.3%) compared to NS group (10%) and US group (3.3%).

Conclusion: The success rate and effective quality of the block were more satisfactory with US technique than the NS or CB technique. The onset time of sensory and motor blockade was significantly less in US group, while the incidence of complications such as vessel puncture was seen only in CB group.

Key words: Brachial plexus, Forearm fracture, Supraclavicular block, Ultrasound guidance

INTRODUCTION

Supraclavicular approach is an easy and effective method of brachial plexus block. It is used to perform surgeries

on the distal half of arm, forearm, and hand as a safe alternative to general anesthesia. The conventional blind (CB) technique depends on subjective response and is associated with significant failure rate, injury to nerves, and vascular structures.¹ In the nerve stimulator (NS) technique, nerve plexus is located by eliciting motor response, which is associated with patient discomfort, patchy block, failure of block, injury to nerves, and vascular structures. Nowadays, the ultrasound (US) technique is being used to locate the nerve plexus and its spatial relationship with other surrounding tissues as it provides the real-time view. US guidance not only determines the size, depth, and exact

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location of the plexus, but also its neighboring structures and achieves a satisfactory and dense blockade, but due to variable user experience, the results may vary.²

The primary aim of the study was to compare the three techniques of supraclavicular approach of brachial plexus block in terms of time taken for block, time of onset, quality of sensory and motor blockade, duration of analgesia, and failure rates. As a secondary objective, we studied the occurrence of complications such as nausea, vomiting, hypotension, arrhythmias, and convulsions.

MATERIALS AND METHODS

After taking Institutional Ethical Board's approval and patient's informed consent, 90 cases of ASA I, II, and III grading of both sexes between age 18 and 60 years, and posted for elective surgery of upper limb of <90 min duration were enrolled in this prospective, comparative, and randomized study. Exclusion criteria included patient's refusal, ASA IV status, infection at the site of block, coagulopathy, allergy to local anesthetic, pulmonary pathology, and pre-existing neurological deficit in the upper limbs. All patients were randomly divided into three different groups using closed envelope method. Group I was CB technique, where the block was administered following eliciting of paresthesia or hitting first rib as end point. Group II was peripheral NS-guided technique where motor twitches were elicited using current strength of 0.6 mA as end point. Group III used US-guided technique in real-time view for locating the brachial plexus as end point for injecting the drug mixture. A SonoSite Micromaxx-HFL linear 38 probe (6-13 MHz) was used for conducting the block in every case. The probe was covered with tegaderm so as to maintain sterility. It was then placed in the coronal oblique plane in the supraclavicular fossa. The subclavian artery, vein, and the brachial plexus were visualized. The brachial plexus and its spatial relationship to the surrounding structures were scanned. The plexus was identified superolateral to the subclavian artery, consistently in all the cases.

Patients in all the three groups were injected 2% xylocaine with adrenaline 1:200,000 in a dose of 7 mg/kg body weight. The drug solution was diluted with normal saline to make a final concentration of 1.5%. The observed parameters included time of procedure, number of skin puncture, onset of sensory and motor blocked, quality of sensory and motor blocked, duration of analgesia, and for any post block complications.

The sensory and motor blocks were then assessed by an independent observer who was not aware of the technique

used for every 2 min till the onset of block and every 5 min thereafter for 30 min. Any failure in establishing the block was converted to general anesthesia.

The procedural time was defined as the time spent between the insertion of needle using any technique and its removal following the administration of full volume of anesthetic solution. The sensory block was assessed by pinprick and cold application every 2 min until the onset of sensory block. The time from the removal of block needle to the time when the patient first says he/she has reduced sensation when compared to the opposite limb was taken as the time of onset of sensory block. Similarly, the time of removal of the block needle to the time when the patient had weakness of any of the three joints, i.e., shoulder, elbow, or wrist upon trying to perform active movements was taken as the time of onset of motor block.

The quality of sensory block was assessed every 5 min after the onset was established using pinprick method. At the end of 30 min, the sensory block in each dermatome was graded as follows; blocked: Complete absence of sensation; patchy: reduced sensation when compared to the opposite limb; no block: normal sensation. Postoperatively, the patients were supplemented with analgesics when they complained of pain or had a visual analog scale score of more than 4, and the duration of analgesia was recorded.

Statistical Analysis

The data were analyzed using the SPSS (version 19) software. The demographic characteristics, hemodynamics, duration of analgesia, and blockade failures were compared using one-way ANOVA test. Variables such as time of motor, sensory blockade and total duration of analgesia between all the three groups were compared using Chi-square tests and Fisher's exact test, whichever appropriate. *Post hoc* intergroup comparisons were made using Bonferroni's correction. $P < 0.05$ was considered significant.

RESULTS

A total of 96 cases were enrolled during the study period, with 32 cases in each group. Due to protocol violation in 4 cases (i.e., delay in surgery for more than 90 min) and patient's refusal to participate in the study, 2 cases were excluded from the study, leaving a total of 90 cases in the study and 30 cases in each group. There were no significant differences between the three groups with regards to demographic data such as age, sex, weight, ASA grading, and pre-operative vitals parameters (Table 1).

Comparison of blockade characteristics between the CB, NS, and US-guided groups revealed that the procedural

time and number of skin punctures were comparable in all the three groups. On comparison, the onset of sensory and motor blockade was significantly less in US group, whereas they were comparable in NS and CB groups (Table 2). The average duration of surgery was comparable in all the three groups. The mean duration of analgesia too was significantly higher in both NS and US group (3 h 21 min and 3 h 25 min, respectively), whereas it was nonsignificant in CB group (2 h 33 min). The incidence of patchy effect (5 cases) and blockade failure requiring general anesthesia (7 cases) were significantly higher in CB group compared to NS group (3 cases each) and US group (1 case each) (Table 2). No incidence of serious side effects or life-threatening complications such as pneumothorax, arrhythmias, hemodynamic instability, or local anesthetic toxicity was observed in any of the groups.

DISCUSSION

This prospective randomized study was aimed at comparing the efficacy of various brachial plexus blockade techniques. A successful brachial plexus block depends not only on the technique used, but also on the experience of the anesthetist, patient's body habitus, and the amount and type of drug injected.

In recent years, real-time ultrasonographic guidance has been introduced for peripheral nerve blocks, which is rapidly evolving and becoming increasingly more useful in the field of regional anesthesia. It has also resulted in improved success rate of supraclavicular brachial plexus block due to ability to visualize plexus, subclavian artery, first

rib, and pleura.³ This study compared different parameters between CB, NS, and USG-guided supraclavicular block.

The average number of needle pricks required to perform the procedure did not vary in any of the three groups, owing to the user experience in performing the procedures through any of these techniques. Similarly, the average procedure time in this study did not show any significant difference in any of the three groups, with 7 min ± 26 s in blind technique, 6 min ± 32 s in NS group, and 7 min ± 3 s in USG-guided group. It is well known that the learning curve of US-guided blocks may require 15–20 procedures, following which the performance time improves for all inexperienced users. As all the investigators in this study were well versed and in routine use of these techniques, it took comparable time to perform the block in all the three groups.

The onset time of sensory and motor blockade was significantly less using US-guided technique (9 min ± 33 s and 14 min ± 3 s, respectively) while the same were significantly higher using CB (11 min ± 31 s and 17 min ± 1 s, respectively) and NS-guided techniques (20 min ± 1 s and 22 min ± 06 s, respectively). In the earlier studies, the reason for delay in the onset of action in supraclavicular blocks has been attributed to distant spread of injected drugs away from the perineural tissues. This distant spread of injectate not only delays the onset of action, but also shown to limit the duration of action of the local anesthetics. Kapral *et al.*,⁴ Casati *et al.*,⁵ and Soeding *et al.*⁶ compared US- and NS-guided techniques in supraclavicular block and found that the extent of sensory and motor blockade was significantly better in the US group when compared with the nerve stimulation group. Hence, the results in our study are comparable with other researchers.

We observed a higher duration of analgesia in both NS- and US-guided groups compared to CB group. This could be explained by more precise delivery of drug closer to the brachial plexus. Similar findings have been observed by Abrahams *et al.*⁷ where they observed a combined mean increase in block duration of 25% as compared with NS group. A higher incidence of patchy effect requiring

Table 1: Comparison of demographic data between different groups

Demographic data	CB group	NS group	US group	Significance
Age (years)	36.4±12.3	31.5±9.8	34.3±13.1	ns
Weight (kg)	57.6±7.8	51.4±13.2	50.6±9.5	ns
Gender (M:F)	17:13	19:11	14:16	ns
ASA grading (I:II:III)	21:7:2	24:5:1	23:4:3	ns

ns: Non-significant, CB: Conventional blind, NS: Nerve stimulator, US: Ultrasound

Table 2: Comparison of blockade characteristics between different groups

Block characteristics	CB group	NS group	US group	Standard deviation	Significance CB:NS:US (P value)
Procedural time (s)	446.0333	392.8000	423.7000	137.19083	1.00:0.48:1.00
Number of skin punctures	2.4000	2.3000	1.8333	1.10746	1.00:0.42:0.304
Onset of sensory blockade (s)	679.6667	1207.7391	572.9310	401.89227	0.548:0.001:0.001
Onset of motor blockade (s)	1031.93	1324.09	842.97	400.462	0.12:0.135:0.001
Mean duration of analgesia (min)	153.4783	203.3448	205.8333	57.43618	0.74:0.019:0.026
Patchy effect	5	3	1		0.75:0.14:0.045
Failure	4	3	1		1.00:0.004:0.002
Vessel puncture	4	1	0		0.018:0.342:1.000

CB: Conventional blind, NS: Nerve stimulator, US: Ultrasound

intravenous anesthetic supplementation was observed using CB technique (5 cases) compared to NS (3 cases) or US-guided techniques (1 case). Not only the CB technique which relies on eliciting paresthesia, even the peripheral NS technique can result in inadequate blockade owing to anatomical variation and thus sparing of peripheral nerves. Again, these spared nerves have been shown to be more effectively blocked using multiple point paresthesia technique, either by CB or NS-guided technique that points toward the merits of nerve bundle visualization using ultrasonography. Owing to the real-time visualization of injected drug spreading around the nerve sheaths, the failure rate of supraclavicular blocks requiring conversion to general anesthesia was least in US group (3.3%) compared to CB (13.3%) and NS groups (10%). These results correlate with the studies done by Liu *et al.*,⁸ Duncan *et al.*,⁹ Chan *et al.*,¹⁰ and Kapral *et al.*⁴

CONCLUSION

From the present study, it was concluded that the success rate and effective quality of the block were more satisfactory with US technique than the NS or CB technique. Moreover, the incidence of complications such as vessel puncture was seen only in CB group.

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Comparison of Conventional Cephalometric Method of Landmark Identification with Digital Monitor Image and Film-based Digital Image

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Abstract

Introduction: After the standardization of the technical procedures, radiography has become one of the most frequently applied aids in human biometric research. While using this method, it is necessary to make a careful check of the accuracy of the reproduction of cephalometric landmarks.

Purpose: The purpose of this study was a comparison of the conventional cephalometric method of landmark identification with digital monitor image and film-based digital image.

Materials and Methods: Eight observers, all orthodontists, recorded 8 landmarks twice on 10 conventional cephalograms, 10 digital hard copy, and 10 monitor images that were obtained from 10 human skulls in standardized fashion. Digital images were displayed on 15 inches, thin-film-transistor monitor. Recordings were transferred into standardized coordinate systems and evaluated separately for each coordinate. After correcting for magnification, precision was assessed with Maloney-Rastogi tests; intra-observer and inter-observer reproducibility was calculated from squared differences.

Results: Effective magnification was larger for the digital images. Significantly different ($P < 0.05$) precision was found for nasion (N), posterior nasal spine (PNS), sella (S), supraspinale (A), and orbitale (Or), but average standard errors were within the confidence interval. Intra-observer and inter-observer reproducibility did not differ significantly among the three image modes. Squared differences were largest for PNS in three modalities.

Conclusion: Results indicate comparable errors in landmark recording for three evaluated modalities.

Key words: Conventional cephalometry, Digital radiography, Landmark identification, Monitor image, Precision, Reproducibility

INTRODUCTION

The assessment of radiography as a diagnostic aid in orthodontics was proclaimed by W. A. Price in 1900 just 5 years after the invention of X-rays.¹ Thereafter, many investigators produced radiographs for evaluation of the craniofacial measurements, but it was only in the year 1931, that Hofrath in Germany and Broadbent in America

concurrently and independently developed standardized technique for the production of cephalometric radiographs using cephalostat.² Since its inception in early thirties, cephalometry has gained sufficient popularity for clinical use as well as for research in field of growth and estimation of treatment response through measurement of anatomic landmarks in number of various analysis. However, to quantify the precision of measurements, the errors and their sources should be pointed out. According to Baumrind and Frantz,³ variations or errors in the angular and linear measurements are of three basic types: Errors in projection, errors in landmark location, and mechanical errors in drawing lines between points on tracing and in measuring with ruler or protractor. Whereas, Chen *et al.*⁴ points out that the major sources of error in the cephalometric analysis include radiographic

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film magnification, tracing, measuring, recording, and landmark identification.⁵ Identification and reproduction of the landmarks precisely are one of the most effective means of avoiding this inconsistency.

Today with the application of computers in orthodontics, digital enhancement of the images can be done to get precision and accuracy in landmark identification, which resulted in the replacement of conventional film-based radiographic machines with digital systems.⁶ Digital X-rays have many advantages over film-based X-rays. Despite these advantages, however, the diagnostic performance of the new digital systems must be evaluated in comparison with that of the established film-screen combination. Various studies have been published comparing digitized and conventional cephalometric radiographs with respect to validity and reproducibility of angular and linear measurements or accuracy of landmark identification.⁶

The aim of our study was to compare conventional cephalograms with digital hard copy cephalograms and digital monitor image for precision and reproducibility of the landmark identification with the images from both modalities obtained from the corresponding radiographic machines of one manufacturer.⁶

MATERIALS AND METHODS

About 10 dry skulls were selected randomly for film-based digital cephalograms, digital monitor images, and conventional cephalograms. Criteria included while collecting data as follows.

1. Skulls without mandible were selected randomly
2. Three dimensional stabilization of skull was done by ear rods in acoustic meatus and nasal pointer at the frontonasal suture area
3. Internal references for the calculation of magnification were provided by three steel balls (diameter 1.0 mm) that were glued to each skull mid-sagittally in three anatomic regions, namely, glabella, maxilla above the anterior spine, and dorsal part of the palatine raphae
4. Eight observers marked 8 landmarks on transparent film placed on conventional, digital monitor image, and digital film-based cephalograms
5. Same size (10 × 8 inch) was maintained for conventional, digital, and monitor images. Adobe photoshop (7.1 Version) and PowerPoint stretch options were used to get the same size on flat screen (thin-film-transistor monitor)
6. Statistical presentation was done by Maloney-Rastogi test and graphical representation by Bland-Altman plots. The difference between the methods were

plotted against the mean $([CO+DH+MO]/3)$, where CO = Conventional, DH = Digital hard copy, and MO = Monitor image⁶

7. Consequently, the following landmarks were selected for evaluation: Sella, nasion, anterior nasal spine (ANS), posterior nasal spine (PNS), orbitale, supraspinale, porion, and basion.

The entire tracing evaluation procedure was repeated for the entire data material consisted of 10 images of 10 skulls acquired in 3 modalities (CO, DH, and MO) with 8 landmarks recorded twice by 8 observers. The time gap between the first and second registration was at least 1 week.

In our study, the transparent films obtained from all images were placed on millimeter-scaled graph paper, and an X, Y coordinate system was constructed with reference ball number 1 and 2 (X-axis) and the reference ball number 3 and 2 (Y-axis). Precision was assessed by including 95% confidence interval (CI) of the differences.⁶ Intra-observer reproducibility was calculated from squared differences between both observations averaged over all skulls, and inter-observer reproducibility was expressed as squared differences between observers averaged for each skull and observation. Differences were compared with Maloney-Rastogi test with $P < 0.05$ considered to be significant.

For digital image processing and enhancement, Multiscale Image Contrast Amplification software was used. This enables the implementation of subsets of specific image processing algorithms such as detail contrast enhancement, edge contrast enhancement, latitude reduction, and noise reduction.

RESULTS

Conventional lateral cephalograms of 10 skulls and their digitally enhanced hard copy and monitor images were compared with 8 different landmarks for location. Location of each landmark was denoted by (X, Y) coordinates.

Mean and standard deviation were calculated. All values were analyzed statistically and compared using Maloney-Rastogi test and Bland-Altman plots. The mean significant disparity of all 8 observers for locating point sella, ANS, and PNS with X-coordinate and nasion, basion, supraspinale, orbitale, and porion with Y-coordinate.

The mean, standard deviation, and P value for all 8 landmarks for all 3 modalities are compared in Table 1. The mean of the sum of the squared differences for different methods was calculated to show the squared difference value with respect to X and Y coordinates

Table 1: Comparison of mean, standard deviation, and significance of all 8 landmarks for all 3 modalities (CO, DH, and MO)

Landmark	Coordinates	CO-DH			DH-MO			MO-CO		
		Mean	SD	P value	Mean	SD	P value	Mean	SD	P value
ANS	X	0.2625	0.7201	<0.05	0.0375	0.6412	<0.05	-0.300	0.8426	<0.05
	Y	0.0139	0.5110	>0.05	-0.0750	0.3800	>0.05	0.0375	0.6214	>0.05
Nasion	X	0.825	1.5064	>0.05	-0.8500	1.4841	>0.05	0.0250	0.6341	>0.05
	Y	0.3000	0.0416	<0.05	-0.5875	1.0331	<0.01	0.2875	1.3341	<0.001
Orbitale	X	-0.2250	1.9169	>0.05	0.1875	1.5976	>0.05	0.0375	2.2105	>0.05
	Y	0.2250	2.2582	>0.05	-0.4125	2.7554	<0.05	0.1875	2.4854	<0.01
PNS	X	-0.2250	3.5951	<0.001	0.0125	2.9601	<0.01	0.2125	3.2737	<0.05
	Y	0.1500	3.4896	>0.05	-0.1375	2.6160	>0.05	-0.012	3.1630	>0.05
Sella	X	0.3625	0.8695	<0.05	-0.0250	0.6888	>0.05	-0.337	1.1613	>0.05
	Y	0.3051	0.8000	>0.05	-0.1500	1.0618	>0.05	0.0500	1.2237	>0.05
Supraspinale	X	1.0500	1.6576	>0.05	-0.6625	1.2937	>0.05	1.1750	6.3871	>0.05
	Y	0.7875	1.5628	>0.05	-0.6250	1.3544	<0.05	-0.162	1.1559	>0.05
Porion	X	-0.2350	1.8169	>0.05	0.1975	1.4976	>0.05	0.0475	2.2405	>0.05
	Y	0.2350	2.3582	>0.05	-0.3125	2.8554	<0.05	0.1975	2.4954	<0.01
Basion	X	0.735	1.4064	>0.05	-0.8800	1.4641	>0.05	0.0350	0.7341	>0.05
	Y	0.3010	0.05526	<0.05	-0.6875	1.0231	<0.01	0.2876	1.4341	<0.001

ANS: Anterior nasal spine, PNS: Posterior nasal spine, SD: Standard deviation

(Table 2). Higher the value, lesser will be the precision and reproducibility of that particular landmark. Hence, we can precisely reproduce ANS than sella and nasion, orbitale, supraspinale in decreasing order and most difficult point to reproduce was the PNS. The calculated mean values of the sum of the squared differences taking different landmarks to evaluate the intra-observer deviation on X and Y coordinates shows how much each observer deviated while locating all 8 landmarks in all 3 modalities (Table 3). As the value of X and Y coordinate increases, more the person deviated from mean.

DISCUSSION

After the standardization of the technical procedures, radiography has become one of the most frequently applied aids in human biometric research. While using this method, it is necessary to make a careful check of the accuracy of the reproduction of cephalometric landmarks. Furthermore, interpretation of cranial radiographs of living subjects can involve a factor of uncertainty. This is especially true in details of the cranial base. For this reason, the study was made on human skulls from which brain had been removed to permit proper inspection and location of landmarks, like in the present study, it was point sella of the cranial base.⁷

The present study compared 3 modalities of landmark identification to check the precision and reproducibility. Furthermore, the comparison of conventional method with digital hard copy and monitor image was performed and statistically analyzed.

To the best of our knowledge, many researchers have compared digital and conventional cephalometry, but very

Table 2: Comparison of intra-observer squared differences between observations for CO, DH, and MO averaged for all skulls

Landmark	CO-DH		DH-MO		MO-CO	
	X	Y	X	Y	X	Y
ANS	5.875	2.625	4.125	1.5	8	3.875
Nasion	29.5	11.75	29.25	14.125	34	18.625
Orbitale	37.25	51.5	25.875	77.625	48.875	62.125
PNS	129.75	122	87.625	68.625	107.63	252.625
Sella	8.875	6.5	4.75	11.5	14.625	15
Supraspinale	38.5	30.625	21.125	22.25	11.625	13.625
Porion	38.25	512.5	26.875	78.625	47.875	61.125
Basion	30.5	12.75	30.25	15.125	35	17.625

ANS: Anterior nasal spine, PNS: Posterior nasal spine

Table 3: Comparison of inter-observer squared differences for CO, DH, and MO averaged over all skulls (P=Person)

Person	CO-DH		DH-MO		MO-CO	
	X	Y	X	Y	X	Y
P1	97.33	9.50	88.33	65.33	87.67	64.17
P2	86.33	99.67	66.00	57.33	63.00	224.33
P3	37.33	82.00	17.83	61.50	26.83	114.83
P4	32.83	20.67	18.17	22.17	35.67	24.17
P5	28.83	29.67	20.17	12.00	26.67	27.67
P6	18.00	9.33	8.00	7.00	25.67	9.00
P7	17.33	8.17	4.50	13.83	17.17	11.00
P8	15.00	41.00	7.33	21.67	17.00	12.67

few studies exist on digital hard copy comparison with conventional cephalogram and monitor image.

Schulze *et al.* did the comparison of direct landmark identification study on monitor images on conventional cephalogram.⁶ Since 1995, Chen *et al.* have conducted serial

studies on landmark identification, but all their studies were mainly concerned with the digitization of landmarks using various software that were available in market at that particular time.^{4,8,9}

In our study, the mean significant disparity for locating point sella was only with x-coordinate. This result favors the study of Schulze *et al.*⁶ but contrasts the observation of Chen *et al.*⁹ The mean significant difference for locating point nasion was with Y-coordinate while comparing all 3 modalities ($P < 0.05$). This is in accordance with Richardson¹⁰ and Liu *et al.*¹¹

The mean significant disparity for locating point supraspinale was with Y-coordinate, which favors the findings of Richardson,¹⁰ who concluded that point A was difficult to reproduce vertically. The mean significant inconsistency for locating point ANS was mainly with X-coordinate. Similar findings were noted by Schulz *et al.*,⁶ Liu *et al.*,¹¹ and Turner and Weerakone¹² in their study.

The mean significant disparity for reproducing point PNS was with X-coordinate ($P < 0.05$). It was observed that PNS was more difficult to locate in young individuals due to the presence of developing third molars in this region. This finding is in favor of the study of Turner and Weerakone¹² and partly in favor of Schulz *et al.*⁶ The mean significant disparity for precise reproduction of point orbitale was with Y-coordinate, i.e., vertical direction. This finding is similar to that observed by Chen *et al.*¹¹ There was slight difficulty in accurately locating point porion, which could be due to superimposition of other anatomical structures of the inner cranium. This was also noticed by Midtgård *et al.*¹³ There was slight difficulty in locating basion on the y-axis ($P < 0.05$) which shows a vertical pattern of distribution, as noted by Baumrind and Frantz³ in his study.

The mean of the sum of the squared differences for different methods was calculated to show the squared difference value with respect to X and Y coordinate. The increase in value indicates less precision and reproducibility of that particular landmark. So, we can precisely reproduce ANS, sella, nasion, basion, orbitale, porion, and supraspinale in decreasing order and most difficult point to reproduce was the PNS.

In the present study, we found that compared to conventional and monitor tracing it was very easy to precisely reproduce the landmarks on a digital hard copy, but still we did not find statistically significant difference between all 3 modalities as far as accuracy in landmark identification and reproduction is concerned.

CONCLUSION

Based on the results of this study, we can make the following conclusions.

1. Precision and reproducibility in landmark identification on conventional, digital hard copy, and monitor image were almost similar
2. It is extremely easy and convenient to locate landmarks in digital hard copy than conventional and monitor image
3. ANS was the most consistent and PNS was the least consistent landmark.

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Efficacy of Vaginal Misoprostol in Second-trimester Abortion

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Abstract

Introduction: Abortion is one of the most fundamental health care needs of a woman! Abortion is defined as the termination of pregnancy by any means before the fetus is viable.

Aim: To provide a review on mid-trimester abortion with vaginal misoprostol which is effective, safe, and acceptable with minimal side effects lasting for a transient period.

Materials and Methods: A prospective study was conducted in the Department of Obstetrics and Gynecology. A total of 100 patients were selected from Outpatient Department and labor room having a gestational age of 13-20 weeks. Irrespective of age, marital status and parity these patients seeking for abortion were induced with vaginal misoprostol for labor induction. The results were analyzed.

Results: Maximum number of patients 44% were in the age of 26-30 years. About 80% of women belonged to urban community, and the majority of women 88% were literate while only 12% were illiterate. About 64% belonged to lower and middle socio-economic class while only 2% belonged to rich/high socio-economic class. Exactly 81% patients had 3 or more children, 5% were primigravidae, and 14% had 1 or 2 children. Contraceptive failure temporary and permanent accounted for 9% of women wanting abortion. Women having gestational age of 17-20 weeks, 100% aborted within 24 h and 76% aborted within 24 h in women having gestational age of 13-16 weeks. About 88% of cases with gestational age of 13-20 weeks had complete abortion within 24 h and did not require surgical evacuation. Exactly 12% of patients with gestational age of 13-16 weeks required surgical evacuation for placental bits and membrane. This observation was found statistically significant.

Conclusion: Misoprostol is highly effective drug for second-trimester abortion. It is inexpensive, safe, stable at room temperature, easily available, easy to use with minimum side effects.

Key words: Efficacy, Gestational age, Mid-trimester termination, Misoprostol, Parity

INTRODUCTION

Abortion is one of the most fundamental health care needs of a woman! Abortion is defined as the termination of pregnancy by any means before the fetus is viable. Viability is considered to be reached at 23-24 weeks of gestation. Mid-trimester is a period ranging from 13 to 28 weeks of gestation which again is subdivided into an early period between 13 and 20 weeks

and a late period between 20 and 28 weeks. In our review, we have limited up to 20 weeks gestations taking in consideration the medical termination of pregnancy (MTP) act.

Medical abortion is a safe option for second-trimester abortion in indicated cases. It is a safe alternative to a surgical method. MTP was legalized in the year 1971.¹ In the year 2002 and 2003, there was an amendment to the MTP act which sanctioned Obstetrician and Gynecologist to provide mifepristone and misoprostol in a clinical setting up to 7 weeks of pregnancy.

The efficacy of misoprostol in second-trimester abortions has been reported.^{2,3}

It is found in clinical studies that vaginal route of misoprostol administration is a more effective as it bypasses extensive

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and rapid first pass metabolism. Although effective but cumbersome, as it requires repeated vaginal examination for misoprostol induction which is inconvenient and at times may be unacceptable to the patients. Misoprostol is marketed as an oral preparation used to prevent and treat gastroduodenal damage induced by nonsteroidal anti-inflammatory drug. However, misoprostol is used for a variety of indications in the practice of obstetrics and gynecology, including medical abortion, medical management of miscarriage, induction of labor, cervical ripening before surgical procedures and the treatment of postpartum hemorrhage.⁴

Misoprostol is a synthetic 15-deoxy-16-hydroxy, 16-methyl analog of the naturally occurring prostaglandin (PG). It is an effective abortifacient and uterotonic drug. It is formulated for oral use but is effective by vaginal, buccal and sublingual administration for the purpose of abortion.⁵ It is stable at room temperature, is easily available, inexpensive and has a long half-life.

Demetroulis *et al.*, 2001,⁶ randomized controlled trial has reported a success of 82.5% as compared to surgical treatment with no difference in relation to incidence, duration or severity of bleeding.

With the improvement of ultrasound technology and noninvasive blood tests, the likelihood of detection of major fetal structural abnormalities in mid-pregnancy has increased considerably. On detection of serious anomalies, women are offered the option of termination. In addition, there are still many reasons other than fetal anomalies, why women seek abortion in the mid-trimester. It is an option for women who are poor surgical candidates and also for those who live in areas where surgical termination is not available.

In the Cochrane review 2011, medical abortion in the second-trimester using the combination of mifepristone and misoprostol was found to have the highest efficacy and shortest abortion interval. If mifepristone is not available, misoprostol alone is a reasonable alternative.⁷

The optimal route for administering misoprostol is vaginal. Apart from pain, the side effects are usually mild and self-limiting.⁷

Misoprostol's effects are dose dependent. Although not approved by the US FDA, in 2002, pregnancy was removed from the label as an absolute contraindication.⁸

MATERIALS AND METHODS

Our study was undertaken in the Department of Obstetrics and Gynecology, Rajendra Institute of Medical

Science, Ranchi. Around 100 patients were selected from the outpatient department and labor room having gestational age of 13-20 weeks. Proper counseling was done, and a written informed consent was obtained before starting the treatment regime. Ultrasonography was done, along with detailed history and proper examination of the patient.

Irrespective of age, marital status and parity, these patients were induced with misoprostol introduced in the posterior fornix. Intravenous antibiotics were administered on admission, to all patients after instilling vaginal misoprostol. A value of 400 µg of misoprostol was introduced and repeated at 4 h interval, up to a maximum of 4 doses. Anti-D immunoglobulin (150 µg) was administered to all those with a negative blood group within 72 h of the first dose.

Exclusion Criteria

- Known allergy or previous reaction to PG
- Active renal or hepatic disease
- Scarred uterus
- Cardiac disease
- Severe anemia
- Maternal coagulopathy.

Indication for seeking mid-trimester abortion:

- Unmarried
- Low socio-economic
- Having a small child or two or more children
- Failure of contraception
- Congenital abnormalities of fetus.

After admitting the patients, relevant laboratory investigations were done. Date and time of induction of the first dose of misoprostol were noted. Patients were observed for painful uterine contraction and 400 µg was repeated at 4 h interval. Date and time of abortion were observed. Any additional treatment if given was noted down along with side effect and complications if any.

RESULTS

This prospective study was performed in 100 patients seeking abortion in the second-trimester. Each patient was given 400 µg of misoprostol in the posterior fornix and repeated at 4 h interval.

- a. Maximum numbers of patients 44% were in the age group of 26-30 years.
- b. Patients with an urban background accounted for 80% of the case while 20% belonged to the rural community. As the institute is situated in an urban area, so it is convenient for the women to come.
- c. The majority number of women 64% belonged to

lower and middle socioeconomic class. Only 2% belonged to rich/high socioeconomic class. The reason for this distinct difference is the use of contraceptive measures and resort to the permanent method of sterilization once their family is complete. Among the lower middle class, the situation is different. They are unable to rear more children and due to unawareness, poverty and poor transport diagnosis of pregnancy is late.

- d. The majority of the cases in the study 88% were literate and 12% were illiterate. Maximum number of cases 70% had studied up until XII Std. The high percentage of literacy in the present study could be because of the fact that the majority of the cases were from urban areas where literacy level is higher than in rural areas.
- e. About 81% of patients who came for mid-trimester abortion had three or more children and only 5% were primigravida. Exactly 14% of cases had one or two children. This shows that parity has a close relation with women wanting abortion. Since they had completed their family hence not desirous for another pregnancy (Table 1 and Graph 1).
- f. Among patients seeking mid-trimester abortion, the common indication was low-socioeconomic status and inability to rear another child in 64% of cases. About 18% of patients had conceived soon after delivery in lactation amenorrhea, hence not aware of gestational age. Having a small child was the reason behind seeking for mid-trimester abortion.
- g. Contraceptive failure was the reason for abortion in 7% of patients and tubectomy failure in 2% of cases (Table 2 and Graph 2).
- h. 50 cases were of 13-16 weeks gestation and majority 39% who sought mid-trimester abortion had a gestation of 16 weeks while 50 cases had gestation 17-20 weeks (Table 3 and Graph 3).
- i. Overall success rate in 13-16 weeks and 17-20 weeks with vaginal misoprostol was 100% in this study. Patients with 13-16 weeks gestation aborted within 24 h in 76% of cases and in 17-20 weeks groups 100% aborted within 24 h (Tables 4-6 and Graphs 4-6).

DISCUSSION

There is a wide variation in doses used at different stage of gestation, means that it is important to have an accurate diagnosis before commencing treatment. For this reason, many health services will make misoprostol available only at a level where both trained staff and facilities for diagnosis are available.

In the largest published series ($n = 1002$, gestation age 13-21 weeks), 97% of women aborted within 24 h, with

mean induction time of 5.9 h for multiparous women and 6.6 h for nulliparous women.⁹

This regime is on the basis of recommendation by the World Health Organization and Royal College of Obstetricians and Gynecologists based on trials that included women predominantly at 20 weeks gestation or less.

- j. 88% of patients had complete abortion within 24 h (Table 6) and did not require surgical evacuation. These patients had gestation of 17-20 weeks. 12% of patients with 13-16 weeks of gestation required surgical

Table 1: Distribution of cases according to parity

Parity	Number of cases
0	5
1	4
2	10
3	32
4	23
5	16
>5	10
Total	100

Table 2: Distribution according to reasons seeking for abortion

Reason for abortion	Number of cases
Unmarried	7
Socio-economic	64
Having small children	18
Contraceptive failure	
Temporary method	7
Permanent method	2
Congenital anomalies	2
Total	100

Table 3: Distribution of cases according to gestational age

Gestational age (weeks)	Number of cases
13-16	50
17-20	50
Total	100

Table 4: Distribution according to induction-abortion interval in 13-16 weeks gestation by vaginal misoprostol

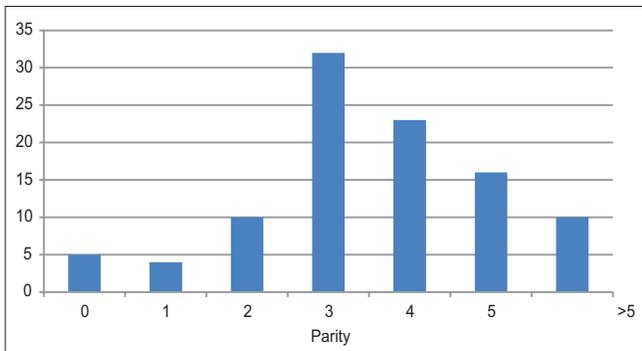
Induction-abortion interval in (h)	Number of cases	Percentage of cases
00-12	2	4
12-24	36	72
24-36	8	16
36-48	4	8
Total	50	100

Table 5: Distribution according to induction-abortion interval in (17-20 weeks) gestation

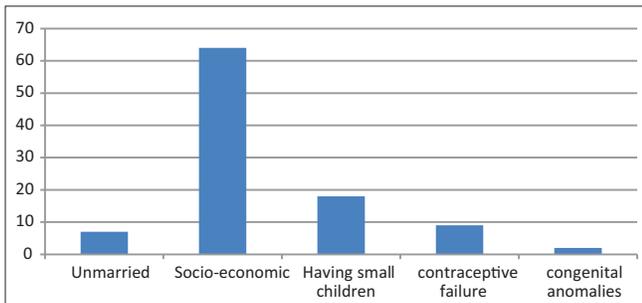
Induction-abortion interval in (h)	Number of cases	Percentage of cases
00-12	11	22
12-24	39	78
Total	50	100

Table 6: Comparison of efficacy of misoprostol in 13-16 weeks gestation and 17-20 weeks in first 24 h

Gestational age (weeks)	Number of cases	Percentage of cases
13-16	38	76
17-20	50	100
Total	88	88



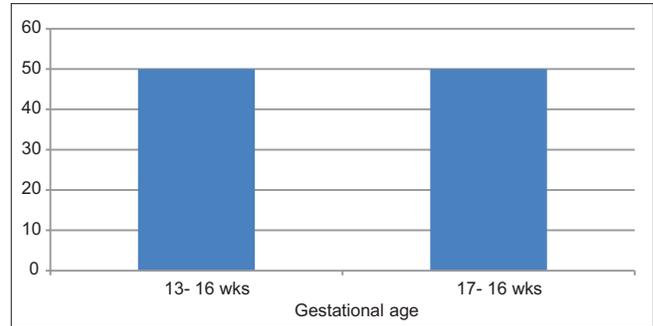
Graph 1: Distribution of cases according to parity



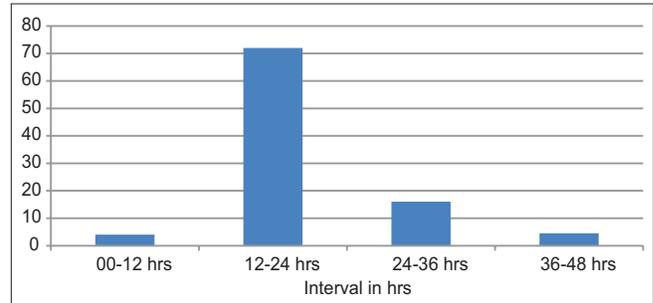
Graph 2: Distribution according to reasons seeking for abortion

evacuation of placental bits and membranes. This observation was found to be statistically significant. Lo *et al.*, noted the pregnancies with <17 weeks gestation had a higher rate of incomplete abortion and operational procedure as compared to more than 20 weeks.¹⁰

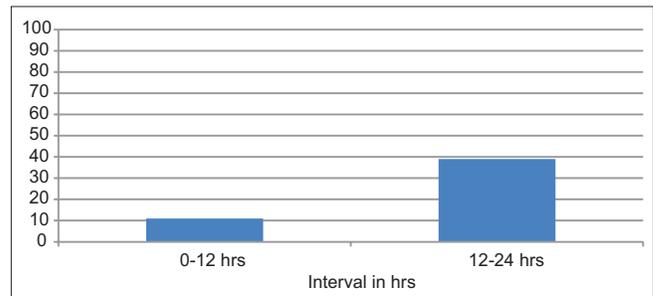
Few studies follow the natural course of placental expulsion without intervention for placental delivery. In women receiving misoprostol alone for labor induction abortion, half of women deliver the placenta within an hour, and there was no increase in bleeding when women were



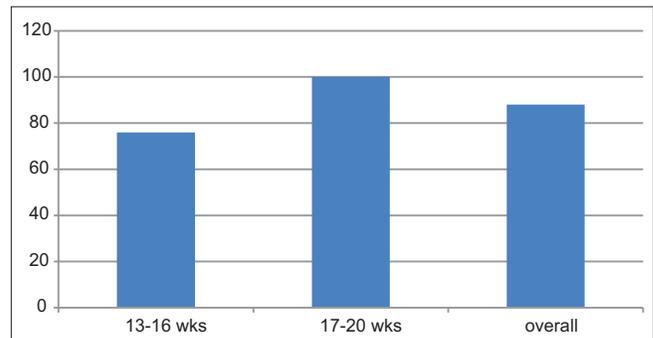
Graph 3: Cases according to gestational age



Graph 4: Induction-abortion interval in 13-16 weeks gestation



Graph 5: Induction-abortion interval in 17-20 weeks gestation



Graph 6: Misoprostol efficacy in first 24 h

observed past 2 h. This study also showed that routine misoprostol administration after fetal expulsion did not decrease the time to placental delivery.¹¹

Dickinson and Evans randomized women to receive intramuscular oxytocin, oral misoprostol or no medication

after fetal delivery. After oxytocin 90% of women expelled the placenta within an hour, compared to 71% and 69% after misoprostol or no medication respectively.¹²

- k. Side effects associated with misoprostol was nausea and vomiting 2%, fever 6%, diarrhea 2% and bleeding 2%. However, these side effects were mild and self-limiting. There was no major complication in this study. Fever is at times confused with infection but resolves within several hours of stopping misoprostol. The incidence of side effects is also lower for vaginal use except for transient fever.¹³

While isolated case reports and retrospective review documents uterine rupture during second-trimester induction with misoprostol, the magnitude of the risk is not known.¹⁴ Second-trimester abortion constitutes 10-15% of all induced abortion worldwide but are responsible for two-third of major abortion-related complications.¹⁵

Because of potential for heavy vaginal bleeding and serious complications, it is advisable that second-trimester abortion takes place in a healthcare facility where blood transfusion facility and emergency surgery including laparotomy are available. When fetal anomaly causes a woman to seek second-trimester abortion, oral administration of misoprostol appears to be the least effective method for terminating the pregnancy and vaginal misoprostol is more acceptable to women.¹⁶

Pregnancies with fetal demise may be treated similarly but the doses necessary to cause fetal expulsion is lower and induction process is typically shorter.¹⁷⁻²⁰

Majority of second-trimester abortion performed in the United States are performed surgically by dilatation and evacuation.²¹

Whereas labor-induction abortion represents approximately 2% of second-trimester abortion in the United States,²² more than 80% of abortions throughout the second-trimester in Sweden and other Nordic countries are inductions.²³

CONCLUSION

The incidence of second-trimester abortion has significantly reduced off-late, thanks to the PNDA act. Yet, when the condition is not favorable, either for the fetus or mother, the benefits of pregnancy termination outweighs the risk of continuation. This process, rightly known as mini-labor, is not only painful physically but also has a psychological impact. Second-trimester abortion carries a higher financial cost to individuals, medical institution and society. It

remains a necessary procedure despite higher risk and cost compared to first-trimester procedure, due to advances in antenatal diagnosis, decreased access to timely early abortion care and medical complications of pregnancy in the second-trimester.

The majority of women have no long-term psychological sequelae, but short time grief may be considerable, particularly for those choosing to terminate a desired pregnancy. Overall misoprostol appears to be more effective than $\text{PGF}_2\alpha$, PGE_2 , high dose oxytocin and ethacryndine lactate when adequate doses are used. Both PGE_2 and $\text{PGF}_2\alpha$ analogs are expensive and require refrigeration, in contrast to misoprostol, which is inexpensive and stable at room temperature.

Misoprostol used alone or in combination with other uterotonic agents have supplanted most other methods, because of high efficacy, cost-effective, wide availability and easy to use.

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Ophthalmic Manifestations in Human Immunodeficiency Virus Patients at Presentation in a Tertiary Care Hospital

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Abstract

Background: Numerous ophthalmic manifestations of human immunodeficiency virus (HIV) infection may involve the anterior or posterior segment of the eye. Anterior segment findings include a variety of external infections and tumors of the periocular tissues. Posterior segment changes include an HIV-associated retinopathy and a number of opportunistic infections of the retina and choroid.

Materials and Methods: Observational cross-sectional study done over a period of 6-month at a Tertiary Care Hospital. A total of 246 HIV positive patients were screened for ophthalmic manifestations. CD4 counts correlated with anterior and posterior segment lesions. Patients already on treatment for eye manifestations were excluded.

Results: Out of the 246 patients, 127 (51.62%) were in the 4th decade of life. About 28 patients (88.60%) had ophthalmic manifestations out of the total 246 patients. Visual acuity was better or equal to 6/12 in 42.85% of patients (12). Posterior segment lesions were found in 18 patients (64.3%), anterior segment lesions in 7 (25%), and both anterior and posterior segment lesions in 3 patients (10.7%). About 50% of patients had CD4 count >500/cumm, ophthalmic manifestations were present at all CD4 counts. 6 patients with anterior segment lesions had CD4 count >200 with only 1 patient having <200. Of the 21 patients with posterior segment findings, 18 had CD4 count <500. All 3 patients with anterior and posterior segment findings had CD4 count <100. HIV retinopathy was present in all ranges of CD4 count. 3 patients with cytomegalovirus (CMV) retinitis had CD4 count <200. Opportunistic infections were predominant in CD4 count in the range of 200.

Conclusion: HIV retinopathy, CMV retinitis, blepharitis, anterior uveitis, and viral keratitis are the ophthalmic manifestations at presentation in order of prevalence in this study. Low CD4 count is a good predictor for CMV retinitis and posterior segment manifestations in patients with anterior segment lesions.

Key words: CD4 count, Cytomegalovirus retinitis, Human immunodeficiency virus retinopathy, Ophthalmic manifestations, Opportunistic infections

INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) is an infectious disease caused by a retrovirus, the human immunodeficiency virus (HIV). This syndrome is characterized by a gradual decrease in circulating CD4+

T-lymphocytes and subsequent development of various opportunistic infections and neoplasia.

The World Health Organization Report in 2014 estimates 35 million people including 3.2 million children have been infected with HIV worldwide.¹ Overall, 58% of HIV patients show ophthalmic manifestations.² Among HIV-positive individuals, the lifetime cumulative risk for developing at least one abnormal ocular lesion ranges from 52% to 100% in various studies.³

The role of the ophthalmologist in the diagnosis of AIDS is becoming increasingly important. Not only does the eye reflect systemic disease but also ocular involvement

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may often precede systemic manifestations so that we can initiate treatment early. In the AIDS patients, the ophthalmologist has an opportunity to make not only a sight saving, but also a lifesaving diagnosis of disseminated opportunistic infections.

The aim of this study is to evaluate the various ophthalmic manifestations in proven HIV seropositive patients at a tertiary care center at presentation and to study the variations at different levels of immunosuppression with the aid of CD4 count.

MATERIALS AND METHODS

The present study was a hospital-based observational cross-sectional study carried out at the Department of Ophthalmology in a tertiary care hospital for a period of 6-month. Institutional Ethics Committee Approval was obtained. The hospital has an ART (antiretroviral therapy) center affiliated to National AIDS Control Organization and catering to surrounding villages in the region. Inclusion criteria: HIV seropositive patients at their first visit to Ophthalmology OP after diagnosis as a part of their routine screening. Patients already on treatment for eye manifestations were excluded. A total of 246 patients were included in the study. Informed consent was taken along with demographic data like age, sex and occupation. Visual acuity noted using Snellen’s vision charts. Field examination, color vision, histopathological examination was done as required. Slit lamp examination with imaging was performed for anterior segment findings. Posterior segment examination was done with the help of +90D lens, direct and indirect ophthalmoscopy. Fundus photography, fundus fluorescein angiography, ultrasound examination were performed for relevant cases. Ancillary investigations, such as magnetic resonance imaging and infectious agent antibody titers, were obtained in cases wherever necessary. CD4 count was obtained in all cases.

RESULTS

Out of the 246 patients that were screened, 51.62% (127) were in their 4th decade. There were 162 males and 84 females in the study. Drivers (30.48%) predominated among males followed by laborers. Among females majority were house wives (76%).

At presentation, 28 patients showed ophthalmic manifestations and 218 patients were asymptomatic with no clinical findings (Chart 1). Among the 28 patients with ophthalmic manifestations, patients had vision as shown in Table 1.

Out of the 28 patients, anterior segment lesions were found in 7 patients, posterior segment lesions in 18 patients and both anterior and posterior segment findings were present in 3 patients.

Out of the 7 patients with anterior segment lesions, 5 patients had Herpes simplex virus keratitis, blepharitis, meibomitis, molluscum contagiosum, herpes zoster ophthalmicus, respectively, 2 patients were diagnosed to have anterior uveitis without any posterior segment findings. Out of the 18 patients with posterior segment lesions, 11 patients had HIV retinopathy, 3 patients had cytomegalovirus (CMV) retinitis, 4 patients had toxoplasmosis, optic neuritis, choroidal melanoma, choroiditis, respectively. 3 patients had both anterior segment and posterior segment lesions. CD4 counts of patients with opportunistic infections are as shown in Table 2 and Figures 1-4.

Table 1: BCVA in patients with ophthalmic manifestations in our study

BCVA in diseased eye	Number of patients n=28 (%)
≥6/12	12 (42.85)
6/18-6/60	8 (28.57)
5/60-3/60	5 (17.85)
2/60-1/60	2 (7.14)
<1/60	1 (3.57)

BCVA: Best corrected visual acuity

Table 2: CD4 count in patients with opportunistic infections

Opportunistic infections	CD4 count (mean)/cumm
CMV retinitis	108
Toxoplasmosis	158
HSV Keratitis	314.5
Herpes Zoster ophthalmicus	256
Molluscum contagiosum	250

HSV: Herpes simplex virus, CMV: Cytomegalovirus

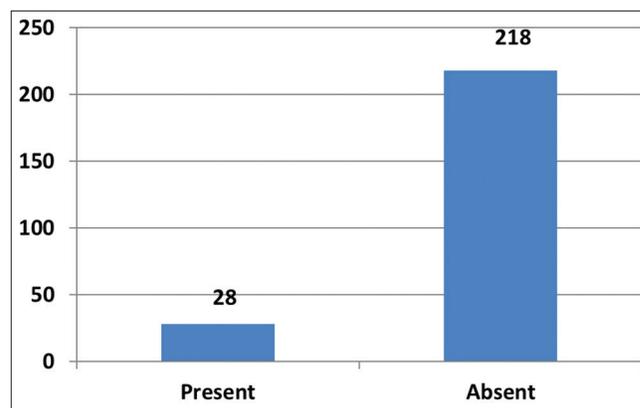


Chart 1: Number of patients with and without ophthalmic manifestations in the study



Figure 1: Fundus picture of right eye depicting features of human immunodeficiency virus retinopathy

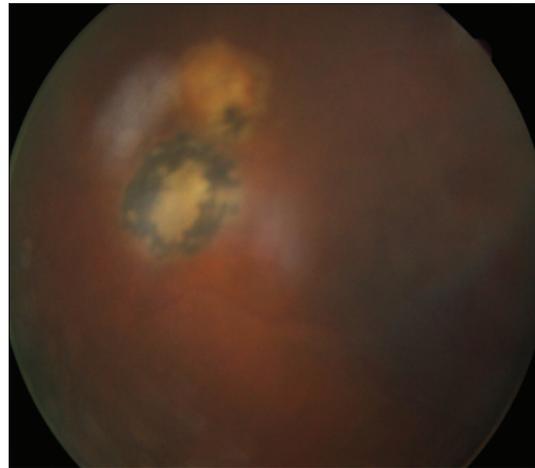


Figure 3: Fundus picture showing features of toxoplasmosis with pigmented retinochoroidal scar

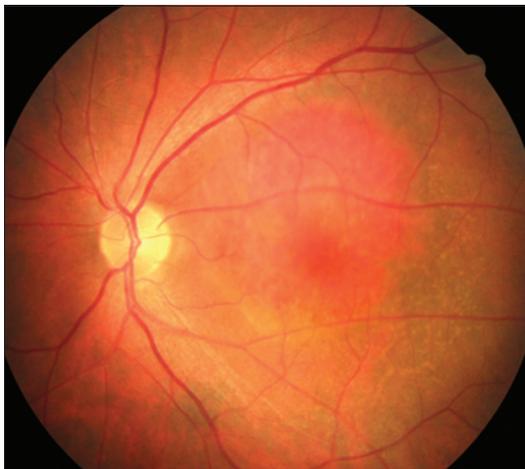


Figure 2: Fundus picture showing non-pigmented choroidal melanoma



Figure 4: Fundus picture showing cytomegalovirus retinitis in the posterior pole surrounding the disc

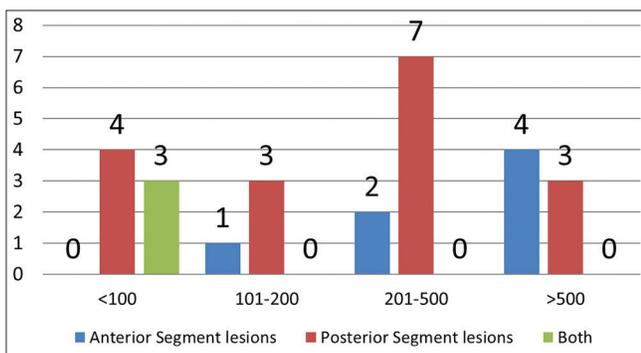


Chart 2: Comparison of 3 groups of patients at all CD4 counts

Out of the patients studied, 132 patients had CD4 count >500/cumm. Ophthalmic manifestations were present at all CD4 counts (Table 3).

The majority of anterior segment lesions were present at CD4 count>200. Of the 21 patients with posterior segment findings, 18 had CD4 count <500. All 3 patients with

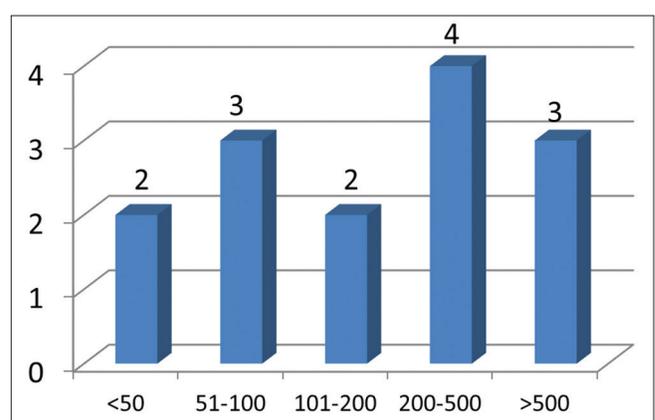
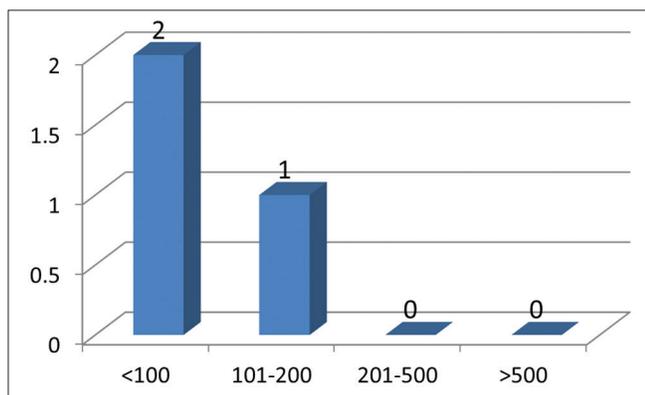


Chart 3: Depiction of relation of human immunodeficiency virus retinopathy with CD4 count

anterior and posterior segment findings had CD4 count <100 (Chart 2). HIV retinopathy is present in all ranges of CD4 count (Chart 3), 3 patients with CMV retinitis had CD4 count below 200 in this study (Chart 4).

Table 3: CD4 count in total patients studied and in those with findings

CD4 count	Over all	With ophthalmic manifestations
<100	18	7
101-200	27	5
201-500	69	9
>500	132	7

**Chart 4: Depiction of relation of cytomegalovirus retinitis with CD4 count**

DISCUSSION

Out of 246 patients screened, mean age group was 31-40 years correlating with Biswas *et al.*, study,⁴ males predominated which correlates with national statistics of HIV population.⁵

About 28 patients were found to have ophthalmic manifestations. Among these 7 had anterior segment lesions,⁶ 18 patients had posterior segment lesions,⁴ 3 patients had both anterior and posterior segment lesions.

HIV retinopathy is the most common ophthalmic manifestation (50%).³ There was no association between anterior segment lesions and CD4 count of the patients. Patients of anterior segment lesions who had CD4-count <100 cells/cumm also had concurrent posterior segment lesion. Posterior segment opportunistic infections showed

association with low CD4-count. 11.4% of HIV patients had ophthalmic manifestations at presentation. Among the patients with ophthalmic manifestations, 43% had CD4 count <200/cumm. HIV retinopathy is the most common presentation and 50% of these patients had CD4 count <200/cumm. Incidence of posterior segment opportunistic infections such as CMV retinitis⁷ and Toxoplasmosis⁸ increases with low CD4 count. Early screening of HIV patients explains low prevalence of ophthalmic manifestations in our study.

CONCLUSION

HIV retinopathy, CMV retinitis, blepharitis, anterior uveitis, and viral keratitis are the ophthalmic manifestations at presentation in order of prevalence. Low CD4 count is a good predictor for CMV retinitis and posterior segment manifestations in patients with anterior segment lesions. There needs to be awareness of ocular involvement among HIV infected individuals and an increased emphasis on regular ophthalmic examination.

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Internal Root Morphology of Maxillary First and Second Molars of South Indian Population by Canal Staining and Clearing Technique

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Abstract

Background: The success of endodontic treatment relies on the precise identification of all root canals followed by cleaning, shaping, and obturation. Maxillary molars present wide variations with regard to the number and type of root canals. The complexity of the root canals varies widely in different ethnic groups.

Aim of the Study: To investigate the root canal anatomy of permanent maxillary first and second molars in South Indian population.

Materials and Methods: Extracted 200 maxillary molars, maxillary first molars (100), and maxillary second molars (100) were collected from the section of South Indian population. Standard access cavities were prepared, and the teeth were immersed in 3% NaOCl to dissolve pulp tissue. Canal staining and clearing technique were used to study the root canal configurations of all the teeth.

Results: All maxillary first molars had three separate roots, whereas in second molars 41% were single rooted, 42 % two roots fused, and 16% three roots fused. The prevalence of second mesiobuccal canal (MB2) in maxillary first molars (84%) was higher than in second molars (38%). In the two-canal MB roots, the Type II, IV, and VI canal systems were the most prevalent. Lateral canals in the apical third of the first molar were 51, 21, and 14% in MB, DB, and P, respectively; and in the second molar were 40, 15, and 5% in MB, DB, and P, respectively. Intercommunications in maxillary first molar were 32% and 4% in MB and DB, respectively. Palatal root curvature at apical third in first molar was buccal 70%, palatal 4%, and straight 20%.

Conclusion: In South Indian population, the prevalence of MB2 canal is more than 80% in maxillary first molars. The presence of lateral canals and intercommunications is also more in first molars. Full understanding of the potential complexities of the root canal system is essential for the successful endodontic treatment of maxillary molars.

Key words: Anatomy, Clearing, India ink, Maxilla, Molars, Root canal, South Indians

INTRODUCTION

Studying the root canal anatomy has both endodontic and anthropological significance. It is important to know the anatomy of teeth and its variations in different ethnic groups as such knowledge can aid in the identification,

cleaning, and shaping of root canals. The presence of undetected canals, ramifications, and radiographically undetected curvatures have been attributed as possible causes for failure of endodontic treatment in maxillary molars.¹ A variety of techniques have been utilized to study the anatomical details of the root canal system. These techniques include microscopic studies, radiographic studies, sectioning of teeth, iontophoresis, injections, metal filling of pulp cavities, plastic embeddings, transparency/clearing, and combined techniques.² Even though there are discrepancies between *in vitro* and *in vivo* studies of root canal morphology, the technique of clearing teeth has considerable value because it makes the external surface

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transparent and helps in three-dimensional visualization of the pulp chamber and root canals.³

The pulp chamber and the root canals take on numerous configurations and shapes. The most frequent of the root canal ramifications are the apical delta, the accessory, and lateral canals.² An in-depth understanding of the complexity of the root canals and adequate cleaning, shaping, and filling of all the minute intricacies of the root canal system is essential for the successful outcome of endodontic treatment.⁴ Maxillary first and second molars have fascinated researchers and clinicians due to their anatomical variations.⁵ Because of the overall similarity of the first molar to the second molar, there may be a tendency for the clinician to treat them alike. In this study, both the teeth were analyzed as to the number of roots, canals, curvature, ramifications of the main root canal, localization and number of foramina, and apical deltas.

MATERIALS AND METHODS

The sample comprised 200 teeth (100 maxillary first molars and 100 maxillary second molars) collected all over from South India. The gender and age of the patients were not known. The teeth were extracted for reasons other than for this study. Teeth were stored in 10% formalin at room temperature during the period of collection. Hard and soft deposits were removed using ultrasonic scaler and washed under tap water. Once the teeth were classified into first and second molars, standard access cavities were prepared using Endo access burs and high-speed handpiece. Canal orifices were located by placing a size 8 K file into the visible orifice. The tooth was discarded if penetration was not possible into at least one canal orifice in the MB root.

The teeth were then placed in 5% sodium hypochlorite solution for 24 h to dissolve the organic tissue from the root surface and the root canal system. The teeth were dried, and Indian ink was injected into the pulp chamber using a hypodermic syringe with a 23-gauge needle and drawn through the canals using suction from apically. After 7 h of drying, the samples were stored in 5% nitric acid for 5 days to aid in the demineralization process. The fresh nitric acid solution was replaced daily and at the end of 5 days, the reliability of the demineralization procedure was verified by inserting a needle in the crown portion of the tooth. Decalcification of teeth was also confirmed by radiographs, which revealed complete radiolucency. Decalcified teeth were washed in running tap water for 4 h and dehydrated in ascending concentrations (70%, 95%, and 100%) of ethanol for 1 day and then rendered transparent by immersing in methyl salicylate for 2 days.

The transparent teeth samples were evaluated using a stereomicroscope at a magnification of 8×. The following observations were made: (1) Number of roots and their morphology; (2) number of root canals per root; (3) root canal configuration in each root using Vertucci's classification with additional modifications; and (4) presence and location of lateral canals and intercanal communications. Lateral canals were defined as those branches of main canals which diverged at right or oblique angles to exit onto the lateral surface of the root. Intercanal communications were defined as those complex canal ramifications that ran from and in between the main canals but did not communicate with the root surface (Figures 1-3).

RESULTS

All maxillary first molars had three separate roots, whereas in second molars 41% were single rooted, 42% two root

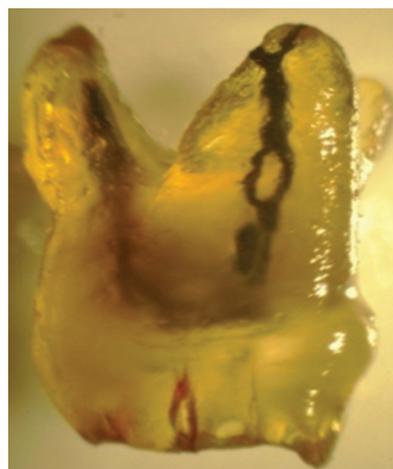


Figure 1: Cleared maxillary first molar showing Vertucci's Type VII root canal system



Figure 2: Cleared maxillary second molar showing accessory canals and ramifications

fused, and 16% three roots fused. The prevalence of second MB canal (MB2) in maxillary first molars (84%) was higher than in second molars (38%).

Tables 1 and 2 show the root canal configuration in maxillary first molars and maxillary second molars, respectively. In maxillary first molars, Type I canal systems were found to be 9%, 85%, and 96% in MB, DB, and P roots, respectively. Type II canal system was found to be 37% and 6% in MB and DB roots, respectively. Type III canal system was found to be 2% in MB root. Type IV canal system was found 20% in MB root. 5%, 7%, and 4% of Type V canal system was found in MB, DB, and P roots, respectively. Type VI was found to be 18% in MB, 2% in DB and Type VII 2% in MB. Additional canal system type (2-1-2-1) of 3% and type (2-3) of 4% were found in MB roots of first molars (Table 1). In maxillary second molars, Type I canal system was found to be 46%, 92%, and 95% in MB, DB, and P roots, respectively. Type II canal system

of 18% was found only in MB. Type IV canal system was found to be 5% in MB root. Type V canal system of 17%, 8%, and 5% found in MB, DB, and P, respectively. 10% of Type VI was found in MB. Additional canal system type (2-3) of 4% found in MB root only (Table 2).

Table 3 shows the percentage of lateral canals in first molar MB, DB, and P roots in apical third to be 51%, 21%, and 14%, respectively. MB, DB, and P showed lateral canals in middle third to be 6%, 3%, and 2%, respectively. Lateral canals in coronal third of MB root were 2%. Lateral canals in second molar MB, DB, and P roots in apical third was 40%, 15%, and 5%, respectively, and 24%, 11%, and 72% in a middle third of MB, DB, and P, respectively. In the coronal third of MB, DB, and P roots, lateral canals were found to be 8%, 1%, and 1%, respectively.

Table 4 shows intercanal communications in MB and DB roots of maxillary first molars to be 32% and 4%, respectively. In the second molar, 6% of intercommunications were seen in fused MB and DB roots, 5% in MB and P fused roots, and 3% in three roots fused.

Palatal root curvature at apical third in first molars was 70% buccal curvature, 4% had palatal curvature, and 20% of palatal roots were found to be straight. In second molars, the palatal root curvature was buccally (78%), distally (4%), and straight (15%) (Table 5). The buccal curvature of palatal roots was found to be less in first molars (average of 10° in 52%) compared to second molars (average of 20° in 45%) (Table 6).

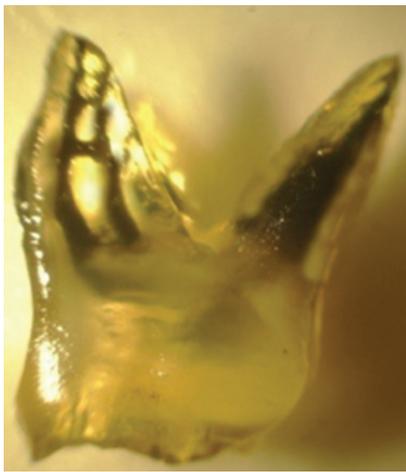


Figure 3: Cleared maxillary first molar showing intercommunications between canals

DISCUSSION

It is extremely important for clinicians to be aware of the complexity of the root canal system that we are

Table 1: Percentage of maxillary first molars with different types of root canal configuration

Root (%)	Number of teeth	Type I (1)	Type II (2-1)	Type III (1-2-1)	Type IV (2)	Type V (1-2)	Type VI (2-1-2)	Type VII (1-2-1-2)	Type VIII (3)	Additional canal type	
										(2-1-2-1)	(2-3)
MB root	100	9	37	2	20	5	18	2	-	3	4
DB root	100	85	6	-	-	7	2	-	-	-	-
Palatal root	100	96	-	-	-	4	-	-	-	-	-

MB: Mesiobuccal, DB: Distobuccal

Table 2: Percentage of maxillary second molars with different types of root canal configuration

Root (%)	Number of teeth	Type I (1)	Type II (2-1)	Type III (1-2-1)	Type IV (2)	Type V (1-2)	Type VI (2-1-2)	Type VII (1-2-1-2)	Type VIII (3)	Additional canal type
										(2-3)
MB root	100	46	18	-	5	17	10	-	-	4
DB root	100	92	-	-	-	8	-	-	-	-
Palatal root	100	95	-	-	-	5	-	-	-	-

MB: Mesiobuccal, DB: Distobuccal

Table 3: Percentage of maxillary molar roots with lateral canals

Roots	Lateral canals (%)		
	Coronal third	Middle third	Apical third
First molar			
MB (100)	2	6	51
DB (100)	-	3	21
P (100)	-	2	14
Second molar			
MB (100)	8	24	40
DB (100)	1	11	15
P (100)	1	7	5

MB: Mesio Buccal, DB: Distobuccal, P: Palatal

Table 4: Number and percentage of maxillary molar roots with intercanal communications

Teeth	Group	Intercommunications (%)
Maxillary first molars	Group I	
	MB Root	32 (32)
	DB Root	4 (4)
	P Root	-
Maxillary second molars	Group II	
	MB+DB Root	6 (6)
	Group III	
	MB+P Root	5 (5)
	Group IV	
	3 roots fused	3 (3)

MB: Mesio Buccal, DB: Distobuccal, P: Palatal

Table 5: Palatal root curvature at apical third

Tooth	Buccal (%)	Palatal (%)	Mesial (%)	Distal (%)	Straight (%)
Maxillary first molars	70 (70)	4 (4)	3 (3)	3 (3)	20 (20)
Maxillary second molars	78 (78)	2 (2)	1 (1)	4 (4)	15 (15)

Table 6: Degree of curvature of palatal root at apical third

Tooth (%)	Buccal curvature in degrees				
	10°	20°	30°	40°	50°
Maxillary first molars	52 (52)	18 (18)	-	-	-
Maxillary second molars	27 (27)	45 (45)	6 (6)	-	-

expected to access, shape, clean, and fill.⁴ Although various techniques have been used in studying the canal morphology, it has been reported by Vertucci (1984)⁶ that the most detailed information can be obtained by demineralization and staining technique which is regarded as an excellent method for three-dimensional evaluation of root canal anatomy.⁷ Martin Trope *et al.* showed that there is difference in canal anatomy in various ethnic groups.⁸ The maxillary first molars generally have three roots and can have as many as three mesial canals, three distal canals, and two palatal canals.⁹ Root number and morphology of South Indian population molars

were different to those in Burmese (2001)¹⁰ and Thai (2002)¹¹ populations, where all first and second molars had completely three separate roots. In this study, it was observed that all maxillary first molars 100% had three separate roots, whereas in second molars only 41% had three separate roots, 42% two root fused, and 16% three roots fused.

The MB root of the maxillary first molar has undergone more research and studies than any other root in the mouth. It generally has one or two canals but a third canal has been reported.⁹ Second MB canal (MB2) of South Indian population molars was different to those in Japanese (1999),¹ Burmese (2001),¹⁰ and Thai (2002)¹¹ populations, where Japanese maxillary first molar present 27% of MB2 canal; Burmese population present 68% in first molar, 49% in second molar; Thai population present 65% of MB2 in first molars, and 55% MB2 in second molars. In this study, MB2 canal was found to be 84% in maxillary first molar and 38% in second molars. In the two-canal MB roots, the Type II, IV, and VI canal systems were the most prevalent. MB2 canals are often very fine and difficult to negotiate; consequently, more errors in instrumentation occur in this tooth than any other. Anastomosis between the two canals in mesial root may take the form of narrow canals or wide fins, both making instrumentation and disinfection challenging.¹²

Accessory and lateral canals are communications between the pulp and the periodontium in the apical, middle, or coronal third of the root.¹³ According to Vertucci (1984),⁶ lateral canals occur most commonly in the apical third of the root (73.5%), followed by middle third (11.4%) and cervical third (6.3%). They are formed by the entrapment of periodontal vessels in Hertwig mesial root mayot sheath during calcification.^{14,15} They serve as avenues for the passage of irritants primarily from the pulp to the periodontium. The observed prevalence of lateral canals in the apical third of Burmese (2001)¹⁰ and Thai (2002)¹¹ populations were 13% and 10.5%, respectively. In the present study, the lateral canals were found to be highest in the apical third of MB root (51% in first molars and 40% in second molars). In this study, intercanal communications were most prevalent in maxillary first molars (MB roots - 32%). Whereas in Burmese (2001)¹⁰ populations, it was 27% in first molars; and in Thai (2002)¹¹ populations, it was 16% in first and second molars.

The clearing technique being three-dimensional also reveals the bucco lingual nature of canals which are usually not discernible in the radiograph. The palatal root curvature is more commonly seen toward the buccal, and this cannot be

visualized from the radiographs.¹² As a result, the clinician may assume that a canal is straight and may over enlarge what is, in reality, a facial or lingual curvature, resulting in ledging or perforation.¹⁶ In this study, palatal root curvature at apical third in the first molar was more commonly toward the buccal (70%), followed by palatal (4%) and straight (20%). The degree of curvature was less in maxillary first molars (average of 10°) compared to second molars (average of 20°). The greater the degree of curvature more likely is the formation of a ledge. A radiograph shows that the instrument or obturation no longer follows the original curve. Relocating and renegotiating the original canal is a problem; correcting the ledge is difficult, even if the original canal is renegotiated.¹⁶

Although clearing technique helps in a detailed investigation of the delicate root canal systems, it has few drawbacks. There can be distortion in the morphology of the tooth as a result of the demineralization process.¹⁷ Moreover, the dye solution may not fully infiltrate into narrow canals and ramifications if the dimension was below the grain size of the injected dye.¹⁸ Recent advances in imaging technology enable the use of micro-computed tomography (MCT) and cone-beam computed tomography in the study of root canal morphology. MCT has been proven to be an effective tool for visualizing the complex root canal anatomy in various studies and can be considered when in-depth morphological analysis is desired.^{19,20}

CONCLUSION

The MB roots of the South Indian maxillary molar possessed a variety of canal system types, over 84% of first molars had MB2 canals and 38% in second molars. The palatal and distobuccal canal mainly had Type I canals. Prevalence of lateral canal was 51% and 41% in first and second molars, respectively, and exhibited highly in the apical third. Outcomes of non-surgical and surgical endodontic procedures are influenced by highly variable three-dimensional anatomy of teeth.

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Effect of Vaginal Administration of Nitric Oxide Donor Isosorbide Mononitrate on Cervical Ripening Before Induction in Term Pregnancy: A Randomized Controlled Study

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Abstract

Introduction: Nitric oxide donors have been shown to cause cervical ripening. The aim of this study was to investigate whether sustained-release isosorbide mononitrate (ISMN-SR) 60 mg administered vaginally is effective for preinduction cervical ripening in term pregnancy and any effect on mother and fetus.

Materials and Methods: A single-blinded study was conducted in Raja Mirasudar Hospital, Thanjavur for a period of 12-month. This study was conducted in 200 patients with uncomplicated singleton pregnancies at term. These patients were randomly allocated to receive either ISMN-SR 60 mg ($n = 100$) or vitamin C 100 mg ($n = 100$) vaginally. Modified Bishop's Score was evaluated after 24 h in each group.

Results: At the commencement of the study, there were no differences between mean ages, Bishop score of the two groups. In the ISMN-SR group, there was a significantly higher increase in the mean modified Bishop score (2.466 vs. 0.561) $P < 0.05$ after 24 h. Percentage of those requiring additional ripening agent found to be lower in the study group (56.7%) compared to control group (91.7%). Cesarean section rates were similar in both groups.

Conclusion: ISMN-SR administered vaginally is effective for pre-induction cervical ripening.

Key words: Cervical ripening, Labor, Nitric oxide, Term pregnancy

INTRODUCTION

Most exciting events in women's life are labor. Many steps are involved normally in a normal course of labor. Labor usually follows a normal pattern and result in delivering a healthy child to the mother and to the world. This study is mainly focused on the effects of nitric oxide (NO) donor isosorbide mononitrate (ISMN) for cervical ripening in term pregnancy. Induction of labor is necessary in situation, where it could be hazardous to wait for the spontaneous

onset of labor. In the case of ripened cervix, the most common methods of labor induction are oxytocin infusion and/or amniotomy. In unripened cervix, it is wise to use local medical or other mechanical methods to achieve ripening. The most common medical agents used for ripening of cervix are prostaglandin (PG) administered intracervically or vaginally. Thus, PG kept via these routes are associated with side effects like hyperstimulation. Hyperstimulation is registered in 5% of women treated with PG, moreover, treatment is not always effective and it has to be repeated. Hence, many cases of failed induction have been reported with PGE₂. Therefore, it is necessary to find an alternative drug that is the more effective and it should not be associated with hyperstimulation. One such drug is NO donors, ISMN.

NO, a free radical synthesized endogenously in human uterine cervix.¹ Studies were performed by Ledingham

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et al., 2000; Vaisanen-Tommiska *et al.*, 2003 shown that it has been up regulated at term pregnancy. Hence, NO was believed to play a major role as ripening agent (Chwalisz, 1997; 1998).^{2,3} Many studies on vaginally administered NO donor have shown ripening effects of this drug (Thomson *et al.*, 1997).^{4,5} Current study aims to give role of NO donor, ISMN on cervical ripening and labor induction.

Drugs commonly used in hospital settings such as PGE₂ and E₁ (PGE₁) were effective for cervical ripening. However, the high incidence rates of myometrial hyperstimulation, uterine tachysystole and fetal distress associated with their use.

ISMN, an NO donor had been shown to induce ripening of cervix NO found to be the final mediator of cervical ripening. NO donor inhibit uterine contractions and promote uterine blood flow. It acts by altering cervical collagen tissue.

NO play a major role in regulating many factors in the inflammatory process of cervical ripening. There are three major isoforms of NO synthases (NOS). All these three major isoforms of NOS are present in human uterine cervix (Bao *et al.*, 2001, Tschugguel *et al.*, 1999).² Moreover inducible NOS have been found in epithelial cells and stromal spindle cells (Tschugguel *et al.* 1999)² and it has also been demonstrated by immunostaining in the uterine cervix at term (Ekerhovd *et al.*, 2000). Many studies have shown that inducible enzymes have been upregulated in human uterine cervix during delivery.² Metabolites of oxides of nitrogen in the cervical fluid are increased at term compared to preterm. Inducible NOS isoform can be induced by cytokines, tumor necrosis factor α , interferon λ or endotoxins in a calcium-independent manner. NO may exert its effect through stimulation of endogenous PG synthesis through cyclooxygenase stimulation³ or through stimulation of at least one matrix metalloproteinase (MMP), MMP-1.⁶

During late pregnancy, there is an alteration in glycosaminoglycan composition of the cervix, which plays an important role in ripening process. Amount of hyaluronic acid that is present in the cervix is increased at term. Together these changes bring an alteration in the binding affinity to collagen thus altering the tissue hydration and cervical extensibility (Rechberger *et al.*, 1996).

NO suppresses the synthesis of proteoglycan (Hauselmann *et al.*, 1998). NO promote apoptosis that has been demonstrated in smooth muscle cells (Romero *et al.*, 1990) and fibroblasts (Leppert, 1998) during cervical ripening. Several lines of evidence from studies of other tissue suggest that this process is stimulated by NO (Nicotera *et al.*, 1997).⁷ Finally, cervix is constituted by only 10-15% of smooth muscle cells, the role of which

has been studied to some extent only. Relaxing effects of cervical smooth muscle following administration of NO donors have been demonstrated *in vitro* in cervical tissue specimens from term women.

Taken together, NO found to be the final mediator of cervical ripening. The present study was performed to evaluate the safety and effectiveness of ISMN treatment for cervical ripening.

MATERIALS AND METHODS

A randomized prospective placebo-controlled study was conducted in Raja Mirasudar Hospital, Thanjavur during the period of August 2014-August 2105. Institutional Ethical Committee approval was obtained.

The participants all had a singleton pregnancy, with gestational age >40 weeks, uncomplicated pregnancy and intact membranes.

Exclusion criteria were antepartum hemorrhage, previous uterine incision, fetal malpresentation, ruptured membranes, preeclampsia, intrauterine growth restriction, oligohydramnios, heart disease, diabetes, patient with H/O headache, palpitation, and hypotension.

Informed consent was obtained from the women. Patients were randomly allocated to one of the two study groups. Induction is necessary, since the progression of pregnancy after 40 weeks, increases the risk of adverse outcomes such as meconium passage, chorioamnionitis, macrosomia, intrauterine death, and need for caesarean delivery.

Baseline Bishop's Score was recorded. The participants were given either ISMN 60 mg, 2 tablets administered 12 h apart into posterior fornix of the vagina or vitamin C 100 mg 2 tablets as placebo.

If Bishop score 6 or higher, labor was induced by oxytocin. In participants, whose Bishop score <6 after second dose, 0.5 mg PGE₂ gel instilled intracervically. Treatment with PGE₂ gel repeated after 6 h, only once, if cervical did not occur and was followed by oxytocin infusion.

The second dose of ISMN repeated only after evaluation of blood pressure, pulse rate, fetal heart rate, and verification of symptoms such as a headache.

Primary outcome variable was Bishop Score of baseline and 12 h after the second dose, duration of labor, whether delivered vaginally or by caesarean section. Other maternal outcome variables were presence or absence of tachycardia, hypotension, headache, and palpitation.

Fetal outcome variables were Apgar score at 1 and 5 min and whether neonatal intensive care unit admission necessary or not. Secondary outcome variable was operative delivery rates and complications such as uterine hyperstimulation, meconium stained amniotic fluid, tachysystole, and post-partum hemorrhage.

The data, from our study, were collected compiled and statistically analyzed using SPSS statistics, software version 20. A statistical test used for analysis were *t*-test and Chi-square test. *P* < 0.05 was taken as significant.

RESULTS

A total of 200 women were randomized.

- 100 to the study group
- 100 to the control group.

Comparisons of Bishop score, PGE₂ oxytocin usage, labor duration between study and control group. All the results are depicted in tabular form. (Tables 1-6).

DISCUSSION

In obstetrics and gynecology, NO donor has been used for the treatment of preterm labor. NO donor has been shown to induce cervical ripening without causing uterine contraction by rearrangements of cervical collagen tissue and ground substance. In contrast to PG, they also inhibit uterine contraction and promote uterine blood flow.

ISMN is a slow releasing NO donor. Levels of NO metabolites in the cervix are known to be increased at term.

A significant improvement in Bishop score was noted in study group after second dose of ISMN. Similar results were reported in earlier studies by Rameez *et al.*, 2007,⁸ Hana *et al.*, 2010, Bullarbo *et al.*, 2007,⁹ Agarwal *et al.*, 2012,¹⁰ Helal *et al.*, 2004.

The need for additional ripening agent PGE₂ was found to be lesser in the study group (56.7% vs. 91.67%). This was in agreement with study by Agarwal *et al.*, 2012, Bollapragada *et al.*, 2009 and Bullarbo *et al.*, 2007.⁹

The requirement for oxytocin was found to be lesser in the study group compared to control group (56.7% vs. 71.7%). However, the differences were not statistically significant. On contrary study by Eddama *et al.*, 2009,¹¹ Habib *et al.*, 2008 show oxytocin requirement found to be lesser in ISMN group and was statistically significant.

Duration of labor was found to be significantly lesser in study compared with that of the control group. This was

Table 1: Demographic characteristics of the study participants

Characteristics	Study group (n=100)	Control group (n=100)	P value
Age (years)	23.78±1.757	23.67±1.820	>0.05
Gestational age (week)	3.62±1.075	3.68±1.172	>0.05
Parity (%)			
Primigravida	53.5	55	>0.05
II Gravida	30	26.7	>0.05
III Gravida	16.7	18.3	>0.05

Table 2: Demographic characteristics of the study and control groups were comparable

Variable	Study group	Control group	P value
Baseline Bishop score	1.80±0.879	1.82±0.39	>0.05
Post intervention Bishop score	4.87±2.466	2.08±0.561	<0.05
PGE ₂ used (%)	56.7	91.7	<0.05
PGE ₂ not used (%)	43.3	8.3	<0.05
Oxytocin (%)			
Used	56.7	71.7	>0.05
Not used	43.3	28.3	>0.05

PGE₂: Prostaglandin E₂

Table 3: Comparison of mode of delivery between study and control group

Variable	n=100 (%)		P value
	Study group	Control group	
Vaginal delivery	65	53.3	>0.05
Outlet forceps	10	15	>0.05
Vacuum delivery	3.3	0	>0.05
LSCS	21.7	31.7	>0.05

LSCS: Lower segment Cesarian section

Table 4: Adverse maternal side effects

Effect	n=60 (%)		P value
	Study group	Control group	
Palpitation	16.7	0	<0.05
Headache	65	1.7	<0.05

Table 5: Comparison of labor complication

Variable	Study group (%)	Control group (%)	P value
Hyper stimulation	0	5	>0.05
PPH	1.7	3.3	>0.05

PPH: Postpartum hemorrhage

Table 6: Fetal variables

Meconium			
With PGE ₂	13.3%	15%	>0.05
Without PGE ₂	1.7%	5%	
Total	15%	20%	
Non-reactive CTG			
With PGE ₂	3.3%	11.7%	>0.05
Without PGE ₂	-	-	
Total	3.3%	11.7%	

PGE₂: Prostaglandin E₂

in agreement with study, Agarwal *et al.*, 2012, Helal *et al.*, 2004, Habib *et al.*, 2008.

The common side effects were palpitation and headache. In the present study, percentage of study group and control group reporting palpitation found to be 16.7% and 0% ($P < 0.05$).

Agarwal *et al.*, 2012¹⁰ found that in his study percentage of those experiencing palpitation in study group as 18% and none in control group. This result was in agreement with the present study.

Habib *et al.*, 2008¹² in his study reported that those experiencing palpitation in ISMN group found to be 13.73% and none in control group. $P = 0.02$ is statistically significant. This result was in agreement with this study. In the present study, no cases of tachysystole and hyperstimulation have been found in ISMN group.

This study confirmed that vaginally administered ISMN neither induced tachysystole nor hyperstimulation.

No abnormal fetal heart tracings were noted in women after ISMN treatment.

Use of ISMN by vaginal route helps in improving Bishop score and reduces the duration of labor. It has no effect on the hemodynamic state of the mother. In contrast to the other cervical ripening agents, NO donor administered vaginally had the advantage of the absence of uterine contraction. Hence, it removed the main reasons that women were monitored during the induction of cervical ripening.

NO donors suitable agents for preinduction cervical ripening. The absence of contraction had obviated the need for fetal monitoring.

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CONCLUSION

The use of ISMN by the vaginal route as ripening agent before induction of labor at term helps in improving Bishop score and reduces the duration of labor. It has no effect on the hemodynamic state of the mother and fetus. In contrast to the other cervical ripening agents, NO donor, administered vaginally, has the advantage of absence of uterine contractions. Hence, it removes the main reason that women are monitored during the induction of cervical ripening. Hence, NO donors are suitable agents for pre-induction cervical ripening at term. The absence of contraction has obviated the need for fetal monitoring such agent could be given on as outpatient basis.

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Scenario of Palliative Radiotherapy at a Cancer Centre in Kashmir

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Abstract

Background: Almost two-third cancer patients who present to hospitals in developing countries have either locally advanced or metastatic disease. Palliative radiotherapy (PRT) is an indispensable modality for control of cancer symptoms in advanced stages and approximately one-half of prescribed radiotherapy is given for palliation of symptoms.

Materials and Methods: Scenario of PRT was analyzed in 125 patients with various malignancies, who either needed radiotherapy at presentation or later sometime after disease progression. We analyzed the data with respect to (i) socio-demographic status, (ii) site or indication of palliation, (iii) dose prescribed, and (iv) response rate. Descriptive statistics were evaluated in terms of frequencies and percentage to allow comparisons.

Results: About 70% ($n = 87$) of the patients were males; median age of the patients receiving PRT was 55 years (range: 18-70); 28% ($n = 37$) patients received PRT at the primary site, whereas the rest (72%) received PRT at the metastatic site. Pain was the most common indication of PRT in 60% patients, followed by brain metastasis (raised Intra Cranial Tension), hemostatic PRT, and cord compression. The median dose prescribed was 20 Gy (range 8-30 Gy) delivered in 1-10 fractions. Overall response rate after 2 weeks of completion of PRT was 65%; the median follow-up of the patients was 109 days (range 7-280 days). The overall long-term symptom control was 20%.

Conclusion: Radiotherapy is a successful, time-efficient, cost-effective, and safe modality to palliate the symptoms of cancer patients in their advanced stages. The optimal use of PRT requires accurate survival prognostication, judicious enrolment of patients on need basis and, choosing regimens that best suit the patients in terms of toxicity and treatment duration.

Key words: Cancer, Metastasis, Pain, Palliative radiotherapy, Survival

INTRODUCTION

Radiotherapy has been used for palliating cancer symptoms soon after its discovery in the 1800's.¹ It is a cost-effective and time-efficient intervention that is associated with a low

toxicity profile and can relieve symptoms, such as pain, obstruction, bleeding, and neurologic symptoms due to the primary or metastatic tumor. While the complexity of palliative radiotherapy (PRT) has increased with the advent of newer technologies, the common sense goals of its delivery remain a good chance for symptom relief with a limited risk of side effects.²

In developed nations, radiation therapy is a potentially valuable, but under-utilized tool in end-of-life care programs that could greatly enhance the quality of life (QoL) in appropriately selected patients with advanced cancer who still have more than a few weeks or months to live.^{3,4}

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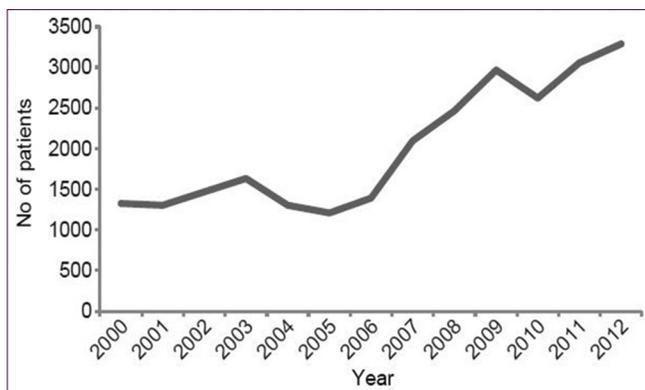
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In developing nations like India where advanced cancer presentations are more common,⁵ radiotherapy is used as much with a curative intent as is being used for palliation.

Over the last one decade, Kashmir valley has witnessed increase in incidence of cancer.⁶

More than half of patients present as locally advanced or metastatic disease⁷ requiring PRT at some point during disease course. In this study, we tried to outline the indications for PRT, the selection of appropriate dose-fractionation schemes, the response to PRT, and long-term symptom control.

MATERIALS AND METHODS

We conducted a retrospective, analytical study in the Department of Radiotherapy SMHS Hospital - a tertiary care hospital of Jammu and Kashmir, from January 2012 to July 2014. All the patients who were selected for the analysis had received PRT either at presentation for a locally advanced or metastatic disease or later after disease progression during follow-up. Written consent was taken from all the enrolled patients before starting PRT. Dose and fractionation were chosen keeping in view the performance score (PS), expected survival, and comorbid medical ailments. PS was calculated via Eastern Cooperative Oncology Group (ECOG) scoring system.⁸ Adjuvant supportive measures were instituted as and when required in the form of corticosteroids, analgesics, antidepressants, and psychotherapy. Symptomatic pain relief and clinical improvement were observed over a period of 2 weeks and above. Differences in pain improvement, time to improvement of symptoms, the durability of symptom control, improvement in QoL were analyzed with respect to demography, dose and fractionation of radiation, and, site of metastasis. Dose and fractionation of radiotherapy were determined by (i) histology of the primary tumor, (ii) duration of neurodeficit, (iii) PS, (iv) expected survival, and (v) feasibility of attending hospital. Endpoints considered

for response were pain control, reversal of neuro-deficit, improvement in QoL.

Eastern Cancer Oncology Group: Classification⁸

Grade	ECOG
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work and office work
2	Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
4	Completely disabled cannot carry on any self-care. Totally, confined to bed or chair
5	Dead

Statistical Analysis

The data were analyzed by an experienced statistician using Student's *t*-test and Chi-square test wherever appropriate. *P* < 0.05 was considered significant.

Table 1: Demographic profile of study population

Demographic profiles	Number of patients (%)
Males	87 (70)
Females	38 (30)
Rural	90 (72)
Urban	35 (28)

Table 2: Site specific dose- fractionation

Site	Number of patients	Symptoms	Dose/ fractions
Esophagus	8	Dysphagia, pain	30 Gy/10#: 6 20 Gy/5#: 2 (recurrence)
Lung	6	Pain, collapse, dyspnea	30 Gy/10#: 3 45 Gy/20#: 3
Skin	4	Pain	8 Gy/1#: 1 15 Gy/3#: 3
Rectum	3	Pain	15 Gy/3#: 1 30 Gy/10#: 2
Head and neck	2	Pain	15 Gy/3#
Sarcoma	2	Pain	30 Gy/10#
GBM (recurrence)	2	Headache, vomiting	15 Gy/3#

GBM: Glioblastoma-multiforme

Table 3: Proportion of metastasis in study group

Site	Number of patients (%)
Bone metastasis	30 (24)
Brain metastasis	25 (20)
Hemostatic	16 (13)
Cord compression	15 (12)
Svc obstruction	12 (9)
Primary site	27 (21)

RESULTS

The outcome of 125 patients were analyzed. The majority of the patients were males (70%) and from rural background (72%) shown in Table 1.

The median age of the patients receiving PRT was 55 years (range: 18-70); pain was the most common symptom (90%) for which PRT was given (Table 2).

Although liver was the most common site of metastasis, bone and brain metastases were the most common sites (24% and 12%, respectively) for which PRT was sought (Table 3).

About 30% of the patients who required PRT had presented in a locally advanced stage who eventually progressed to metastatic disease. Breast and lung were the most common primaries which metastasized to bones, other primaries were prostate, nasopharynx, urinary bladder, and melanoma (Table 4). The most common fractionation used in bone metastasis was 8 Gy single fraction.

Brain metastasis constituted the second most common site of metastasis with lung as primary in 7 patients. Two patients with small cell carcinoma lung (SCLCa) and one with melanoma had multiple metastases and succumbed after 2 months of RT (Table 5). The most common fractionation used was 30 Gy/10#.

Exactly 16 patients had received hemostatic radiotherapy of which 8 had hemoptysis and 5 had hematuria. Other indications were bleeding from fungating squamous cell carcinoma skin which has recurred locally and were not amenable to surgical intervention. Fractionation used was 20 Gy/5#. One patient received PRT for bleeding per rectum with underlying advanced rectal cancer (Table 6).

Around 15 patients had clinical and radiological evidence of cord compression of whom four each was secondary to myeloma and prostatic cancer (Table 7). Three patients had breast as their primary, two had lung, and one each had non-Hodgkin's lymphoma (NHL) and carcinoma unknown primary site (CUPs).

Hypo-fractionation schedule of 8 Gy/1# was chosen for two patients with prostate cancer because of poor performance status and complicated cord compression (compression with fracture) which was not amenable to neurosurgical stabilization. One patient each with CUPs and myeloma received 8 Gy/1# as both had disseminated visceral metastasis and paraplegia of more than 1 week. One patient each with prostate, breast and myeloma who received 15 Gy/3# had multiple sites of cord compression.

Table 4: Profile of patients receiving radiotherapy for bone metastasis

Dose/fractionation	Primary site	Number of patients	Total (%)
8 Gy/1#	Lung	5	11 (36)
	Breast	2	
	Prostate	3	
15 Gy/3#	Nasopharynx	1	4 (13)
	Lung	2	
	Breast	2	
20 Gy/5#	Nasopharynx	3	7 (23)
	Breast	3	
	Urinary bladder	1	
30 Gy/10#	Prostate	3	8 (26)
	NHL	2	
	Breast	2	
	Melanoma	1	

The most common fractionation used in bone metastasis was 8 Gy single fraction
NHL: Non-Hodgkin's lymphoma

Table 5: Profile of patients receiving radiotherapy for brain metastasis

Dose/fractionation	Primary site	Number of patients	Total
30 Gy/10	Lung	5	12
	Breast	4	
	Anaplastic thyroid	2	
	Melanoma	1	
25 Gy/05	Lung	2	03
	Choriocarcinoma	1	

The most common fractionation used was 30 Gy/10#

Table 6: Profile of patients receiving hemostatic radiotherapy

Primary site	Number of patients	Dose/fractionation	Total patients
Lung (hemoptysis)	05	20 Gy/5#	8
Urinary bladder (hematuria)	03		
Lung (hemoptysis)	03	15 Gy/3#	8
Urinary bladder (hematuria)	02		
Skin (fungation)	02		
Rectal cancer (advanced)	01		

Table 7: Profile of patients receiving radiotherapy for cord compression

Primary site	Number of patients	Total	Dose/fractionation
Myeloma	2	08	30 Gy/10#
Lung	2		
NHL	1	03	15 Gy/5#
Breast	2		
Prostate	1		
Breast	1	04	8 Gy/1#
Myeloma	1		
Prostate	1		
CUPs	1		
Prostate	2		
Myeloma	1		

CUPs: Carcinoma unknown primary site, NHL: Non-Hodgkin's lymphoma

Eight patients received protracted course of PRT of 30 Gy/10# for cord compression, had reasonable PS (ECOG of 1-2), had bone as the only site of metastasis, NHL patient had two sites of nodal disease and presented with a paraspinal mass), had expected survival of more than 6 months, primary diseases under remission and none of them had any neuro-deficit. The dose in NHL patient was later escalated to 45 Gy as the patient had contraindication to chemotherapy.

About 12 patients were irradiated for superior vena cava obstruction (SVCO), of which six (2 Hodgkin's disease [HD], 2 NHL, 1 thymoma and 1 small cell lung cancer [SCLCa]) presented with SVCO while as six developed later during the course of treatment and relapse. Fractionation used was 15 Gy/5# (Table 8).

Of the six patients, one each with SCLCa and NHL had rapid worsening of clinical symptoms in the form of deteriorating sensorium, whereas one each with HD and SCLCa had impending airway obstruction for which radiotherapy was started upfront. One patient with NHL had a medical contraindication to chemotherapy, and another with HD had refused chemotherapy. All these patients had received corticosteroids as adjunctive treatment.

PRT as a primary treatment modality was given in 27 patients of whom esophageal cancer constituted approximately one-third (29%). Dysphagia and pain were the prime indications. PRT of 30 Gy/10# was used in six patients whereas two patients who had recurred after radical radiotherapy received 20 Gy/5#. Six patients of primary lung cancer received PRT for pain, dyspnea and collapse. 30 Gy/10# and 40 Gy/20# were two schedules used; former used for infirm and low expected survival patients. Four recurrent skin cancer (squamous cell) patients received

PRT at the primary site (thigh in three and abdominal wall in one) for fungating and infiltrating large volume disease not amenable for resection. Pelvic pain due to unresectable rectal cancer was another indication for PRT in three patients one of whom had recurrent disease after radical RT. 30 Gy/10# was given in two patients whereas the one with recurrent disease was given 15 Gy/3#. Four patients, two each, with recurrent retroperitoneal sarcoma with distant metastasis and recurrent glioblastoma-multiforme (GBM) received PRT for pain, obstruction and raised intra-cranial pressure, respectively (Table 2).

We observed that complete relief of pain (CRP) from bone metastasis was observed in 40% of patients, partial relief in 90% and no response was seen in 20% of patients. Overall response rate (ORR) was 70-80% (Table 9).

CRP was seen in patients who had (i) breast and NHL as primary, (ii) solitary metastatic site, (iii) ECOG score of 0 or 1, and (iv) age less than 50 years and male sex. No difference in pain relief and survival was seen as regards to dose and fractionation, but retreatment rates were high in single fraction group.

All patients with brain metastasis except those with primaries as melanoma and anaplastic thyroid cancer showed overall improvement 60-70% of symptoms (Table 10).

While the improvement lasted 2-3 months, most of them succumbed to their primary disease. Different "dose-fractionation" did not alter the outcome nor did the sex and age of the patient.

Hemostatic PRT appeared to be very effective in controlling bleeding in lung cancer and urinary bladder cancer patients with complete cessation of hemoptysis and hematuria in over 60% of patients.

The effect was more pronounced in small cell histology in lung cancer. Overall response was 60%, but patients with skin and rectal cancer had only partial control. The two fractionation schedule appeared to be equally effective (Table 11).

Six patients out of 12 who received PRT for SVCO had over 90% response and included NHL, HD and SCLCa as primary disease. Two patients one with non-small cell lung cancer (NSCLCa) and other thymoma had 50% response. All patients with HD, NHL and SCLCa and one patient with NSCLCa received radical dose of RT later. All of them received same dose of PRT of 15 Gy/5#. All patients were below 50 years of age except one SCLCa and one NSCLCa. All patients had ECOG PS of 1 or 2. ORR was 75% (Table 11).

Table 8: Profile of patients receiving radiotherapy for SVCO

Primary site	Number of patients	Dose/fractionation
Non-small cell Ca	5	15 Gy/5#
Small cell Ca	2	
Non-Hodgkin's lymphoma	2	15 Gy/5#
Hodgkin's disease	2	15 Gy/5#
Thymoma	1	15 Gy/5#

SVCO: Superior vena cava obstruction, Ca: Cancer

Table 9: Response rate of treated patients

Symptom	Complete response	Partial response	No response
Bone pain (%)	40	90	20

Table 10: Response rate in various malignancies

Brain metastasis	Primary lung cancer	Primary breast cancer	Primary choriocarcinoma	Malignant melanoma	Anaplastic thyroid cancer
Response (%)	70	65	75	15	10

Table 11: Response rate of various treated malignancies

SVCO	Lung (NSCLCa)	Lung (SCLCa)	NHL	HD	Thymoma
Response (%)	50	95	95	92	50

SVCO: Superior vena cava obstruction, NSCLCa: Non-small cell lung cancer, SCLCa: Small cell lung cancer, NHL: Non-Hodgkin's lymphoma, HD: Hodgkin's disease

Table 12: Response rate of patients with cord compression

Primary	100%	50%	Stable/no progression	No response/progression
Prostatic	-	-	1	2
CUPs	-	-	-	1
Breast	1	1	1	-
NHL	1	1	-	1
Myeloma	1	1	1	-
Lung	1	1	-	-

CUPs: Carcinoma unknown primary site, NHL: Non-Hodgkin's lymphoma

Table 13: Overall response rate with PRT

Disease	Symptom	Percentage
Ca esophagus	Pain, dysphagia	70
Ca lung	Pain, dyspnea	65
Ca skin	Pain	50
Ca rectum	Pain	50
GBM	Pain	50
Sarcoma	Pain	50
Head and neck	Pain	50

PRT: Palliative radiotherapy, GBM: Glioblastoma multiforme, Ca: Cancer

Two patients with complicated cord compression due to metastatic carcinoma prostate who received single fraction showed the progression of neurodeficit, whereas the patients with CUPs and myeloma with more than 1 week paraplegia did not show any improvement. One patient each with prostate, breast and myeloma as primaries had stable disease and no progression in neurodeficit was observed. Of the eight patients who received 30 Gy/10# one each with NHL, breast, myeloma and lung as primaries had complete recovery whereas four had over 50% recovery of neurodeficit (Table 12).

Overall response to dysphagia was 70% in patients receiving PRT for cancer esophagus, though median survival did not improve in these patients and none survived beyond 6 months. Fractionation did not seem to affect the time to improvement, neither sex nor age. All the patients were more than 60 years of age.

Pain and dyspnea improved in four of the six lung cancer patients; all the four were small cell variant. Response lasted for an abbreviated period of average 2-month after which patients progressed and were put on supportive care only. Two non-responders had non-small cell histology, had ECOG of 3 and were more than 60 years age.

About 50% pain improvement was seen in 3 out of 4 skin cancer patients irrespective of dose-fractionation schedule. Two rectal cancer patients who had 70% response with 30 Gy/10 fractions (30 Gy/10#) schedule were below 60 years and were receiving RT for the first time, and concurrent chemotherapy was used in these set of patients. Recurrent rectal cancer patient showed 30% response. Of the six patients two each with sarcoma, GBM and head and neck cancer showed up to 50% relief. All had recurrent disease (Table 13).

DISCUSSION

Radiotherapy is an indispensable treatment modality in cancer care being administered with palliative intent in up to 40% to 50% of the patients of any radiation oncology department.⁹ The goal of PRT is to achieve durable symptom relief at the shortest expense of time and resources while inflicting the least possible toxicity.¹⁰ Palliative RT is based on the principles of maximizing symptom relief with minimal consumption of time and resources, and causing the least possible concern to the patient with regards to span of treatment and toxicities afforded. Lower total time as well as lower total dose is the hallmark of palliative RT.¹¹

Although painful bone metastasis is the most common reason for the delivery of PRT, approximately 66% of PRT is delivered for the management of other symptoms.¹² Bone metastases are a very common manifestation of malignancy, and radiotherapy provides partial (50%) pain relief in 60-80% and complete pain relief in 30-50% of patients within days to weeks after the initiation of therapy.¹³ As is evident in our analysis, pain relief was equivalent with fractionation regimens of 30 Gy/10#, 20 Gy/5#, or a single 8 Gy/1#.¹⁴ As per literature retreatment rates may be higher in those who receive a single fraction and a second course of therapy can be expected to provide a reasonable rate of pain relief.¹⁵ Pain relief secondary to bone metastasis seems to be independent of dose-fractionation, whereas response

in symptoms of cord compression due to lymphomas, small cell cancer appear to correlate with histology and dose. Moreover, female patients seemed to have a more prolonged survival as compared to men presumably due to higher number of breast cancer patients who have a long survival even with bone metastasis.

PRT has traditionally been used as a non-invasive means of palliating dysphagia in patients with incurable esophageal cancer.¹⁶ Options of palliating esophageal cancer for dysphagia are stenting, brachytherapy or feeding jejunostomy. Brachytherapy was not available at our center and stenting was not elected in view of low PS. However, overall survival seems to be unaffected by PRT and PS and comorbid conditions play a role in overall survival. SVCO is a life threatening sequelae of advanced cancer. Most of the cancers causing SVCO are sensitive to chemotherapy as well as radiotherapy; however for cancers less radio-responsive to chemotherapy, radiotherapy is an efficacious tool of management. We analyzed in this study that patients with SVCO secondary to lymphoma and SCLCa had more than 90% response and that RT doses were escalated to definitive dose levels following good clinical response. Many patients with metastatic lung cancer, and selected patients with locally advanced disease, are routinely treated with thoracic radiotherapy with palliative intent to relieve tumor-related symptoms (hemoptysis, bronchial obstruction, cough, shortness of breath, and chest pain) and to improve health-related QoL.¹⁷ We saw age, PS and histology were variables which affected the response in our study. Poor outcome in low PS patients may be due to use of a low-dose, hypofractionated regimen and omission of chemotherapy. Rectal cancer is prone to recur locally¹⁸ and the outcome of a recurrent rectal cancer is even post adjuvant treatment is dismal. We saw more radiological and symptomatic improvement in RT naive unresectable rectal cancer compared to the re-irradiation cohort; this might in part be due to use of concurrent chemotherapy in newly diagnosed advanced unresectable cancer. In cord compression, complete recovery of neurodeficit in NHL, breast, myeloma and lung as primaries suggest a radio-responsive primary, single site of compression, compression without fracture and a protracted fractionation, good prognostic indicators for response. Short fractionation was chosen in patients with low PS and poor chances of recovery as corroborated with literature.¹⁹

Hemostatic PRT appears to be effective in controlling bleeding in advanced cancers of lung, urinary bladder, rectum and skin and improving QoL. Our results of greater than 60% overall response are corroborated in various studies.²⁰ Short fractionation schedules should be preferred. Single or reduced fraction regimens appear to be

as effective as multiple fractions in controlling bleeding.²¹ Brain metastasis is the terminal event in most malignancies and survival does not exceed beyond 6-7 months in most cases even after palliative RT or drugs like temozolomide. Radio surgery is a relatively promising intervention for patients with solitary metastasis, reasonable PS but patients in our study who fulfilled the criteria did not afford due to financial constraints. Some less well-recognized favorable parameters seem to be a response to steroid treatment, serum lactate dehydrogenase, age, sex in lung primaries, and site and histology of primary tumor.²²

CONCLUSION

Poor health awareness, quackery, late referral to a tertiary care centre and financial constraints, all play an important role in advanced presentation of cancer in developing nations like India. PRT seems to be an important tool in improving QoL and pain relief albeit without an improvement in long-term survival. PS and age independently affect the outcome in all settings of palliative care, but long-term outcome to PRT in all demographic settings is same. To conclude PRT should be considered at all stages of advanced cancer as it is least invasive, cost-efficient, and associated with minimum toxicities.

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Effect of Alcohol Consumption on Indices of Serum Iron and Ferritin in a Tertiary Care Hospital of Rural, Maharashtra

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Abstract

Background: Alcohol increases body iron stores. Alcohol and iron may increase oxidative stress and the risk of alcohol-related liver disease. The relationship between low or “safe” levels of alcohol use and indices of body iron stores, and the factors that affect the alcohol iron relationship have not been fully characterized. Other aspects of the biological response to alcohol use have been reported to depend on iron status.

Aims and Objectives: (1) To study the serum iron indices (serum iron, transferrin saturation, and ferritin) in alcoholics. (2) To study the relation of age, sex, type of alcohol, amount of alcohol, duration of alcohol, and the alcoholic liver disease on iron markers.

Materials and Methods: A comparative study of 100 cases. It is calculated with a confidence interval of 95% and absolute precision of 10%. 25 controls, age and sex matched healthy subjects not consuming alcohol are taken in the study as controls.

Results: All the cases, in the study, were males 100% ($n = 100$). The majority of the cases 52% (52 cases) had history of consuming country liquor. About 14% (14 cases) had history of consuming beer. Only 4% (4 cases) had history of consuming rum. Mean values for serum iron, transferrin saturation, and ferritin varied with the duration of alcohol consumed and was not statistically significant (P value 0.59, 0.70 and 0.09, respectively). Mean values for serum iron and ferritin increased significantly with the increased amount of alcohol consumed (P value 0.003, <0.001, respectively).

Conclusion: Alcohol consumption is associated with increasing levels of serum iron, transferrin saturation and ferritin. Serum iron and ferritin levels increases with the increase in the amount of alcohol consumed.

Key words: Alcohol consumption, Duration of alcohol, Serum iron, Serum ferritin level, Serum transferrin level

INTRODUCTION

Alcoholism also called as alcohol dependence is a condition where there is clear evidence of alcohol use responsible for physical or psychological harm. Alcohol causes impaired judgment or dysfunctional behavior which may lead to disability or have adverse consequence for interpersonal relationship.¹ Alcohol is consumed by the majority of the

population at some times in their life. At low doses can have some beneficial effects such as decreased incidence of myocardial infarction, stroke, gallstones possibly vascular, and Alzheimer’s dementia, but consumption more than two standard drink-per day increase the risk for health problems in many organ systems.² Chronic liver disease in the clinical context is a disease process of the liver that involves progressive destruction and regeneration of the liver parenchyma leading to fibrosis and cirrhosis.³ Hepatic iron deposition unrelated to hereditary hemochromatosis is common in Cirrhosis.⁴ It is known since long time that iron stores are increased in alcoholics and heavy drinkers.⁵⁻⁷ Increase in indices of iron stores, such as serum ferritin has also been described in subjects drinking a small amount of alcohol.⁸ It has been suggested that iron accumulation is one of the mechanisms involved in chronic liver disease.^{9,10}

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Hence, mortality is greater from alcoholic liver cirrhosis in subjects with higher hepatic iron content.¹¹ There is evidence that both iron and alcohol can initiate free radical formation and produce oxidative stress within liver and hence hasten the progression toward cirrhosis.^{9,12,13} Conditions such as Porphyria cutanea tarda, hepatocellular carcinoma, hepatitis C may be promoted or exacerbated by high iron content alcohol or both.¹⁴⁻¹⁷ The relationship between alcohol intake and iron stores are therefore of interest both at the high end of alcohol intake spectrum and general population.

MATERIALS AND METHODS

This study was conducted in Medicine OPD and Indoor Patients admitted in Krishna Institute of Medical Sciences, Karad, over a period of 2-year. Study design: Comparative study and sample size: 100 cases, it is calculated with a confidence interval of 95% and absolute precision of 10%. 25 controls, age and sex matched healthy subjects not consuming alcohol are taken in the study as controls. Inclusion criteria: Persons consuming two or more drinks per day for more than 1 year duration and with or without liver cirrhosis. Exclusion criteria: (1) Cirrhosis of liver due to other cause, (2) Patient who has received iron therapy, (3) Patient who has evidence of gastrointestinal bleeding in last 3 months. After informed and written consent, subjects (cases and controls) meeting the above criteria are taken in the study. Detailed questionnaires regarding the alcohol intake in cases was taken and quantified into number of drinks per day. Through clinical examination was done with emphasis on vital function, height, weight, body mass index, and signs of liver cell failure.

RESULTS

The present study was performed in Department of Medicine, Krishna Institute of Medical Sciences, Karad, Maharashtra, India. Patients are divided into two groups. (1) Cases (those consuming alcohol), (2) control (those not consuming alcohol).

All the cases were male. The mean age in cases was 44.93 ± 11.85 years and in controls, it was 33.6 ± 9.10 years (Table 1 and Graph 1).

Around 32 (32%) cases have history of consuming alcohol for 6-10 years. About 27 (27%) cases have history of consuming alcohol for 11-15 years. Exactly 27 (27%) cases have consumed for 1-5 years and 13 (13%) cases for about 16-20 years. Only 1 case (1%) has history of consuming alcohol for more than 20 years (Table 2 and Graph 2).

It is observed that the mean value for sr. iron, transferrin saturation and ferritin vary with the age of the cases. However, the difference in their mean value is not statistically significant (*P* value 0.66, 0.99, and 0.87) (Table 3).

The mean values for serum iron and serum ferritin were found to be greater in people consuming brandy (172.58 ± 12.34 µg/dL and 573.08 ± 177.26 µg/L, respectively) than other alcohol types, but are not statistically significant (*P* = 0.42 and 0.206, respectively). The mean value for transferrin saturation is found to be greater in cases those who are consuming brandy (53.75% ± 2.86%) and wine (50.28% ± 2.28%) than other alcohol types and the difference are statistically significant (Table 4 and Graph 3).

The mean values for serum iron, transferrin, and ferritin are found to vary with duration of alcohol consumed. However, the difference in their mean values with the duration of alcohol consumed is not statistically significant (*P* value 0.59, 0.70 and 0.09, respectively) (Table 5 and Graph 4).

The mean values for serum iron and serum ferritin are found to increase with the amount of alcohol consumed. The mean values were (159.30 ± 10.82 µg/dL) and

Table 1: Age distribution

Age (in years)	Cases n=100 (%)	Control n=25 (%)
20-29	7 (7)	9 (36)
30-39	31 (31)	6 (24)
40-49	23 (23)	10 (40)
50-59	25 (25)	0 (0)
>60	14 (14)	0 (0)
Mean±SD	44.93±11.85	33.6±9.10

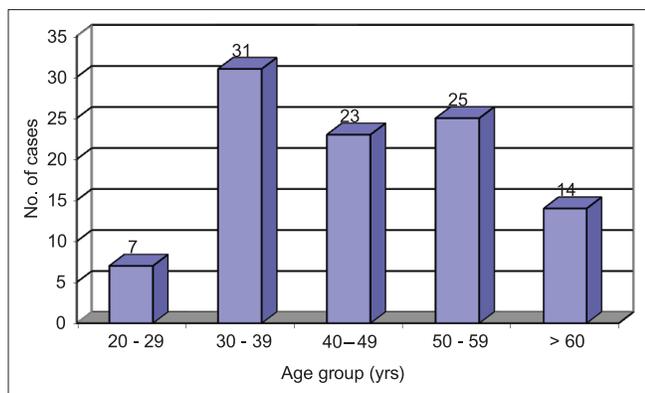
SD: Standard deviation

Table 2: Duration of alcohol consumed in cases

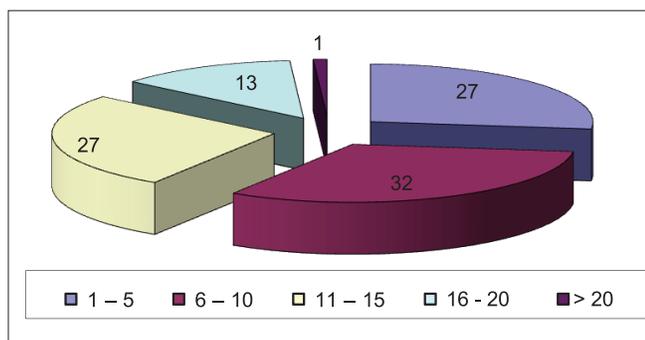
Duration of alcohol consumed (years)	Number of subjects (%) (n=100)
1-5	27 (27)
6-10	32 (32)
11-15	27 (27)
16-20	13 (13)
>20	1 (1)

Table 3: Age and iron indices in cases

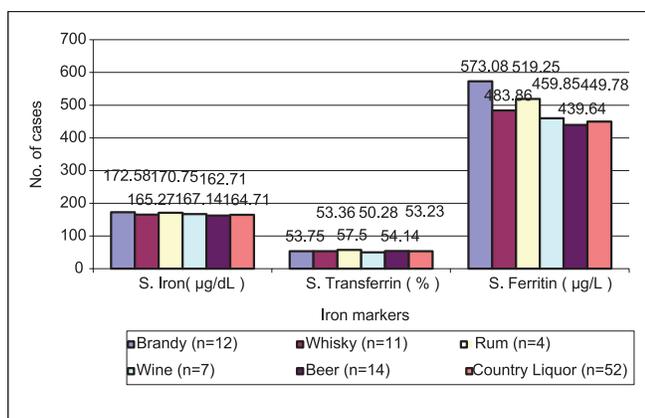
Age (years)	Serum iron (µg/dL)	Transferrin (%)	Ferritin (µg/L)
20-29	162.85±15.90	53.57±3.35	437.28±123.93
30-39	166.06±15.89	53.51±3.52	458.93±163.99
40-49	163.73±13.88	53.39±3.10	478.69±182.99
50-59	166.12±13.00	53.24±4.01	467.20±139.99
>60	170.42±8.94	53.35±3.38	504.21±141.60
<i>P</i> value	0.66	0.99	0.87



Graph 1: Age distribution in cases



Graph 2: Duration of alcohol consumed



Graph 3: Alcohol and iron indices

(357.45 ± 100.41 µg/L) in cases consuming 1-5 drinks per day and (174.66 ± 11.95 µg/dL) and (589.58 ± 141.20 µg/L), respectively, in cases consuming alcohol more than 15 drinks per day. The difference in mean for rise in serum iron and ferritin with increase amount of alcohol intake was found to be statistically significant (P = 0.003, 0.001, respectively) (Table 6 and Graph 5).

It is observed that the mean value for serum glutamic-oxaloacetic transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT) vary with the rise in serum ferritin. However, this was not statically significant (P value 0.84, 0.58, respectively) (Table 7).

Table 4: Type of alcohol and iron indices in cases

Type of alcohol	Serum iron (µg/dL)	Serum transferrin (%)	Serum ferritin (µg/L)
Brandy (n=12)	172.58±12.34	53.75±2.86	573.08±177.26
Whisky (n=11)	165.27±15.80	53.36±4.80	483.86±175.65
Rum (n=4)	170.75±5.31	57.50±2.08	519.25±156.54
Wine (n=7)	167.14±10.22	50.28±2.28	459.85±129.49
Beer (n=14)	162.71±9.77	54.14±3.05	439.64±145.73
Country Liquor (n=52)	164.71±15.21	53.23±3.30	449.78±148.04
P value	0.42	0.029	0.206

Table 5: Duration of alcohol consumed and iron indices in cases

Duration alcohol consumed (in years)	Serum iron (µg/dL)	Serum transferrin (%)	Serum ferritin (µg/L)
1-5 (n=27)	169.29±8.71	53.59±3.36	526.37±154.33
6-10 (n=32)	165.06±16.53	53.56±3.19	440.71±146.78
11-15 (n=27)	164.18±9.44	52.62±4.03	431.92±129.47
16-20 (n=13)	164.00±21.56	54.07±3.30	492.92±200.20
>20 (n=1)	175±0	55.0±0	652.0±0
P value	0.59	0.70	0.09

Table 6: Amount of alcohol consumed and iron indices in cases

Number of drinks/day	Serum iron (µg/dL)	Serum transferrin (%)	Serum ferritin (µg/L)
1-5 (n=20)	159.30±10.82	53.80±4.04	357.45±100.41
6-10 (n=34)	162.97±15.20	53.26±3.54	432.02±140.20
11-15 (n=34)	169.70±12.16	53.67±3.27	533.05±148.48
>15 (n=12)	174.66±11.95	52.33±2.87	589.58±141.20
P value	0.003	0.650	0.001

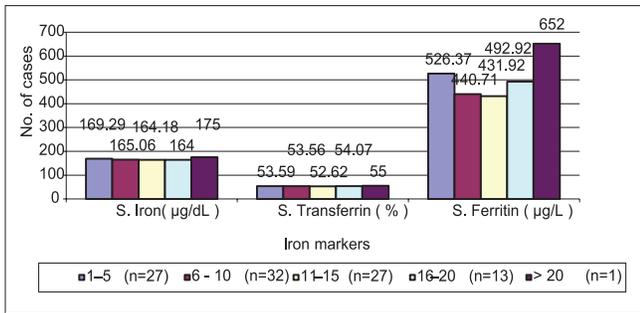
Table 7: Ferritin and liver enzymes

Ferritin (µg/L)	SGOT (IU/L)	SGPT (IU/L)
<300	55.07±29.49	45.53±20.60
300-399	50.59±28.41	39.59±15.31
400-499	45.25±28.69	38.07±18.01
500-599	50.76±29.62	41.41±16.84
>600	46.50±24.79	36.30±13.02
P value	0.84	0.58

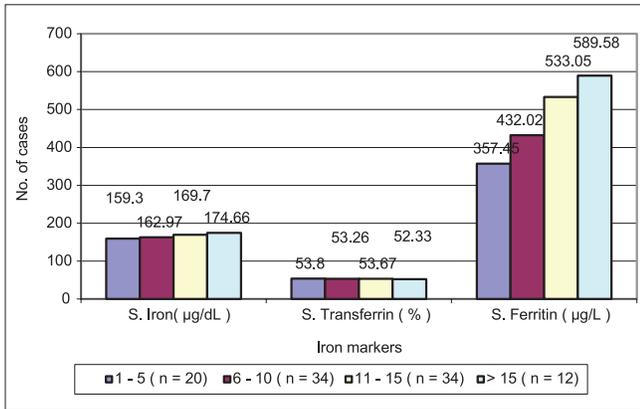
SGOT: Serum glutamic-oxaloacetic transaminase, SGPT: Serum glutamate pyruvate transaminase

DISCUSSION

It has been observed from the study, alcohol causes increase in the serum iron markers – serum iron, transferrin saturation, and ferritin. Alcohol increases the absorption of iron from the intestine by increases body iron stores. Under certain circumstances such an effect might be beneficial whereas in others it may be harmful. Particularly in men who are less likely to be iron deficient and who consume more alcohol on average than women, the synergistic effect of alcohol and iron lead to, or exacerbate liver damage.



Graph 4: Duration of alcohol consumed and iron indices



Graph 5: Number of drinks per day and iron indices

A number of conditions apart from iron overload are known to increase serum ferritin including acute liver injury, inflammation or infection and malignant disease. The subjects were grouped into cases (those consuming alcohol) and controls (those not consuming alcohol).

Age, Sex and Iron Indices

Age

In the present study, the majority of the cases are in the age group of 30-39 years. The mean age at presentation was 44.93 ± 11.85 years. This observation was similar to the observation made by Whitfield *et al.*,¹⁸ and Anttila *et al.*¹⁹ The mean age of cases in the study by Whitfield *et al.*¹⁸ was 44 years and of Anttila *et al.*¹⁹ was 49 years. However in the study by Milman *et al.*,²⁰ the mean age at presentation was 55 years. In the present study, age of the patient was not significantly associated with iron indices. This observation was similar to Fleming *et al.*²¹ study, where age was not related to ferritin. However, in the study conducted by Baker,²² age was positively correlated with serum ferritin with $P < 0.01$.

Sex

In the present study, all cases were males.

Alcohol and iron indices

In this study, the mean values for serum iron, transferrin, and ferritin were increased significantly in alcoholic subjects. These observations were similar to the observations by

Friedman *et al.*,²³ Milman *et al.*,²⁰ Bell *et al.*,²⁴ Milman *et al.*,⁸ Fleming *et al.*,²¹ Whitfield *et al.*,¹⁸ Jurczak *et al.*, and Ioannou *et al.*²⁵

Study	Serum iron	Serum transferrin	Ferritin
Friedman <i>et al.</i> ²³ (1988) <i>n</i> =1250 (male - 591, female - 614) Age - 16-19 years	Increased	Increased	Increased
Milman <i>et al.</i> ²⁰ (1993) <i>n</i> =82 (male - 53, female - 29) Age - 18-84 years	Increased	Increased	Increased
Bell <i>et al.</i> ²⁴ (1994) <i>n</i> =111	-	Increased (15.2%)	Increased (58%)
Ford <i>et al.</i> ²⁶ (1995)	-	Increased transferrin saturation >60% in 16% patients	Ferritin >1000 unit; ng/ml in 16% patients
Milman <i>et al.</i> ⁸ (1996) <i>n</i> =2235 (male - 1044, female - 1191) Age - 30-60 years	Increased	-	Increased
Fleming <i>et al.</i> ²¹ (1998) <i>n</i> =634 Age - 67-93 years	Increased	Increased	Increased
Whitfield <i>et al.</i> ¹⁸ (2001) <i>n</i> =3375 (male - 1134, female - 2241)	Increased	Increased	Increased
Ioannou <i>et al.</i> ²⁵ (2004) <i>n</i> =8839	-	Increased	Increased
Present study (2008) <i>n</i> =100 (M=100) Mean age 44.9 ± 11.85 years	Increased	Increased	Increased

Type of Alcohol and Iron Indices

Majority of the cases 52% (*n* = 52) had history of consuming country liquor. Only 4% cases had history of consuming rum. This observation was similar to the observation made by Gupta *et al.*²⁷ in their study, where most of the patient had history of consuming country liquor. The reason for country liquor being the most common type of alcohol is due to the extensive network at outlets serving country liquor and to its low price. In the present study, the mean serum iron and ferritin was more in subjects consuming brandy than in other types of alcohol and mean transferrin saturation was greater in subjects consuming brandy and wine but the difference was not significant. However, Whitfield *et al.*,²⁵ in their study observed a significant effect of beer intake but not wine or spirit intake on serum ferritin in both men and women. For both iron and transferrin saturation, both wines and spirits showed similar effects to beer. None of the beverages had any significant effect on transferrin.

Duration of Alcohol Consumed and Iron Indices

Most of the cases 32% had history of consuming alcohol for 6-10 years. 27% cases had consumed alcohol for

11-15 years and only 1% consumed alcohol for >20 years. In the present study, the mean serum iron, transferrin saturation, and ferritin did not increase with the duration of alcohol consumed. These observations were similar to the observation by Whitfield *et al.*¹⁸ who found no difference in the mean levels of iron and transferrin between patients who had alcohol intake. However, ferritin levels were increased in patients with alcohol dependence.

Amount of Alcohol Consumed and Iron Indices

In this study, the majority of the cases 68% (68 cases) had history of consuming 6-15 drinks per day. This was in contrary to the observations made by Gupta *et al.*²⁷ in their study, where most of the patients had history of consuming 5-6 drinks per day. This heavy drinking pattern was probably due to illiteracy among the people and due to easy availability of the alcohol in the society. In the present study, it is observed that the mean iron and ferritin increased significantly with the amount of alcohol consumed. These observations were similar to the observation by Whitfield *et al.*¹⁸ where the mean iron, transferrin saturation and ferritin increased with the increase in the amount of alcohol consumed. The increasing amount of alcohol intake causes increased necroinflammation of the hepatocytes which release the iron and ferritin from the hepatocytes. Also increased alcohol intake results in increase in the levels of carbohydrate-deficient transferrin (CDT), which are taken up by the CDT receptors present on the hepatocytes which are up regulated in the habitual drinkers.

Liver Enzymes and Ferritin

In the present study, the mean value for SGOT and SGPT of the cases were increased significantly compared to controls (SGOT more than SGPT). However, the liver enzymes SGOT and SGPT did not vary significantly with the ferritin levels. No enzyme -ferritin correlation was found. However, in the study by Whitfield *et al.*,¹⁸ the liver enzymes SGOT and SGPT were highly and significantly (positively) correlated with the ferritin values in both men and women. This enzyme-ferritin correlation may be due to an indirect association, because iron overload is associated with liver damage, higher values of the liver function tests are to be expected in subjects with higher ferritin levels. The present study did not show this type of correlation. This could be because the majority of the patients were having cirrhosis and maximum liver damage had already occurred in these cases when they were included in the study.

Observations of the study are summarized as follows:

1. The mean age of the patients in cases was 44.9 ± 11.85 years and in control was 33.6 ± 9.10.
2. All the cases in the study were males 100% (*n* = 100).
3. Majority of the cases 52% (52 cases) had history of

consuming country liquor. 14% (14 cases) had history of consuming beer. Only 4% (4 cases) had history of consuming rum.

4. 32% (32 cases) had history of consuming alcohol for 6-10 years. 27% (27 cases) had history of consuming alcohol for 11-15 years. Only 1% (1 case) had history of consuming alcohol for more than 20 years.
5. 68% (68 cases) had history of consuming 6-15 drinks per day. 20% (20 cases) has history of consuming 1-5 drinks per day. Only 12% (12 cases) had history of consuming more than 15 drinks per day.
6. Mean values for serum Iron, transferrin saturation and ferritin varied with the age of the patient and it was not statistically significant (*P* value 0.66, 0.99, and 0.87, respectively).
7. Mean values for serum iron, transferrin saturation and ferritin were increased significantly in subjects consuming alcohol as compared to those not consuming alcohol (*P* < 0.001).
8. Mean values for serum Iron and ferritin was higher in cases consuming brandy (172.5 ± 12.34 µg/dL, 573.08 ± 177.26%, respectively) than with other types of alcohol but was not statistically significant (*P* = 0.42 and 0.206, respectively). Mean value for transferrin saturation was higher in cases consuming brandy (53.75 ± 2.86 µg/L) and wine (50.28 ± 2.28 µg/L) than other alcohol types and was statistically significant (0.04).
9. Mean values for serum Iron, transferrin saturation and ferritin varied with the duration of alcohol consumed and was not statistically significant (*P* value 0.59, 0.70, and 0.09 respectively).
10. Mean values for serum iron and ferritin increased significantly with the increased amount of alcohol consumed (*P* value 0.003, <0.001 respectively).
11. Mean values for SGOT and SGPT were increased significantly in cases (48.89 ± 27.78 IU/L and 39.59 ± 16.61 IU/L) as compared to controls (29.60 ± 18.59 IU/L and 27.04 ± 6.29 IU/L, respectively) (*P* = 0.001).
12. Mean values for SGOT and SGPT varied with the rise in serum ferritin but was not statistically significant (*P* value 0.84, 0.58, respectively).

CONCLUSIONS

1. Alcohol consumption is associated with increasing levels of serum iron, transferrin saturation and ferritin.
2. Serum iron and ferritin levels increases with the increase in the amount of alcohol consumed.
3. The duration of the alcohol and type of alcohol consumed has no influence on the serum iron indices.
4. Iron indices have no effect on the liver enzymes (SGOT and SGPT).

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Mantle Cell Lymphoma and Variants: A Clinicopathological and Immunohistochemical Study

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Abstract

Introduction: Mantle cell lymphoma (MCL) is an intermediate grade lymphoma characterized by reciprocal translocation $t(11;14)(q13;q32)$ which results in cyclin D1 overexpression. Several variant forms of MCL are recognized, namely, blastoid, pleomorphic, small cell, and marginal zone type. The former two are considered aggressive. The purpose of the study was to study and compare the clinicopathological and immunohistochemical (IHC) features of MCL and its variants.

Materials and Methods: All cases diagnosed as MCL in our institution over a period of 4½ years were included in this study. Histomorphology was reviewed and a panel of IHC comprising CD3, CD5, CD10, CD20, CD23, cyclin D1, Bcl6, Bcl2, Ki67, c-myc, and p53 was done on all cases.

Results: Twelve cases of MCL were identified: Four classical, six blastoid, one pleomorphic, and one small cell variant. They were grouped into non-aggressive (classical and small cell variant) and aggressive (blastoid and pleomorphic variant) groups. The aggressive group had a higher mitotic rate, Ki67 proliferative index, MCL International Prognostic Index, and poor outcome. Aberrant phenotypes such as CD5-, CD10+, and/or Bcl6+ in varying combinations were encountered in both the groups. Some cases in the aggressive group also showed strong p53 and c-myc expression.

Conclusions: Our study highlights that MCL can have different histological appearances which can lead to diagnostic confusion with various other lymphomas. Since aberrant IHC expressions are also frequent, a cautious approach using a panel of IHC markers is essential for a correct diagnosis. Blastoid and pleomorphic subtypes may strongly express p53 and c-myc and have a poor outcome.

Key words: Aberrant, Blastoid, Cyclin D1, C-myc, p53, Pleomorphic, Small cell

INTRODUCTION

Mantle cell lymphoma (MCL) is an intermediate grade B-cell lymphoma and comprises 2-10% of all non-Hodgkin lymphomas (NHL). It is characterized by reciprocal translocation $t(11;14)(q13;q32)$ between

the *CCND1* and the immunoglobulin heavy chain (*IgH*) genes which results in cyclin D1 overexpression. Besides the classical form, which is the most common, several morphological variants are recognized, namely, blastoid, pleomorphic, small cell and marginal zone types.¹ The former two are considered aggressive. Typical immunohistochemical (IHC) profile of MCL shows positivity for CD20, CD5, cyclin D1, and Bcl2, although variations do exist. Secondary molecular and genetic events involved in the progression of MCL are more frequently encountered in the blastoid and pleomorphic types. The aim of the present study was to study and compare the clinical, histopathological, and IHC features of MCL and its variants.

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MATERIALS AND METHODS

All cases diagnosed as MCL over a period of 4½ years (January 2011 until June 2015) in the Department of Pathology were included in this study. Information about clinical features, relevant investigations, treatment, and outcome were retrieved from the hospital records. Besides hematoxylin and eosin (H and E) sections, IHC sections were reviewed, and additional IHC staining carried out. All the cases were stained for CD3 (PS1, Biogenex), CD5 (4C7, Novocastra), CD10 (56C6, Biogenex), CD20 (L-26, Novocastra), CD23 (1B12, Novocastra), cyclin D1 (ERP-224-32, Biogenex), Bcl6 (LN22, Novocastra), Bcl2 (124, Dako), Ki67 (MM1, Novocastra), c-myc (9E10, Biogenex), and p53 (DO-7, Dako). The blastoid and pleomorphic variants were also stained for TdT (Sen28, Novocastra). All the primary antibodies were pre-diluted and ready-to-use. The detection kit used was “NovoLink polymer” from Leica Biosystems, Newcastle upon Tyne, United Kingdom.

For IHC, 4 µ paraffin sections were cut and mounted on poly-L-lysine coated slides. The sections were then deparaffinized through two changes of xylene followed by re-hydration in descending grades of ethanol, to bring sections to water. Heat-induced antigen retrieval was done in citrate buffer at pH 6.0. Subsequent steps included endogenous peroxide block, protein block, incubation with primary antibody, post-primary block and incubation with Novolink polymer. Interval washings were done with 50 mM Tris-buffered saline, pH 7.6. Final color development was achieved using 3,3'-diaminobenzidine followed by hematoxylin counter stain. Appropriate positive and negative controls were also run with each batch of staining.

Staining of Ki67, c-myc and p53 was semi-quantitatively scored by accessing percentages of positively stained nuclei in multiples of 10. For c-myc and p53, average intensity of nuclear staining was recorded as weak (+), moderate

(++) or strong (+++). For the other IHC markers, results were recorded as positive if more than 10% neoplastic cells were positive.

Fluorescent *in situ* hybridization (FISH) for *t*(11;14) (q13;q32) was done in two cases (cases no. 1 and 5).

RESULTS

Twelve cases (4.8%) of MCL were identified out of a total of 252 cases diagnosed as lymphoma. Of these, four had classical morphology (case no. 1 to 4), six were blastoid (case no. 6-11) and one each was pleomorphic (case no. 12) and small cell type (case no. 5). For comparative study, classical and small cell types were grouped into non-aggressive category (Group A), while blastoid and pleomorphic types were grouped as aggressive (Group B).

The age range of patients was 45-85 years with a mean of 64 years and median of 67 years. Eleven out of 12 patients were male. Generalized lymphadenopathy (LN) (9/12), hepatomegaly (8/12), splenomegaly (4/12), bone marrow (BM) involvement (10/12), peripheral blood (PB) spill (5/12), and extra nodal involvement (ENI) (6/12) were frequent findings. ENI was found in the gastrointestinal tract (GIT) (3/12), pleural cavity (3/12), peritoneal cavity (2/12), lung (1/12), and liver (1/12). Two cases in the aggressive group and one in the non-aggressive group also had bulky confluent lymph node masses. About 10 cases had stage IV and two had stage III disease. The mean serum lactate dehydrogenase (LDH) level was 659 U/L. The clinical features and laboratory parameters are shown in Tables 1 and 2.

Table 3 shows the histopathological features of all the MCL cases. Growth pattern in the lymph nodes was mixed in 10 cases; 8 of these had diffuse and nodular

Table 1: Relevant clinical features and Ann Arbor staging of 12 mantle cell lymphoma patients²

Case ^a	Age/sex	LN	Hepatomegaly	Spleno megaly	Extra nodal	Peripheral blood spill	Bone marrow	Stage ^b
1	70/M	Generalized	+	+	-	-	+	IVB
2	45/M	Cervical	+	-	-	-	+	IVB
3	72/M	Mediastinal	+	-	Lung	-	+	IVB
4	58/M	Generalized	+	-	GIT, PE, As	+	+	IVB
5	69/M	Cervical, tonsil, mediastinal	-	-	-	-	+	IVA
6	52/M	Generalized	+ nodules	+	Liver	+	+	IVXB
7	65/M	Generalized	+	+	PE, As	+	+	IVB
8	65/M	Generalized	-	-	GIT	+	+	IVB
9	85/M	Generalized	+	-	-	-	+	IVA
10	45/F	Generalized	-	+	GIT, PE	+	+	IVB
11	73/M	Generalized	-	-	-	-	-	IIIA
12	77/M	Generalized	+	-	-	-	-	IIIXB

As: Ascites, GIT: Gastrointestinal tract, LN: Lymphadenopathy, PE: Pleural effusion. ^aCases 1-4 classical, case 5 small cell variant, cases 6-11 blastoid variant, case 12 pleomorphic variant. ^bCotswold's modification of Ann Arbor Staging.

pattern, 2 had mantle zone (MZ) and nodular pattern (Figure 1a), and one purely nodular growth pattern. In one patient (case no. 3) only the BM trephine biopsy was available, which showed a nodular and interstitial pattern of infiltration. The neoplastic lymphoid cells in classical type showed centrocyte-like morphology with round indented nuclei, coarse chromatin, and inconspicuous nucleoli (Figure 2a). The blastoid variants showed lymphoblast-like morphology with slightly enlarged, rounded nuclei having fine chromatin and small nucleoli (Figure 2b). The nuclei were more enlarged and pleomorphic in the pleomorphic subtype (Figure 2c). The small cell variant showed cells with small, condensed, hyperchromatic nuclei, morphologically resembling small lymphocytic lymphoma (SLL) (Figure 2d). Other diagnostic histopathological findings included the presence of pink histiocytes and hyalinized blood vessels. Tumor cell proliferation as assessed by mean mitotic activity was 8/10 high power field (hpf) for Group A and 48/10 hpf for Group B. The median Ki67 proliferative fraction was 30% for Group A and 70% for Group B.

The IHC profile of the cases is shown in Table 4. All cases were positive for CD20, cyclin D1 and bcl2 (Figure 1b and c). Ten cases were positive for CD5 (Figure 1d). The intensity of cyclin D1 nuclear staining was heterogeneous, being weaker in the blastoid cells as compared to the centrocytic. Aberrant phenotypes such as CD5 negative (2/12), CD10 positive (2/12), Bcl6 positive (4/12), and CD3 positive (2/12) were found in various combinations in six cases. The case with small cell histology was CD5 negative and strongly positive for CD10 and bcl6 (Figure 3a-d). Aberrant expression in blastoid variants was generally of weak intensity. Two cases (cases no. 1 and 5) tested for *t(11;14)(q13;q32)* by FISH were positive, which included the small cell variant with aberrant phenotype.

Prognostic parameters and outcome of all the cases are shown in Table 5. In the non-aggressive, Group A, the mean MCL International Prognostic Index (MIPI) was 4 while in the aggressive, Group B, it was 7.5. Strong expression of c-myc (intensity 3+) was present in 2 cases

Table 2: Comparative clinical features, laboratory parameters and Ann Arbor staging of non-aggressive (Group A) and aggressive (Group B) subgroups of Mantle cell lymphoma

Group	Age (years)	Sex	Gen LN	Hepatomegaly	Splenomegaly	ENI	PB spill	BM	LDH (U/L)	Stage
A. Non-aggressive (n=5)	45-70 Median: 69	M=5	2	4	1	2	1	5	Mean: 510	IV=5
B. Aggressive (n=7)	45-85 Median: 65	M=6 F=1	7	3	3	4	4	5	Mean: 808	IV=5 III=2

BM: Bone marrow, ENI: Extra nodal involvement, Gen: Generalized, LDH: Lactate dehydrogenase, LN: Lymphadenopathy, PB: Peripheral blood

Table 3: Comparative histopathological features and Ki67 proliferative index of non-aggressive (Group A) and aggressive (Group B) subgroups of Mantle cell lymphoma

Group	Pattern	Cell morphology	Mitosis/10 Hpf	Ki67%
A. Non-aggressive (n=5)	MZ+N=2 D+N=2 D+I=1 (BM)	Centrocytic=4 Small cell=1	Range: 3-11 Mean: 8	Range: 10-30 Median: 30
B. Aggressive (n=7)	D+N=6 N=1	Blastoid=6 Pleomorphic=1	Range: 35-63 Mean: 48	Range: 60-100 Median: 70

BM: Bone marrow, D: Diffuse, Hpf: High power field, I: Interstitial, MZ: Mantle zone, N: Nodular

Table 4: Immunohistochemical profile of 12 cases of mantle cell lymphoma

Case	Type	CD20	Cyclin D1	Bcl2	CD5	CD10	CD23	Bcl6	CD3	TdT
1	Classical	+	+	+	+	-	-	-	-	ND
2	Classical	+	+	+	+	-	-	-	-	ND
3	Classical	+	+	+	+	-	-	-	-	ND
4	Classical	+	+	+	+	-	-	+w	-	ND
5	Small cell	+	+	+	-	+	-	+	-	ND
6	Blastoid	+	+	+	-	-	-	-	-	-
7	Blastoid	+	+	+	+	+w	-	+w	-	-
8	Blastoid	+	+	+	+	-	-	+w	+w	-
9	Blastoid	+	+	+	+	-	-	-	+w	-
10	Blastoid	+	+	+	+	-	-	-	-	-
11	Blastoid	+	+	+	+	-	-	-	-	-
12	Pleomorphic	+	+	+	+w	-	-	-	-	-

ND: Not done, w: Weak

Table 5: Prognostic parameters and outcome of 12 patients with mantle cell lymphoma

Case	Type	MIPI ^a	c-myc ^b	p53 ^b	Outcome
1	Classical	3 (low risk)	70% (++)	70% (++)	Relapse at 2 years and 3 months
2	Classical	4 (Int. risk)	ND	ND	No follow-up
3	Classical	7 (high risk)	0%	10% (+)	No follow-up
4	Classical	3 (low risk)	80% (++)	30% (+)	No follow-up
5	Small cell	3 (low risk)	60% (++)	60% (+)	In remission at 3 years
6	Blastoid	ND	50% (++)	40% (+)	Progressive disease at 3 months of follow-up
7	Blastoid	11 (high risk)	60% (++)	90% (+++)	Expired before treatment
8	Blastoid	6 (high risk)	80% (+++)	40% (++)	Expired before treatment
9	Blastoid	3 (low risk)	0%	10% (+)	In remission at 1 year
10	Blastoid	8 (high risk)	30% (+++)	40% (++)	Relapse at 1 year; progressive disease after 6 months
11	Blastoid	8 (high risk)	40% (++)	40% (+)	Expired after 6 months
12	Pleomorphic	9 (high risk)	10% (+)	70% (+++)	On induction therapy since 2 months

ND: Not done, Int: Intermediate, MIPI: Mantle cell lymphoma International Prognostic index. ^aMIPI 0-3 Low risk, 4-5 Intermediate risk, 6-11 high risk. ^b+weak, ++ moderate, +++ strong positive intensity of staining

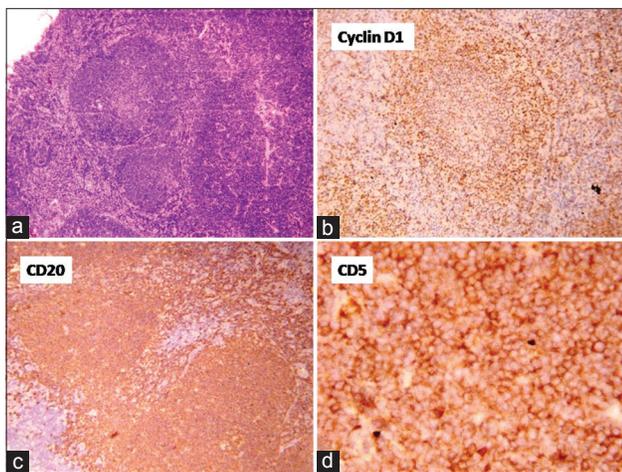


Figure 1: (a) Mantle zone and nodular pattern of growth (H and E, $\times 40$). (b-d) Immunohistochemistry showing cyclin D1, CD20, and CD5 positivity in classical mantle cell lymphoma. 3,3'-diaminobenzidine chromogen

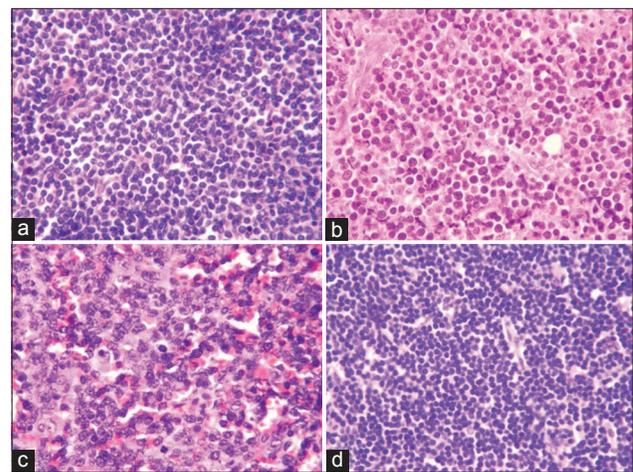


Figure 2: Histological types of mantle cell lymphoma. (a) Classical centrocyte-like (b) Blastoid (c) Pleomorphic (d) Small cell chronic lymphocytic leukemia/small lymphocytic lymphoma-like (H and E, $\times 400$)

of blastoid MCL while strong expression of p53 (intensity 3+) was found in one case each of blastoid and one pleomorphic MCL (Figure 3e and f). None of the Group A cases showed strong intensity of c-myc or p53 staining. Weak to moderate intensity of staining was found in all the subtypes. Three patients of blastoid MCL expired, two had progressive disease, and one is in remission. One patient of pleomorphic type was on induction therapy.

DISCUSSION

Epidemiology

MCL is an intermediate grade B-cell lymphoma and comprises 2-10% of all NHL.¹⁻⁴ In the data published from two large Indian studies, MCL constituted 2.1% and 3.4% of all NHL as compared to 4.8% in our institutional series.^{5,6} MCL with classical histology is the most common and comprises 80-90% of cases. The remaining 10-20% of cases are variants of MCL and include blastoid, pleomorphic, small cell and marginal zone subtypes.^{1,7-9}

MCL is common in middle-aged or elderly individuals with a median age of 60 years.^{1,7,10} Our patients had a mean age of 64 years and median of 67 years. There is a striking male predilection with the male to female ratio in different studies ranging between 2.3-4.5:1.^{3,6,7,10,11} This strong gender preference was also reflected in our study.

Clinical Features

Most patients of MCL, irrespective of their histological subtype, present with advanced stage disease (stage III or IV), with lymph nodes being the most common site of involvement. ENI is frequent, and commonly includes the spleen, BM, PB, GIT, Waldeyer's ring and pleura.^{1,5-7} All our cases had LN and advanced stage disease (either stage III or IV) at presentation. Generalized LN, splenomegaly, and PB spill were more common in the aggressive group. In a study of 187 patients of MCL, a higher percentage of ENI (66%), PB spill (48%) and BM infiltration (82%) was found in the blastoid subgroup.⁸ Among the six cases of blastoid MCL in the present study, four cases each had ENI

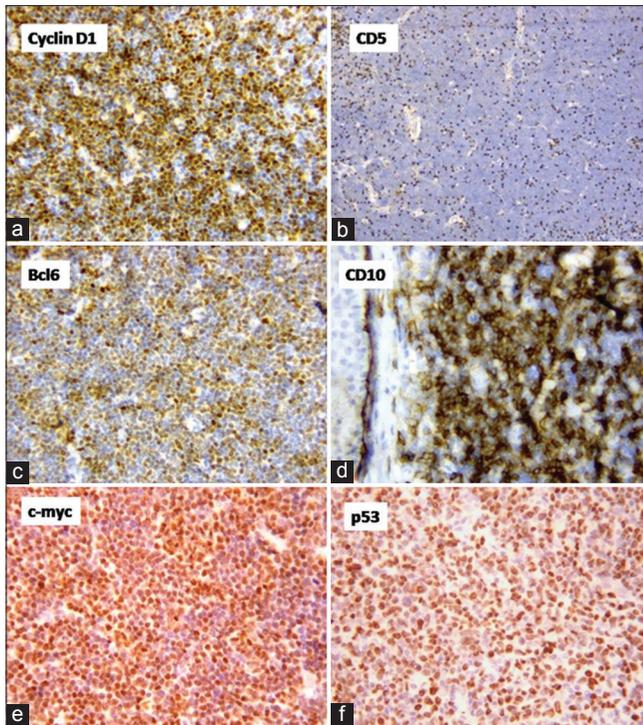


Figure 3: (a-d) Small cell variant showing aberrant CD5-, Bcl6+ and CD10+ phenotype with cyclin D1 expression (e) Blastoid mantle cell lymphoma (MCL) with strong c-myc expression (f) Pleomorphic MCL with strong p53 expression. 3,3'-diaminobenzidine chromogen

and PB spill, and five had BM infiltration. GIT and pleural cavity were the other commonly involved extra nodal sites.

Histopathology

Histopathology of nodal MCL shows complete or partial effacement of architecture with a diffuse, nodular, MZ, or a mixed pattern of growth. Out of these, mixed (nodular and diffuse) and diffuse patterns are the most common.^{1,5,6,11} Most cases in our study showed a mixed nodular and diffuse pattern of involvement. There was no apparent difference in the pattern of involvement between aggressive and non-aggressive groups. However, areas with MZ pattern were seen only in the classical category.

The lymphoid cells of classical MCL are small to intermediate in size and have centrocyte-like morphology. Mitotic activity is variable but generally low. In the blastoid variant, the nuclei are larger with round to irregular contours, fine chromatin, and inconspicuous nucleoli. The pleomorphic subtype shows lymphoid cells with greater variation in size and shape, coarser chromatin, and conspicuous nucleoli at least in some cells. Blastoid and pleomorphic phenotypes may represent a continuum with some cases showing both the morphologies in different areas of the same lymph node. At times, it may be difficult to segregate blastoid from pleomorphic cells because of intermediate morphology.¹² One case categorized

as pleomorphic type in our series had areas showing both blastoid and pleomorphic morphology. Blastoid and pleomorphic subtypes show high mitotic activity (>20-30/10 hpf) often with tingible-body macrophages. The small cell variant is an uncommon and indolent subtype of MCL. It is characterized by smaller lymphoid cells with condensed nuclear chromatin resembling cells of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL). Mitotic activity and Ki67 proliferative index is lower than classical subtype.¹³ The marginal zone-like variant shows foci of cells with abundant pale cytoplasm or monocytoid B-cells mimicking marginal zone lymphoma. Hyalinized small vessels and pink histiocytes are other important diagnostic findings in MCL.¹ BM infiltration by MCL is usually diffuse or nodular, and may occasionally show paratrabeular or intrasinusoidal growth pattern.¹²

Since MCL can show morphological diversity, several other lymphomas enter into the differential diagnosis such as CLL/SLL, follicular lymphoma, marginal zone lymphoma, lymphoblastic lymphoma and diffuse large B-cell lymphoma. Hence, IHC is essential for an accurate diagnosis.

Immunohistochemistry

Typical IHC profile of MCL shows positivity for CD20, CD5, cyclin D1, and Bcl2 with negativity for CD10, CD23, and BCL6. Aberrant phenotypes are not uncommon and can be encountered in cases with both classical and blastoid morphology, the frequency being higher in the latter.¹ These variations include CD5-, CD23+, CD10+, Bcl6+, and cyclin D1- in isolation or in various combinations.^{14,15} In our series, six out of 12 cases showed aberrant IHC. The case with small cell morphology, not only showed aberrant loss of CD5 but was also positive for CD10 and Bcl6, bringing in a differential diagnosis of follicular lymphoma. However, positivity for cyclin D1, established the diagnosis, which was later also confirmed by FISH for $t(11;14)(q13;q32)$. The aggressive group in our series also showed greater phenotypic aberrancy. A small number of morphologically typical MCL cases are cyclin D1 negative. These can be identified using SOX11, a novel diagnostic marker for MCL, having more than 90% sensitivity.¹⁶

Our results support the fact that immunophenotypic variations are common in MCL, and recognizing this variability is important for accurate sub-classification of B-cell lymphomas. In cases with inconclusive IHC, molecular testing becomes essential for confirmation of diagnosis.

Molecular Genetics

The characteristic reciprocal translocation $t(11;14)(q13;q32)$ is the initial molecular event in MCL and

can be identified in up to 99% of cases by FISH.¹⁷ The translocation results in constitutive over-expression of cyclin D1 which is a cell cycle regulator and drives the cell beyond the G1/S-phase check point, leading to B-cell proliferation. Subsequently, several secondary genetic events in the form of gains and losses occur causing disease progression. Besides cell cycle deregulation, other molecular mechanisms implicated in pathogenesis are alterations in DNA damage response pathway and activation of cell survival pathways. Different studies have identified alteration in the *ATM*, *TP53*, *c-myc*, and *Bcl6* genes in association with disease progression.^{9,18-21}

Since *c-myc* and *p53* gene alterations have been implicated with aggressiveness and poor outcomes in patients with MCL, we studied their protein expression by IHC. Correlation between *c-myc* and *p53* molecular alterations and protein expression by IHC in lymphomas has been documented in some studies.²²⁻²⁵ Strong intensity of c-myc expression (3+) was found in two cases of blastoid MCL. Similarly, strong expression (3+) of p53 was observed in one case of blastoid and one case of pleomorphic MCL. None of the cases in the non-aggressive group showed strong expression of these two markers. The percentage of tumor cells expressing these markers were, however, very variable.

Treatment and Prognosis

Based on the MIPI score, treatment options for MCL patients include observation alone, combination chemotherapy with R-CHOP or R-Bendamustine and BM stem cell transplant, either autologous or allogenic.²⁶ At the time of relapse, agents directed at activated pathways in MCL cells such as bortezomib (nuclear factor kappa B inhibitor) or lenalidomide (anti-angiogenesis) can be used.²⁶

Clinically, MCL displays an aggressive course, with a continuous relapse pattern and a median survival of only 3-7 years. The main biological parameters related to an unfavorable prognosis in MCL are high MIPI score, blastoid and pleomorphic morphology, and an increased level of proliferation.^{9,18,21,27,28}

Clinically, MIPI is the prognostic model most often used and incorporates Eastern Cooperative Oncology Group performance status, age, leukocyte count, and LDH levels. In a large study on data from 455 MCL patients, the median overall survival directly correlated with MIPI.²⁷ In our series, the blastoid and pleomorphic subtypes had a higher mean MIPI score, a higher mitotic and Ki67 proliferative index, and poorer outcome as compared to the classical and small cell subtypes. The small cell variant generally has a lower proliferative fraction and an indolent clinical course.¹² One patient of small cell variant in our series who had an

MIPI of 3 (low risk), mitotic index of 3/10 hpf and Ki67 proliferative fraction of 30%, is in remission at 3 years.

CONCLUSIONS

Because of varying cytoarchitectural and morphological appearances MCL can be confused with various other lymphomas. Though cyclin D1 is a reliable marker for all forms of MCL, aberrant IHC expressions are also common. Hence, a cautious approach with a panel of IHC markers is essentially recommended for an accurate diagnosis of MCL. In cases with inconclusive IHC, molecular testing becomes necessary for confirmation of diagnosis. Strong p53 and c-myc expression by IHC along with higher Ki67 proliferative indices may be seen in the aggressive subtypes and might contribute toward poor prognosis.

ETHICAL APPROVAL

This article does not contain any studies with human participants or animals performed by any of the authors.

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Prevalence of Fear of Hypoglycemic Attack in Patients with Uncontrolled Diabetes Mellitus and Correlation Analysis in Diabetes

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Abstract

Background: Diabetes is chronic illness in nature, and patients are having difficulties in achieving optimal diabetes control. As there is no cure for diabetes, the main aim of diabetes treatment is to optimize glycemic control. People with uncontrolled diabetes are at higher risk of psychological problems such as fear of hypoglycemic attack (FHA) than the general population.

Aim: To study the prevalence of FHA in patients with uncontrolled diabetes mellitus (DM) and correlation analysis of these factors in diabetes.

Settings and Design: Tertiary care private sector in northern Karnataka. This study was cross-sectional observational study.

Materials and Methods: We included person diagnosed with DM having uncontrolled diabetes status measured by one previous hemoglobin A1c (HbA1c) between 8.2% and 15.0%. The existence of FHA was evaluated by fear of hypoglycemic survey (FHS) tool. Socio-demographic data and duration of diabetes were obtained from semi-structured questionnaires.

Statistical Analysis: The data were analyzed using Pearson correlation analysis.

Results: We included total 100 patients in this study. Results suggest a high level of neuropathy and retinopathy. The most common FHA was "Eat large snacks at bed time" and "Eat something as soon as I feel the first sign of low sugar." There was a strong correlation between Hb1Ac and FHS total score.

Conclusion: We found higher levels FHA among uncontrolled DM. Strong positive correlation exists between uncontrolled diabetes and Hb1Ac.

Key words: Fear, Hemoglobin A1c, Hypoglycemic attacks, Uncontrolled diabetes mellitus

INTRODUCTION

Fear of having a hypoglycemic episode is one of the most common worries for people with type 1 and type 2 diabetes and is associated with sub-optimal glycemic control. The fear of hypoglycemia is related to thoughts of being out of control, being vulnerable and dependent on others and

the public humiliation and embarrassment, as well as fear for one's own safety and of dying. Other factors that may lead to excessive worry include the inability to feel the symptoms of hypoglycemia (hypoglycemic unawareness or reduced hypoglycemic awareness) and misattributing symptoms of anxiety to hypoglycemia.^{1,2}

Hypoglycemia was shown to be independently associated with lower patient utility, and that disutility increases with severity of hypoglycemic episode in the present study. Similar, although non-significant, results were obtained in a study of Swedish type 2 diabetic patients treated with oral antihyperglycemic agents and/or insulin. Based on the EQ-5D, Lundkvist *et al.* reported a utility decrement of 0.047 ($P = 0.120$) for patients experiencing any

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hypoglycemia in the preceding month, after adjusting for gender, insulin use, and hypoglycemia group (symptomatic, mild or severe).³ The relationship between severity of hypoglycemic episode and patient disutility in the present analysis was similar to that reported for French patients with type 2 diabetes treated with a combination of metformin and sulfonylurea.

Hypoglycemia is practically a part of life for individuals with type 1 diabetes and individuals with long-term type 2 diabetes.⁴ It is also known as a main barrier to achieving glycemic goals. In particular, severe and recurrent hypoglycemia lead to fear of hypoglycemia, which negatively affects diabetes adherence and metabolic control. Patients with high hypoglycemia fear may engage in behaviors such as overeating, taking less insulin than required, or limiting daily-life activities (e.g., exercising, driving, shopping, visiting friends) to avoid hypoglycemia. However, these types of coping strategies lead to poor metabolic control and increase the risk of health problems related to diabetes and psychosocial difficulties.¹ The signs and symptoms of hypoglycemia differ from one individual to another. Factors such as old age, long diagnosis period, and the existence of complications impair hypoglycemia awareness. Studies have determined that 33% of individuals with diagnosis periods longer than 15 years have hypoglycemia unawareness (i.e., they are unaware of the signs and symptoms of hypoglycemia). This has been found to increase the risk of serious hypoglycemia, which increases hypoglycemia fear. In particular, patients who experience sudden hypoglycemic attacks worry about losing control, experiencing hypoglycemia while alone or sleeping or making a mistake or having an accident during an attack.⁵ Because they might not have time to treat their hypoglycemia and might lose consciousness suddenly, hypoglycemia has the potential to be life threatening.

Vexiau *et al.* reported HFS scores that increased by 7.9 for any hypoglycemia, and by 5.8 for mild episodes, 11.1 for moderate, and 13.4 for severe episodes after adjusting for patient and disease characteristics. Although these decrements are smaller overall than those found in the present study, the positive linear association between severity of hypoglycemic episode and greater fear is consistent. In general, patients who experience severe and/or frequent hypoglycemic episodes report lower general health and greater fear of hypoglycemic events compared with patients who do not experience hypoglycemia.

The need to avoid hypoglycemia and the long-term consequences of hyperglycemia remain a challenge in disease management. Patients may prioritize the immediate risk of hypoglycemia over the possibility of future health problems. It has been suggested that patients may

intentionally take less diabetes medication (i.e. reduce treatment compliance) or over-eat to increase their blood glucose level to avoid hypoglycemia.^{6,7} Hypoglycemic episodes not only impact the daily clinical management and well-being of patients, but the fear resulting from the side effect may negatively impact long-term diabetes outcomes if acceptable glucose levels are not maintained.

Studies on fear of hypoglycemic in uncontrolled diabetes are very few, especially in Indian setting very knowledge about diabetes and its complication are less. Hence, we evaluated these short comings in Indian setting

Aims and Objective

To study, the prevalence of fear of hypoglycemic disorder in uncontrolled diabetes mellitus (DM).

Design

Cross-sectional study using standard screening tools.

Setting

Tertiary care centre in northern Karnataka.

Inclusion Criteria

1. DM was defined according to the World Health Organization criteria
2. Either they are on oral hypoglycemic agents and/or on insulin therapy
3. Age between 18 and 65 years
4. With one previous HbA1c of between 8.2% and 15.0%, identified by the treating physician.

Exclusion Criteria

- a. Pregnancy or attending a pre-pregnancy clinic
- b. Acute or serious medical illness as defined by treating physician
- c. Advanced diabetes complications (such as registered blind or serum creatinine values >300 mmol/l)
- d. Known hemoglobinopathy or severe mental disorder.

Tools

Semi-structured questionnaire to measure socio-demographic data and hypoglycemia fear survey (HFS) to measure fear of hypoglycemia. HFS, developed by Cox *et al.* (1987), is a 27-item questionnaire with two subscales that measure (a) behaviors aimed at avoiding hypoglycemia and its negative consequences and (b) worries about hypoglycemia and its negative consequences. Responses are made on a 5-point Likert scale where 0 means never and 4 means always. Both subscales were used in this study, and higher scores indicated increased fear of hypoglycemia. Internal consistency reliability (Cronbach's alpha) for the behavior subscale, worry subscale, and total HFS was found to be 0.77, 0.91, and 0.90, respectively.

RESULTS

Socio-demographic Data

We included total 100 number of subject who fulfilled inclusion and exclusion criteria. Semi-structured questionnaire was used to look for socio-demographic data. The results suggest mean age of presentation was 57 years, the majority were males, and married, belongs to Hindu religion from urban background with mean educational status of 7 years (Tables 1 and 4).

To evaluate for diabetic status and its related complication, we used clinician based evaluation and some bedside and laboratory test. The results are as shown in Table 2. Mean duration of diabetes was 8 years with minimum new case to maximum 30 years duration. Mean hemoglobin A1c (Hb1Ac) was 8.32. The maximum possible score in fear of hypoglycemic attack (FHA) was 135 and minimum score by this scale was 27. We found mean score of FHA 35 with minimum score 27 and maximum score 65.9 (Table 5). The most common FHA behavior was observed was “eat large snacks at bed time” followed by “Eat something as soon as I feel the first sign of low sugar” and “Carry fast acting sugar with me.” The least fear was observed in “Avoid lot of exercise when I think my sugar is low.” These behaviors were developed following few episode of hypoglycemic attack or instruction by the treating physician. Avoiding exercise comes only when person on regular exercise for diabetes (Table 3). The most common worry among these individuals were “feeling dizzy or passing out in a public” followed by “Having seizure or convulsion and having a reaction while driving.” The least worry or not single patient have bothered about “Embarrassing myself/my friends/family in social situation.”

Table 1: Demography

Age minimum	30
Maximum	84
Mean±SD	56.98±12.0
Sex	
Male	61
Female	39
Marital status (%)	
Married	98
Unmarried	2
Education	
Minimum	0
Maximum	18
Mean±SD	7.94±4.8
Religion (%)	
Hindu	96
Muslim	4
Region (%)	
Rural	42
Urban	58

SD: Standard deviation

The correlation analysis has shown a strong positive correlation between Hb1Ac and total score of FHA, i.e., 0.79. This suggests higher the Hb1Ac higher will be the fear of hypoglycemic score and lower the Hb1Ac lower the FHA score. In another analysis between duration of diabetes and FHA score, it was a weak positive correlation. A value of 0.12 suggests FH is irrespective of duration of DM.

DISCUSSION

The socio-demographic data of this study represents clinical profile of private sector institution. Majority of them were in the middle age group. About 60% were male and another 40% were female. The prevalence of type 2 DM was the more common in the community and also treatment seeking is more in this population. The mean duration of diabetes was 8 years which suggest majority were suffering with diabetes for significant duration and stress and psychiatric disorder are more among longer duration suffering. Similar results have been found by Amit Raval *et al.* study where the mean duration of the study was 8 years.⁸ We have included minimum Hb1Ac should be more than 8 which suggest uncontrolled diabetes. The prevalence of various psychological phenomenon such as burnout and FHA was more common among these population. The maximum possible score in FHA was 135 and minimum score by this scale was 27. We found a mean score of FHA 35 with minimum score 27 and maximum score 65. This suggests though majority of them were suffering from one or other symptoms of FHA but symptoms were not high enough to seek psychiatric help.

Table 2: Diabetic profile

Duration of diabetes	
Minimum	New case
Maximum	30 years
Mean±SD	7.9±7.3
Hb1Ac	
Minimum	8.2
Maximum	14.21
Mean±SD	8.32±1.8
Neuropathy (%)	
Yes	33.3
No	66.7
Nephropathy (%)	
Yes	10
No	90
Retinopathy (%)	
Yes	21.7
No	78.3
Stroke/MI (%)	
Yes	11.7
No	88.3
Diabetic foot (%)	
Yes	13.3
No	88.3

SD: Standard deviation, MI: Myocardial infarction

Table 3: Fear of hypoglycemia attack

Behavior	Never	Rarely	Sometimes	Often	Very often
Eat large snacks at bed time	43	42	15	0	0
Avoid being alone when my sugar is likely to be low	65	32	2	2	0
If test a urine, spill little sugar on safe side, if test blood glucose, run little high to be safe side	78	20	0	0	2
Keep my sugar higher when I will be alone for while	55	37	2	2	4
Eat something as soon as I feel the first sign of low sugar	47	48	3	2	0
Reduce my medication when I think my sugar is too low	78	20	3	0	0
Keep my blood sugar higher when I plan to be in a long meeting or a party	58	37	3	2	0
Carry fast acting sugar with me	57	38	2	3	0
Avoid lot of exercise when I think my sugar is low	92	7	0	2	0
Check my blood sugar often when I plan to be in a long meeting or out to party	67	28	0	2	4
Worry					
Not recognizing/realizing I am having reaction	78	18	0	0	4
Not having food fruit, juice with me	75	22	3	0	0
Feeling dizzy or passing out in a public	60	32	3	2	3
Having reaction while asleep	93	5	0	0	2
Embarrassing myself/my friends/family in social situation	100	0	0	0	0
Having reaction while alone	95	5	0	0	0
Appearing stupid or drunk	98	2	0	0	0
Loosing control	92	8	0	0	0
No one be around to help me during reaction	96	2	0	0	2
Having reaction while driving	76	22	0	0	2
Making mistake or having accident at work	86	12	2	0	0
Getting bad evaluation at work because of something that happens when my sugar is low	92	6	0	0	2
Having seizure or convulsion	75	25	0	0	0
Difficulty thinking clearly when responsible for others	88	12	0	0	0
Developing long term complication from frequent low blood sugar	92	8	0	0	0
Feeling light headed or faint	95	5	0	0	0
Having insulin reaction	97	3	0	0	0

N=100 (in percentage)

Table 4: Correlation analysis of hypoglycemic fear survey and diabetic profile

Correlations	DM duration	HbA1c	Total score (27)
DM duration			
Pearson correlation	1	0.142	0.154
Sig. (2-tailed)		0.159	0.126
N	100	100	1000
HbA1c			
Pearson correlation	0.142	1	-0.026
Sig. (2-tailed)	0.159		0.796
N	100	100	100
Total score (27)			
Pearson correlation	0.154	-0.026	1
Sig. (2-tailed)	0.126	0.796	
N	100	100	100

DM: Diabetes mellitus, HbA1c: Hemoglobin A1c

The most common FHA behavior was observed was “eat large snacks at bed time” followed by “Eat something as soon as I feel the first sign of low sugar” and “Carry fast acting sugar with me.” The least fear was observed in “Avoid lot of exercise when I think my sugar is low.” These behaviors were developed following few episode of hypoglycemic attack or instruction by the treating physician. Avoiding exercise comes only when person on regular exercise for diabetes. But in our patient population, this behavior is least observed probably they are not aware about role of exercise in blood sugar control. The most common worry among these individuals were “Feeling

Table 5: score of FHA

Parameters	Total score (27)	DM duration
N		
Valid	100	100
Missing	0	0
Mean	35.07	9.21
Median	33.00	7.00
Standard deviation	8.384	8.037
Minimum	27	0
Maximum	65	30

DM: Diabetes mellitus

dizzy or passing out in a public” followed by “Having seizure or convulsion and having reaction while driving.” The least worry or not single patient have bothered about “Embarrassing myself/my friends/family in social situation.”

The correlation analysis has shown a strong positive correlation between Hb1Ac and total score of FHA, i.e., 0.79. This suggests higher the Hb1Ac higher will be the fear of hypoglycemic score and lower the Hb1Ac lower the FHA score. The interpretation suggests in those who are suffering from uncontrolled diabetes are prone for developing FHA. In another analysis between duration of diabetes and FHA score, it was a weak positive correlation. A value of 0.12 suggests FH is irrespective of the duration of DM.

CONCLUSION

This study is the unique study due to the evaluation of hypoglycemic attack study done on uncontrolled DM patients. Second, this study has shown a high prevalence of psychological symptoms among this population. This also showed strong positive correlation between HB1Ac and FHA score. Hence, we need evaluate patients with uncontrolled DM for the prevalence of psychological problems and should be addressed properly.

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Prediction of Mesiodistal Width of the Mandibular Permanent Canines and Premolars by Utilizing the Mesiodistal Width of Mandibular First Permanent Molars and Incisors

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Abstract

Introduction: Prediction of mesiodistal (MD) width of unerupted permanent canines and premolars is an essential aspect of mixed dentition analysis. Several methods are used to predict tooth width. The best methods demonstrate high values of correlation and determination coefficients. In this study, we aimed to determine the linear regression equation that would predict the sum of the MD widths of mandibular permanent canines and premolars based on the sum of widths of the four mandibular permanent incisors and first permanent molars.

Materials and Methods: The sample consisted of 100 dental casts, obtained from Indian patients (50 male, 50 female, age ranges from 13 to 18 years). MD widths were measured with an electronic digital caliper. Paired and unpaired *t*-tests were used to determine measurement consistencies and the inter-examiner calibration, respectively. Unpaired *t*-test was also used to determine right/left side and sex differences. Paired *t*-test was also used to compare the predicted and actual sum of width of mandibular permanent canines and premolars.

Results: We found high values of correlation (*r*) and determination (*r*²) coefficients (i.e., *r* = 0.746 and *r*² = 0.557). On average, there was no difference between predicted and actual widths of the mandibular permanent canines and premolars, and the standard errors of estimation were 1.69, 1.48, and 1.69 mm for the males, females, and the total sample, respectively.

Conclusion: The proposed method showed good accuracy and was easy to use, but it must be tested for other population.

Key words: Linear regression equations, Malocclusion, Mesiodistal diameter, Mixed dentition analysis, Prediction

INTRODUCTION

The universe of malocclusion commonly identified in orthodontics is a result of dental problems, skeletal problems, and a combination of dental and skeletal problems.^{1,2} Orthodontic literature reveals that a large number of cases of malocclusion develop during the mixed

dentition stage, which spans an interval from the 6th to the 12th year of life.³⁻⁵

The mixed dentition analysis is performed once the four permanent mandibular incisors and the first permanent molars are erupted in the oral cavity.^{6,8} This analysis intends to predict the widths of unerupted permanent canines and premolars and determines the difference between the amount of dental arch space that is available and the amount of tooth material that should be accommodated. The first attempt to estimate tooth mesiodistal (MD) widths was made by Black,⁹ who proposed tables based on average widths. Thereafter, many methods of predicting the MD width of unerupted canines and premolars in the mixed dentition have been reported. These methods use three

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distinct ways to achieve their purposes. The first employs direct measurements of the teeth from radiographs with or without the use of a prediction formula as reported by Nance,¹⁰ Jensen *et al.*,¹¹ and Staley *et al.*¹² The second uses prediction tables based on the measurements of other erupted permanent teeth, as reported by Ballard and Wylie,⁸ Carey,¹³ Moyers,¹⁴ Huckaba,¹⁵ Tanaka and Johnston,¹⁶ and Ferguson *et al.*¹⁷ The third method involves a combination of the previous two methods, i.e., the use of prediction tables associated with the measurements of erupted and unerupted teeth, as recommended by Hixon and Oldfather,¹⁸ Staley and Kerber,¹⁹ Bishara and Staley,⁷ Ingervall and Lennartsson,²⁰ and Staley *et al.*²¹

Teeth tend to have a remarkably close relationship in their proportional sizes in the same person. If a patient has large incisors, then large canines and large premolars can be expected.^{4,8,14,15} In addition, there are also tooth size differences in various populations and between the sexes (males generally have larger teeth than females). Literature has shown considerable differences on form, age at eruption, and congenitally missing teeth among and within racial or ethnic groups.²²⁻³⁵

This study has been carried out to determine linear regression equations to predict the sum of the MD width of unerupted mandibular permanent canines and premolars in Indian population from Mumbai, by utilizing the width of mandibular four permanent incisors and first permanent molars as predictors.

MATERIALS AND METHODS

This study was carried out only in the mandibular arch because the arch length is generally diminished (particularly in the mandibular arch) during the transition from mixed to the permanent dentition.^{10,33,43}

The sample for the present study consisted of 100 pretreatment study casts, belonging to the patients who were reported to the Department of Orthodontics for treatment and clinically having full complement of teeth till the first permanent molars.

All casts met the following criteria, as stated by many authors: permanent dentition till first permanent molar; no history of previous orthodontic treatment; all the teeth fully erupted and free of interproximal restoration, distortion, fractures, and caries; no occlusal or proximal attrition; not form, size, or number alterations; all the subjects ranged from 13 to 18 years.

All the impressions and study casts were obtained from high-quality alginate (Zhermack® clinical, Tropicalgin, a

chromatic alginate impression material, ISO 1563 - ADA 18) and orthodontic model stone (Kalstone®, dental stone type III).

For accurate measurements, a digital vernier caliper (Digimatic caliper, Mitutoyo) with a 0.01 mm resolution, ± 0.02 mm accuracy, and 0.01 mm repeatability (manufacturer specification) was used to measure the MD width of the teeth (Figure 1).

The digital vernier caliper was adjusted to the greatest MD diameter (contact points) of teeth, parallel to the occlusal surface and perpendicular to the long axis, according to the methods of other investigators.^{4,11,17,18,37,44}

To determine the measurement consistencies, a primary investigator measured MD widths of 20 models from the first mandibular molar on one side to the first molar on the other side, 3 times at intervals of 15 days (i.e., a total of 60 models).

The inter-examiner calibration was done by a second investigator who also measured the same models twice separated by 2 weeks.

Paired and unpaired *t*-tests were used to determine measurement consistencies and the inter-examiner calibration, respectively. Unpaired *t*-test was also used to determine right/left side and sex differences. Paired *t*-test was also used to compare the predicted and actual sum of the width of mandibular permanent canines and premolars.

Pearson correlation was used to determine the correlation coefficients (*r*) between the sum of the MD widths of the mandibular permanent canines and premolars (SCPM) and the MD widths of both mandibular first permanent molars plus the MD widths of the four permanent mandibular incisors (SMI) for males, females, and both sexes.

New regression equations were calculated to determine the sum of the MD widths of the mandibular permanent canines and premolars (SCPM) for both male and female population separately and combined. The MD widths of both mandibular first permanent molars plus the MD



Figure 1: Digital vernier caliper used in the study

Table 1: Comparison of linear regression equations in various studies for males, females, and both sexes

Study	Male	Female	Male+female
Ballard and Wylie (1947)			X=9.41+0.527Y
Hixon and Oldfather (1957)			X=0.6474Y+3.493
Tanaka and Johnston (1974)			Y=9.18+0.54X
Ferguson <i>et al.</i> (1978)			Y=9.9350+0.5288X
Frankel and Benz (1986)	Y=0.72X+5.97	Y=0.49X+10.34	Y=0.64X+8.30
al-Khadra (1993)			Y=8.6+0.55 (X)
Lee-Chan (1998)			Y=7.5+0.6X
Yuen <i>et al.</i> (1998)	Y=8.22+0.58X	Y=6.66+0.64X	
Nourallah <i>et al.</i> (2002)			Y=4.93+0.52X
Diagne <i>et al.</i> (2003)	Y=5.45+0.72X	Y=8.74+0.56X	Y=5.67+0.70X
Melgaco <i>et al.</i> (2006)	Y=8.9+0.58X	Y=9.2+0.55X	
Altherr <i>et al.</i> (2007)	Y=0.59X+8.47	Y=0.65X+6.20	
	Y=0.35X+15.30	Y=0.47X+11.52	
Melgaco <i>et al.</i> (2007)	Y=7 + 0.824X	Y=9.2+0.766X	Y=6.55+0.829X
Uysal <i>et al.</i> (2009)	Y=4.17+0.73X	Y=4.51+0.71X	Y=3.74+0.75X
Present study (2009)	Y=0.770X+8.761	Y=0.632X+14.07	Y=0.792X+7.4

widths of the four permanent mandibular incisors (SMI) were used as predictors. Correlation and determination coefficients were also determined.

RESULTS

The results showed a significant statistical difference between the MD tooth widths of males and females (widths were generally larger in males than females). No statistically significant difference was found in tooth widths between the right and left sides. A positive correlation between the mandibular permanent canines and premolars with those of the mandibular permanent molars plus the four mandibular permanent incisors was found, which is highly significant. The linear regression equations in this study are compared with others in Table 1. The new regression equations, correlation (*r*), and determination (*r*²) coefficients developed for males, females, and both sexes in this study are shown in Table 2.

The mean values, mean differences, standard deviations, and statistical significance for each group of teeth (SMI and SCPM) for males, females, and total sample are given in Table 2. Statistically significant differences were found between the values of SMI and SCPM. To predict SCPM based on the values of SMI, the following linear regression equation was determined:

$$Y = a + bX$$

In which, Y (dependent variable) equals the predicted sum of the MD widths of the permanent mandibular canines and premolars on both sides in millimeters

X (independent variable) equals the sum of the MD width of the four permanent mandibular incisors plus the MD

Table 2: Mean values, mean differences, and standard deviations in millimeters for each tooth and sex group

Sex group	n	Mean±SD		Mean difference (SMI-SCPM)	Significance (P value)
		SMI	SCPM		
Male	50	46.24±2.04	44.39±2.33	1.85	0.001
Female	50	44.04±2.12	41.92±2.01	2.11	0.001
Male+ female	100	45.14±2.35	43.16±2.49	1.98	0.001

SMI: Sum of molars and incisors, SCPM: Sum of canines and premolars, SD: Standard deviation

widths of both mandibular first permanent molars on both the sides in millimeters.

The constant *a* is the y-intercept and constant *b* is the slope of the regression. The values of constants *a* and *b* are indicated below:

Male patients: $Y = 8.761 + 0.770X$

Female patients: $Y = 14.07 + 0.632X$

Both sexes: $Y = 7.4 + 0.792X$

Based on these new equations, predicted values for the sum of the widths of the permanent canines and premolars were obtained and compared with actual values in Table 3. A graphical representation of predicted and actual sum of widths of the permanent canines and premolars is shown in Figure 2 for both sexes.

DISCUSSION

The three measurements taken by the primary investigator were compared with paired *t*-test as well as ANOVA.

Table 3: Actual and predicted sum of widths of mandibular permanent canines and premolars, mean differences, and standard deviations in millimeters

Sex group	n	Mean±SD		Mean difference (predicted - actual values of SCPM)	Significance (P value)
		Actual values of SCPM	Predicted values of SCPM		
Male	50	44.39±2.33	44.37±1.57	0.025	0.920
Female	50	41.92±2.01	41.90±1.34	0.022	0.916
Male+ female	100	43.16±2.49	43.15±1.86	0.007	0.968

SCPM: Sum of canines and premolars, SD: Standard deviation

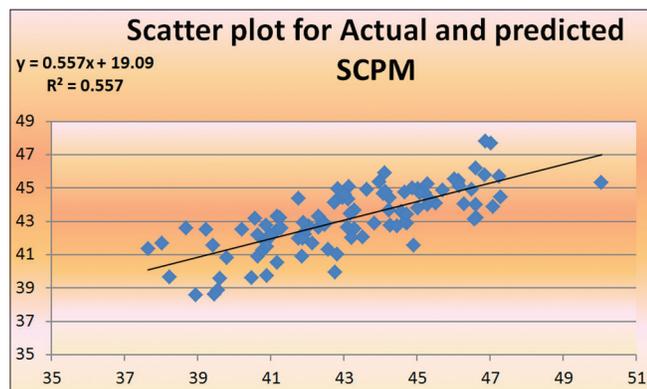


Figure 2: Actual versus predicted values of the sum of mandibular permanent canines and premolars for both sexes

No statistically significant difference ($P > 0.005$) was found between these measurements which implies great measurement precision and repeatability.

In addition, 1st and 2nd measurements of the primary and second investigator were compared with unpaired *t*-test. No statistically significant difference ($P > 0.005$) was found between the values measured by both the investigator, which were nearly the same.

Several authors found differences between male and female tooth widths.^{6,11,14,29,33,37-42,47-49} In this study, we also found a statistical difference between male and female tooth widths. Males generally have larger teeth than females.

The present study shows that there was no statistically significant difference ($P > 0.005$) in the widths found between right and left sides. This implies that the widths of the teeth were same on both the sides of the arch. This symmetry was also found by other investigators.^{6,16,33,37,39,41,42}

The data were analyzed separately for male and female samples. However, higher correlation and determination coefficients were found when both samples were evaluated

together. These higher coefficients can be explained by the increase of sample size from 50 to 100 patients (considering both sexes).

In accordance with other studies, it seems that the combined width of only four permanent incisors is not a good prediction model for the MD widths of unerupted mandibular permanent canines and premolars.^{36,37,41-50}

In this study, we found high values of correlation and determination coefficients when the MD widths of the mandibular first permanent molars were added to those of the four mandibular permanent incisors.

The values of SMI were similar to those of SCPM, with mean differences of 1.85 mm for males and 2.11 mm for females. However, these differences were statistically significant ($P < 0.001$) as shown in Table 2. Thus, simple linear regression equations were determined to predict the values of SCPM based on SMI.

The differences found between the predicted and actual values of SCPM for males, females, and combined sexes were close to zero. The mean differences were 0.025 mm for the male sample, 0.022 mm for the female sample, and 0.007 mm for the total sample (Table 3). The results show that there were minimal differences in the predicted and actual widths for the canines and premolars, which shows the reliability of the linear regression equations developed for the male, female, and total sample of the study.⁵¹⁻⁵⁷

CONCLUSION

Based on the results of the study, the following conclusions were made:

1. No significant differences were found between the MD widths of the teeth on both sides of the arches.
2. There were statistically significant sex differences in tooth sizes in Indian population. Males had significantly larger teeth than their female counterpart.
3. New linear regression equations were developed to predict the sum of the MD widths of the mandibular permanent canines and premolars based on the sum of widths of the four permanent mandibular incisors and first permanent molars for the Indian population.
4. The simplified equations proposed are easy and practical to use and require no sophisticated software or specific equipment.
5. The linear regression equations were found to be reliable as no statistically significant difference was found between the predicted and actual width of the mandibular permanent canines and premolars.

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Biofilm Production and Antibiotic Susceptibility Pattern of Coagulase Negative Staphylococci from Various Clinical Specimens in a Tertiary Care Hospital

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Abstract

Introduction: Coagulase-negative staphylococci (CoNS) have become a common cause of nosocomial infections, particularly bloodstream infections and infections related to the prosthesis. They account for about 9% of the nosocomial infections. They cause infections in debilitated or immunocompromised patients and in patients fitted with urinary catheters, cardiac valves, pacemakers, and artificial joints. CoNS are becoming a problem in treating such infections by showing a considerable amount of antibiotic resistance. Biofilms play an important role in the pathogenesis and drug resistance of CoNS infections.

Materials and Methods: The present study was undertaken to study the biofilm production (slime production) and antibiotic susceptibility pattern of CoNS isolated from various clinical specimens.

Results: The distribution of CoNS from various clinical specimens was as follows: Blood 44 (42.72%), urine 29 (28.16%), pus 16 (15.53%), catheter tip 6 (5.83%), endotracheal tube 5(4.85%) and 1 (0.97%) each from peritoneal fluid, sputum and pleural fluid. *Staphylococcus epidermidis* 63 (55.34%) was the most commonly isolated species followed by *Staphylococcus haemolyticus* 22 (21.36%) and *Staphylococcus saprophyticus* 13 (12.62%). Congo red agar was used for studying biofilm production. Biofilm production was seen in 51 (49.51%) of isolates of CoNS. *S. epidermidis* was the predominant species showing biofilm production 27 (52.94%).

Conclusion: Antibiotic susceptibility testing showed multidrug resistance to commonly used antibiotics. All the isolates were sensitive to vancomycin, but all were resistant to penicillin.

Key words: Biofilm production (slime production), Coagulase-negative staphylococci, Nosocomial infections

INTRODUCTION

Historically coagulase-negative staphylococci (CoNS) have been considered as saprophytes with little pathogenic potential. However, under appropriate conditions they can produce serious human infections. They cause infections in

debilitated or immunocompromised patients, also in patients fitted with urinary catheters, cardiac valves and artificial joints.¹

Some strains of CoNS produce a viscous extracellular material or slime (biofilm). These strains adhere to various biotic and abiotic surfaces. The test for biofilm production helps in deciding the pathogenicity of CoNS and is routinely used in diagnostic laboratories. Biofilm is defined as multicellular communities of bacteria, surrounded by extracellular polymeric matrix produced by the bacteria, which helps it to attach to various biotic and abiotic surfaces.^{2,3} This three-dimensional biofilm structure is made up of extracellular matrix which comprises polysaccharides, proteins, enzymes, DNA, bacterial glycolipids, water and

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aggregates of microorganisms.⁴ Biofilm development depends on many physical, chemical and biological factors.⁵ In staphylococci polysaccharide intercellular adhesin (PIA), also known as a poly-N-acetylglucosamine is responsible for intercellular adhesion.⁶ It is a partially deacylated polymer of β -1, 6-N-acetylglucosamine, which with the other polymers such as teichoic acids and proteins can form a major part of the extracellular matrix. Recently, PIA homologs are identified in many pathogens with biofilm formation ability, which shows that the three-dimensional matrix formation plays an important role in bacterial virulence.⁷⁻⁹ Biofilm protects CoNS, against both; antibiotics used to treat infections and host immune system responses.

Hence, the present study is undertaken to study the biofilm production and antibiogram of CoNS.

MATERIALS AND METHODS

The present study is conducted on various clinical specimens obtained from the patients attending tertiary care hospital. Clinical sample is processed according to standard laboratory procedures. Speciation is done by the following tests-carbohydrate fermentation, phosphatase production, nitrate reduction, ornithine decarboxylation, urease production, novobiocin disc-test, and Polymyxin B resistance.

Biofilm production is studied using Congo red agar. Congo red dye was prepared as concentrated aqueous solution and autoclaved at 121°C for 15 min and added when the agar is cooled to 55°C. Plates are inoculated and incubated aerobically for 24-48 h at 37°C.

A positive result is indicated by black colonies with dry crystalline consistency. Non slime producers remained pink. Antibiotic susceptibility testing was done by Kirby-Bauer disc diffusion method following the Clinical and Laboratory Standards Institute (CLSI) guidelines.¹⁰ Antibiotics tested vancomycin (30 mcg) cefoxitin (30 mcg), netilmicin (30 mcg), co-trimoxazole (25 mcg), Cefotaxime (30 mcg), norfloxacin (10 mcg), ciprofloxacin (5 mcg), chloramphenicol (30 mcg), penicillin-G (10 units), erythromycin (15 mcg), amikacin (10 mcg), gentamycin (10 mcg), and ampicillin (10 mcg).

RESULTS

A total of 103 strains of CoNS isolated in pure form from various clinical specimens are included in the study. The distribution of CoNS is as follows: Blood 44 (42.72%), urine 29 (28.16%), pus 16 (15.53%), catheter tip 6 (5.83%), endotracheal tube 5 (4.85%) and 1 (0.97%) from peritoneal fluid, sputum and pleural fluid, respectively.

Maximum numbers of CoNS were isolated from blood specimen (Table 1 and Figure 1). *Staphylococcus epidermidis* 63 (55.34%) was the most commonly isolated species followed by *Staphylococcus haemolyticus* 22 (21.36%) and *Staphylococcus saprophyticus* 13 (12.62%). Slime production was seen in 51 (49.51%) of isolates of CoNS. *S. epidermidis* was the predominant species showing slime production 27 (52.94%) (Table 2 and Figure 2).

Antibiotic susceptibility testing is performed by Kirby-Bauer disk diffusion method following the CLSI guidelines. Multidrug resistance was seen to commonly used antibiotics. All the isolates were sensitive to vancomycin, but all were resistant to penicillin. Maximum sensitivity was seen to netilmicin 71 (68.93%). Cefoxitin is used as a marker of methicillin resistance. (Table 3 and Figure 3).

Table 1: Distribution of CoNS in various clinical specimens

Specimen	Total number of CoNS	Percentage
Blood	44	42.72
Urine	29	28.16
Pus	16	15.53
Catheter tip	6	5.83
Peritoneal fluid	1	0.97
ETT	5	4.85
Sputum	1	0.97
Pleural fluid	1	0.97
Total	103	100

CoNS: Coagulase negative staphylococci, ETT: Endotracheal tube

Table 2: Slime production in different species

Species	Total	Percentage
<i>S. epidermidis</i>	27	52.94
<i>S. haemolyticus</i>	19	37.25
<i>S. Saprophyticus</i>	3	5.88
<i>S. Schleiferi</i>	1	1.96
<i>S. lugdunensis</i>	1	1.96
<i>S. cohnii</i>	0	0
Total	51	100

S. epidermidis: *Staphylococcus epidermidis*, *S. haemolyticus*: *Staphylococcus haemolyticus*, *S. Saprophyticus*: *Staphylococcus saprophyticus*, *S. Schleiferi*: *Staphylococcus schleiferi*, *S. lugdunensis*: *Staphylococcus lugdunensis*, *S. cohnii*: *Staphylococcus cohnii*

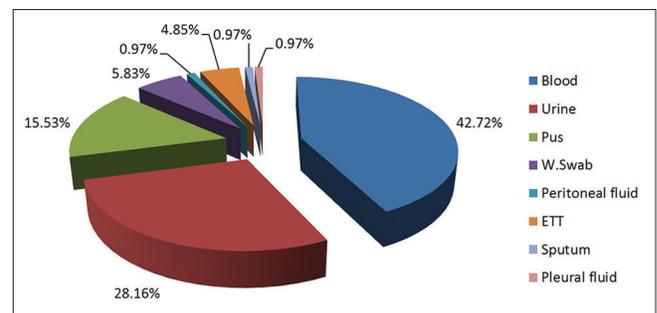


Figure 1: Distribution of coagulase negative staphylococci in various clinical specimens

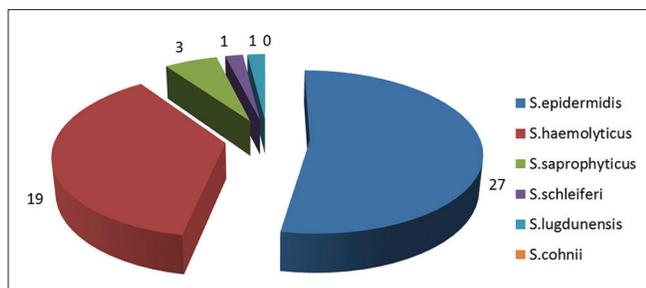


Figure 2: Slime production in different species

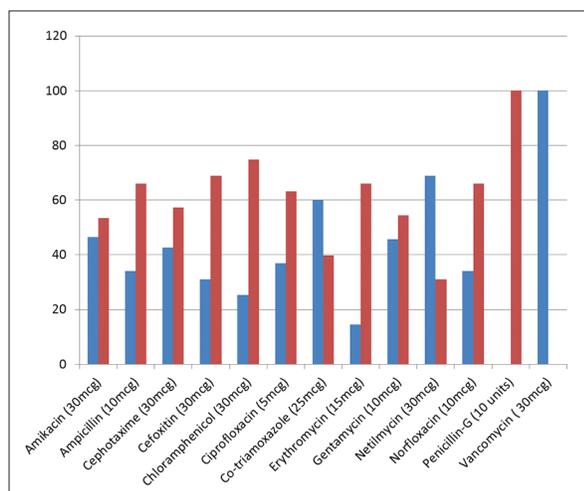


Figure 3: Antibiotic sensitivity pattern of coagulase negative staphylococci

DISCUSSION

CoNS cause hospital infections. An important step in the development of catheter or implant-associated infections caused by CoNS is the adhesion and attachment of these bacteria to biomaterial surfaces.

Among the various mechanisms involved in bacterial adhesion, the production of an extracellular polysaccharide substance called slime plays a relevant role. It strengthens the surface permitting the agglomeration of bacterial cells into biofilms. These biofilms render the cells less accessible to the defense system, thus impairing the action of antibiotics and in term represents the basic survival strategies of these micro-organisms.¹¹

The slime matrix serves as a barrier to the diffusion inward of the antibiotics and may thus protect the enclosed staphylococci. Furthermore, there is evidence that ESS may specifically inhibit the action of some antibiotics.¹²

Table 3: Antibiotic susceptibility pattern in CoNS

Antibiotic (mcg)	Sensitive	Percentage Sensitive	Resistant	Percentage Resistant
Amikacin (30)	48	46.60	55	53.39
Ampicillin (10)	35	33.98	68	66.02
Cephotaxime (30)	44	42.72	59	57.28
Cefoxitin (30)	32	31.07	71	68.93
Chloramphenicol (30)	26	25.24	77	74.76
Ciprofloxacin (5)	38	36.89	65	63.11
Co-trimoxazole (25)	62	60.19	41	39.81
Erythromycin (15)	35	14.56	68	66.02
Gentamycin (10)	47	45.63	56	54.37
Netilmycin (30)	71	68.93	32	31.07
Norfloxacin (10)	35	33.98	68	66.02
Penicillin-G (10 units)	0	0	100	100
Vancomycin (30)	103	100	0	0

Coagulase-negative staphylococci

CONCLUSION

CoNS are emerging as potential pathogens in the hospital settings. Biofilms have a role in the pathogenesis and drug resistance of CoNS infections. Various infection control measures are required to be taken to decrease transmission and reduce infections caused due to CoNS.

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Assessment of Vascularity of Femoral Head after Post-traumatic Fracture Neck of Femur of Variable Period

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Abstract

Background: Fracture neck of femur always poses a big challenge to surgeons. In our country, the majority of them come from low socio-economic status and have to do hard field labor to maintain a household. So, preservation of femoral head should be given the priority during their treatment.

Objectives: It is presumptive to have some idea about the vascular status of the femoral head as they often present late. Our objective is to study the histopathology of femoral head sacrificed during operation so that we can have an idea regarding the vascular supply of femoral head and to determine up to which extent we can conserve the femoral head.

Materials and Methods: This is an institutional based longitudinal observation study conducted at IPGMER and SSKM Hospital Kolkata from May 2013 to April 2014 comprising 32 patients aged 55 years and above having fresh post-traumatic fracture neck of femur admitted for hemiarthroplasty. All sacrificed heads were studied histopathologically from different quadrants for vascularity changes for a variable period up to 4 weeks.

Results: All data are statistically evaluated. There is a gradual decrease in viability and vascularity of different quadrants of the femoral head with increasing time except foveal areas. There were no statistical sex differences of vascularity changes. The significant difference found in displaced and undisplaced fractures.

Conclusions: As there is a proportional relationship between time elapsed after trauma and avascular necrosis change, assessment of vascularity of femoral head should be done before sacrificing it routinely.

Key words: Avascular necrosis, Femoral head vascularity, Fracture neck femur, Viability

INTRODUCTION

Post-traumatic osteonecrosis is a major complication of fracture neck of the femur due to its characteristic blood supply. It is estimated to be 10-30%. It is an injustice to sacrifice femoral head in the form of hemiarthroplasty, which is expensive and a major procedure rather than head preserving surgery without knowing its vascular status.

So, some idea of vascularity of femoral head needs to be known according to their age, sex, duration, and type of fracture. Many studies of femoral head vascularization have assessed the lesion of impact on head viability.¹⁻⁵ Vascular input to the femoral head is threatened by fracture since the epiphysis, and most of the neck is intracapsular. Trueta and Harrison⁶ provide the reference here, completing the work of Howe *et al.*⁷ and Judet *et al.*⁸ In an anatomic study of 15 injected samples, Trueta and Harrison determined the essential vascular elements of the femoral head as being the retinacular vessels originating from the medial circumflex artery; intra-osseous cervical vessels play a minor role and those originating downstream of the neck do not feed anything more than the lateral quarter of the head. These findings were confirmed by Sevitt and Thompson.⁹ The

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lateral circumflex artery supplies few ant retinacular vessels. The medial circumflex artery is extracapsular, with branches penetrating the capsule to become the inferior, posterior, and superior retinacular vessels. The retinacular arteries lie medially to the femoral head and mainly comprise the superior and inferior retinacular vessels. The anterior and posterior vessels are of less importance. Taken together, these arteries form Hunter's arterial circle.¹⁰ There are between four and six superior retinacular vessels, which have the largest diameters, at a mean 0.8 mm. They penetrate the head at the superomedial and terminal part of the neck, at the cervicocephalic junction, to form the cervical branches: the superior metaphyseal and lateral epiphyseal arteries, of which the latter is the main artery, feeding 70-80% of the femoral head. It runs along the old growth plate, anastomosing with the ligament teres vessels, and lies near the retinacular reflection area of the femoral neck. The ligament teres artery branches from the obturator artery when passes the fovea; it anastomoses with the terminal branches of the lateral epiphyseal artery.⁷ The role played by this anastomosis would seem from the literature to be controversial. Sevitt and Thompson¹⁰ do not consider the ligament teres vessels to be essential to the survival of the head: After sectioning the neck, only a small part of the fovea was injected in two-thirds of their anatomic specimens, feeding only a very small part of the head. Catto,¹¹ Chandler *et al.*,¹² and Crock,¹³ on the other hand, consider the anastomosis system between the ligament teres and lateral epiphyseal arteries to be essential to revascularization of the femoral head after neck fracture. In our study, we have assessed histologically the vascularity of femoral head of variable period after intracapsular fracture neck of the femur.

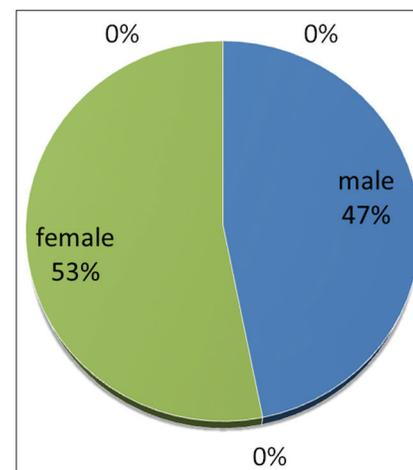
MATERIALS AND METHODS

We have conducted a longitudinal observational study comprising 32 patients of 55 years and above from May 2013 to April 2014, all having fresh post-traumatic intracapsular fracture neck of the femur (Figure 1). Those having age less than 55 years, pathological fracture, neglected fracture, and fracture having a radiological sign of avascular necrosis (AVN) are excluded from our study. We collected all sacrificed femoral head after hemiarthroplasty. The depressed area in the head where the ligamentum teres is attached marked as foveal/apex area, the junctional area with the neck marked as a base. Rest of the head was divided by two lines into four quadrants, i.e., superoanterior, superoposterior, infero-anterior, and infero-posterior. Total six areas denoted by dots like one dot, two dot, and three dots and so on one for each area (Figure 2). After cutting each quadrant into small pieces and putting them into 10 × 10 separate polythene bags with 10% formal saline send to the

pathology department (Figure 3). Next day again, the pieces were put into HNO₃/H₂SO₄ solution to decalcify. After staining with eosin-hematoxylin, we examined different quadrants under a microscope for vascularity changes and tissue necrosis. The earliest microscopic signs^{11,14,15} indicative of bone ischemia are seen in the marrow space starting from the 2nd day there is loss of nuclear staining of marrow cells and large round and ovoid spaces filled with fat appears. The fatty and hematopoietic marrow become then ghosted, and the small vessels show evidence of ischemia (Figure 4). After 15 days, the osteocytic lacunae are empty, and the trabecular surface is devoid of cells. At the border of the necrotic zone, there is a proliferation of capillaries accompanied by fibroblasts and foamy histiocytes, which are responsible for the breakdown of necrotic fatty marrow while dead bone is partly removed by osteoclasts and substituted by newly formed trabeculae; alternatively, woven bone is laid down on the surface of dead trabeculae. So, by observing such changes, the duration and amount of avascular changes have been determined (Figures 5 and 6).

RESULTS

This study includes 32 patients (male - 15, female - 17); left side was more common than the right side and mostly of garden type 3 or 4 variety of fractures (Pie Diagram 1).



Pie Diagram 1: Distribution of sex

Maximum number of cases found in 55-70 years of age group. 25 cases were displaced, and 7 cases were undisplaced fracture neck of the femur. Of the 32 femoral heads, 10 heads were found in the 1st week, 14 in 2nd, 6 in 3rd, and 2 in 4th weeks. Time duration represents the date of injury until the date of surgery (Tables 1-3).

1st week, 10 cases showing 8-10% of necrosis and viability of femoral head around 90%. 2nd week 14 cases and its

Table 1: Relationship between duration of fracture and % of necrosis of different quadrant of the femoral head

Duration of fracture (week)	Number of case	Base (%)	Foveal (%)	Sup-anterior (%)	Sup-posterior (%)	Inf-anterior (%)	Inf-posterior (%)	Average % of necrosis
1 st	10	8.76	8.2	8.4	8	8	7	8
2 nd	14	22.9	7.8	18.9	14.5	16	14	15
3 rd	6	28	7.8	25	25.3	24	21.67	22
4 th	2	46.3	11	37	37	35.5	29	32

Table 2: Average percentage of avascular changes according to displacement

Displacement /type	Average % of avascular change irrespective of time and zone
Undisplaced	7.82
Displaced	18.35

Table 3: Average percentage of avascular changes according to age

Gender	Average % of avascular changes
Male	17
Female	15



Figure 1: X-ray showing fresh undisplaced fracture neck femur of 65 years old woman



Figure 2: After removal of femoral head and 4 quadrants marked by diathermy



Figure 3: Femoral head kept in 10% formalin in sterile polythene and level the bag

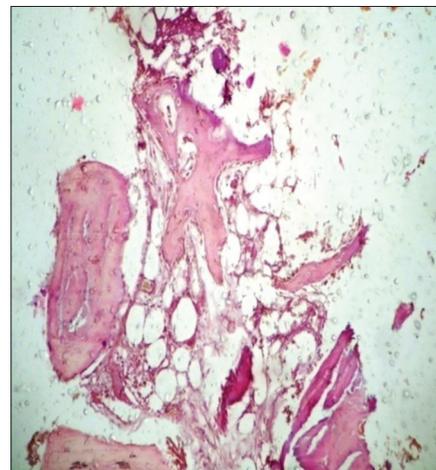


Figure 4: Living lamellar bone lined by osteoblasts with presence of osteocytes in the lacunae (H and E, x100)

necrosis of femoral head around 15%. The viability of femoral head remains half of the femoral head. 3rd week 6 cases and its necrosis and viability accordingly 21-25% and 70-75%. The 4th week has only two cases and necrosis of femoral head is highest (31-35%) and viability (60-65%).

All data were statistically evaluated. We use Statistical version 6 (Tulsa, Oklahoma: Stat Soft Inc., 2001) and

Table 4: Necrosis of different quadrant of femoral heads of all patients

Total number of case	Male/ female	Displaced	Base (%)	Apex (%)	Superoanterior (%)	Superoposterior (%)	Infero-anterior (%)	Infero-posterior (%)	OT days
1	M	Lateral	20	9	17	13	18	13	13
2	F	Superior lateral	24	10	19	14	20	13	12
3	F	Lateral	12	11	13	12	13	14	6
4	M	Lateral	24	9	20	21	19	16	13
5	F	Undisplaced	12	6	14	7	5	6	7
6	F	Lateral	60	11	35	33	37	29	26
7	M	Lateral	11	21	12	18	17	18	6
8	M	Lateral	20	9	19	20	14	20	11
9	F	Lateral	29	11	25	22	24	19	18
10	M	Undisplaced	10	8	10	5	9	6	7
11	M	Lateral	25	10	17	16	19	18	13
12	M	Lateral	37	9	29	28	29	25	20
13	F	Undisplaced	12	6	11	8	11	7	7
14	F	Lateral	24	9	19	8	19	14	13
15	F	Lateral	34	10	26	23	26	26	19
16	M	Lateral	28	8	26	20	25	20	12
17	M	Superior	11	13	10	12	10	13	7
18	F	Lateral	65	11	39	33	34	29	27
19	F	Lateral	27	8	25	16	18	16	13
20	M	Lateral	29	7	26	17	20	16	14
21	F	Superior lateral	19	8	16	11	13	13	10
22	F	Undisplaced	10	7	9	5	6	6	5
23	M	Lat	28	9	30	26	29	25	20
24	F	Undisplaced	5	9	4				7
25	F	Lateral	18	3	15	10	10	10	12
26	M	Lateral	30	7	22	18	18	15	17
27	M	Lateral	28	7	20	20	18	17	16
28	F	Undisplaced	4	7	8	6	4	6	6
29	M	Lateral	22	7	18	15	15	12	13
30	F	Lateral	6	6	5	7	5	6	7
31	F	Lateral	25	5	15	10	10	12	14
32	M	Undisplaced	25	8	12	15	10	10	12

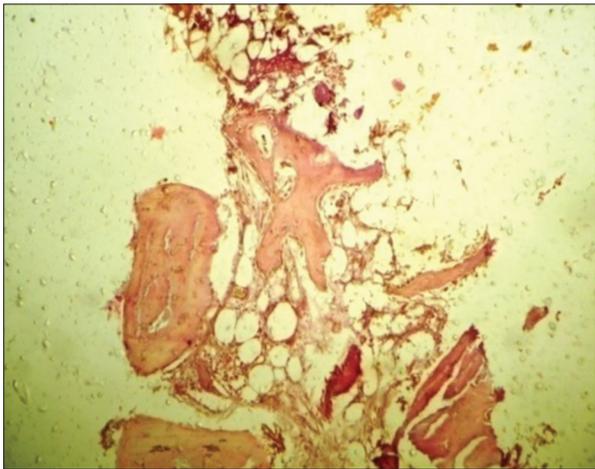


Figure 5: In the right lower corner dead woven bone with loss of osteoblastic rimming and osteocytes. The color of dead bone is more eosinophilic than alive bone (H and E, ×100)

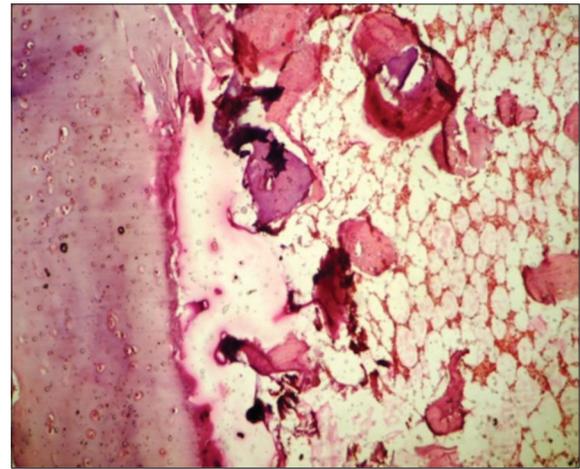


Figure 6: Dead bones and cartilage with loss of vascularity, areas of hemorrhage and increased fat spaces (H and E, ×400)

Pearson’s Chi-squared test (χ^2) to test a null hypothesis (Table 4).

In our statistical calculation, decrease in vascularity of all quadrants of the femoral head is comparable with

increasing time after fractures except foveal zone. There is strong correlation between displaced fracture and loss of vascularity. No significant difference observed between sexes regarding viability changes. The highest amount of avascular changes observed was 35.16% in a female patient who was operated 27 days after injury, while the least

avascular changes, that is, 3% observed also in a female patient who was operated just 7 days from injury.

DISCUSSION

Fracture neck of femur usually affects elderly population, though this is not an emergency but treatment should begin as early as possible because chances of non-union, AVN changes increases with time duration. We usually do hemiarthroplasty or total hip replacement surgery in elderly patients. If we know about the vascularity and viability status of the femoral head after fracture, we can properly plan our management regarding whether femoral head can be preserved or not.

We have selected patients of 55 years or more of recent post-traumatic fractures because there is often a bias toward doing head sacrificing surgeries because of their age and they often come 2-3 weeks later. However, this type of surgery is more costly and do not match their lifestyle.

We took fresh fractures up to 4 weeks of duration and excluded old neglected ones and also those having pathological fractures, fractures having osteoarthritic changes to eliminate confounding factors.

In our study after histological and statistical analysis of 32 heads, we have not found any significant age and sex differences in vascularity changes. Age and sex are not a dependent factor in our study.

Defining displaced and undisplaced fractures we use Garden's classification system, as this is more familiar to us and reproducible. The process of histopathological examination like tissue preservation, staining and high and low power microscopical slide examination was also very simple and standardized; results are reproducible. There is no other study that clearly mentioned about the displaced and undisplaced fracture vascularity. Our Study shows a significant difference of vascularity changes of displaced and undisplaced fractures probably more damage to retinacular vessels and more tamponade effects of the intact capsule.

The study also shows the viability of femoral head gradually decreases with increasing of fracture duration. More the fracture duration, there is less vascularity. We observe that in 1st week 8-10% of necrosis and viability of femoral head around 90-92%, whereas in 4th-week necrosis of femoral head is highest 32-35% and viability lowest.

Sherman and Phemister 1947,¹⁶ Phemister 1948¹⁷ studied histology of femoral head and showed slow osteocyte loss; the bone is dead shortly after the vascular injury. However,

our study did not find rapid bone dead in spite slow loss of vascularity and viability.

After studying different quadrants of the femoral head only, apex part survived till late may be due to intact blood supply through ligamentum teres, which was damaged less than retinacular and ascending cervical vessels.

We have lots of study regarding the assessment of femoral head vascularity, but most of them used radiological assessment, very few of them used histological assessment, and we do not have that data even in Indian patients. The result we are getting from this study will help us to have an idea that in whom we can predict that femoral head is still viable, and we can go for radiological assessment of vascularity by MRI, which is a must before head preserving surgery. Thus, we can avoid doing MRI in all patients, specially in those cases in whom we do not expect the head to be viable so can reduce the cost of treatment. As India being a developing country and more than 50% of its population still living in villages, we must give it a chance to preserve the femoral heads of such patients and it will be really helpful if we have some guidelines in choosing the right candidate.

So, from the above discussion head preservation surgeries (such as compression hip screw, dynamic hip screw with or without bone grafting) for fracture neck of femur are very justified in middle and old aged active group, in minimally displaced fractures within 4 weeks instead of head sacrificing to take a chance of revascularization and union with the remaining viability.

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Significance of Silver Binding Nucleolar Organizer Regions in Oral Squamous Cell Carcinomas

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Abstract

Background: Cell proliferation is an important factor in the prognosis of malignant neoplasia. The number of argyrophilic nucleolar organizer regions (AgNORs) per cell has been considered as an indicator of the cellular proliferative activity. A study is carried out to examine whether AgNOR numbers relate to the growth rate in squamous cell carcinoma (SCC) of the oral cavity.

Aim: To verify the relationship between total AgNORs mean value (mAgNOR) and/or the percentage of cells exhibiting five or more AgNOR dots/nucleus/100 cells AgNORs (proliferative index [pAgNOR]) with histopathologic grading of oral SCC according to Broder's grading.

Materials and Methods: This was a prospective study done over a period of 3 years from May 2012 to June 2015. A total of 50 cases of oral SCC were graded into three groups according to Broder's grading, namely well-differentiated, moderately differentiated, and poorly differentiated. For NOR study, 3-5 μ m-thick sections were stained with 50% aqueous silver nitrate solution. The predominant microscopic pattern of NORs was determined. Quantitative and qualitative analyses of NORs were obtained of all cells present on each histological field. AgNORs were stained by a one-step silver method and examined in representative paraffin sections from 50 cases of oral SCC.

Results: The mAgNORs per nucleus was 3.3057 ± 0.11 for the well-differentiated group, 5.324 ± 0.43 for the moderately differentiated, and 8.167 ± 0.22 for the poorly differentiated. The proliferative index in well-differentiated pAgNOR count is 25%, in moderately differentiated count it is 49.7%, and in poorly differentiated count it is 65.4%.

Conclusions: AgNOR staining technique seems to be a useful diagnostic tool since differences in AgNOR numeric values can be identified in the different types of oral SCC. This technique is easy to handle and inexpensive, thus justifying its large use in histopathology.

Key words: Argyrophilic nucleolar organizer regions, Nucleolar organizer regions, Oral squamous cell carcinoma

INTRODUCTION

In 1941, Broders¹ related the extent of malignancy in neoplasms and emphasized the correlation between histological tumor differentiation, their treatment, and prognosis. The majority of oral and pharyngeal cancers were squamous cell carcinoma (SCC). Out of which, 91.6% occurred in the oral cavity.² Oral SCC represents the third most common form of malignancy in the developing

countries whereas in the developed countries, it is the eighth most common malignancy.^{3,4} The most widespread is the chewing of betel quid with tobacco that have been demonstrated as an increased risk for cancers of the oral cavity.

Quantification of argyrophilic nucleolar organizer regions (AgNORs) is a valuable parameter in tumor pathology. Studies have shown the higher number of AgNORs in malignant lesions such as SCC, which are associated with poor prognosis. NORs are the loop of DNA that encode ribosomal RNA and are considered important in the synthesis of protein. They are located on the short arm of acrocentric chromosomes - 13, 14, 15, 21, and 22. Many of them bind silver, a property attributed to proteins associated with these sites, particularly the acidic

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nonhistone components. NOR staining thus represents actively transcribing NORs (thus rDNA) and the frequency of NORs per nucleus may prove to be useful as replication markers.^{5,6} AgNORs reflect the state of activation and the proliferation activity of the cell and degree of malignant transformation of certain tissues. The amount of AgNOR is proportional to the proliferative activity of neoplastic cells into the cell cycle, which progressively increase from G₀ to S phase.⁷ A rapidly dividing tumor population had a greater proportion of cells in the early stages of G₁. Conversely, tumors with a low rate of cell proliferation display a single NOR.⁷ The silver staining technique is not able to recognize rDNA and rRNA, but the acidic proteins associated with these sites of rRNA transcription are designated as B23, C23, “AgNOR” proteins, and RNA polymerase I.⁸ NORs have got importance nowadays more because the frequency within the nuclei is much higher in malignant cells than in normal cells, reactive, or benign neoplastic cells.⁸

Morphological Characteristics - Qualitative Assessment

Morphological variations of AgNORs were assessed regarding the size and shape of the individual AgNOR dots and their pattern of distribution, as defined by Khan *et al.*, 2006,⁹ who identified different patterns of AgNOR size and distribution:

The grading of size variation was performed according to Khan *et al.*⁹ and scores of distribution were given as following:

- 0 - More or less uniform in size;
- 1+ - Two different sizes;
- 2+ - More than two different sizes (but not those of 3+);
- 3+ - Including all grades and sizes.

The dots dispersion grading was performed according to Khan *et al.*⁹ and scores of AgNOR dots were given as following:

- 0 - Limited to nucleoli;
- 1+ - Occasional dispersion outside nucleoli;
- 2+ - Moderate dispersion outside nucleoli;
- 3+ - Widely dispersed throughout nucleus.

MATERIALS AND METHODS

The present study is undertaken in the Pathology Department of Mahatma Gandhi Medical College and Hospital, Jaipur. A total of 50 cases were studied from May 2012 to June 2015. The cases are referred from ENT Department having growth in the oral cavity (Figure 1a and b) biopsy taken, and sent for histopathological examination. These are broadly classified into three groups according to Broder’s¹ grading of histopathological reports as well differentiated (Figure 2a and b), moderately differentiated (Figure 3a

and b), and poorly differentiated (Figure 4a and b), SCC (Table 1).

The biopsy specimens which were received subjected to proper fixation in 10% formal saline after that followed by

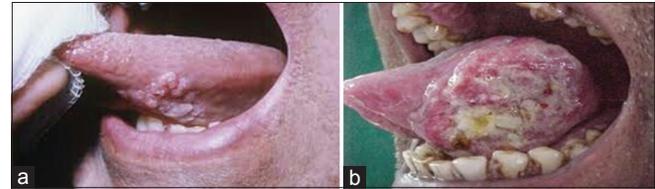


Figure 1: (a) Carcinoma of base of tongue, (b) carcinoma of lateral border of tongue

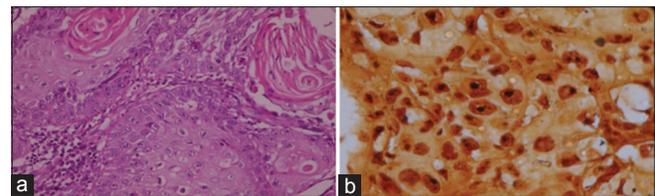


Figure 2: (a) Well- differentiated squamous cell carcinoma (H and E, x40), (b) more or less uniform size argyrophilic nucleolar organizer regions (AgNORs) dots/nucleus (AgNOR stain, x100)

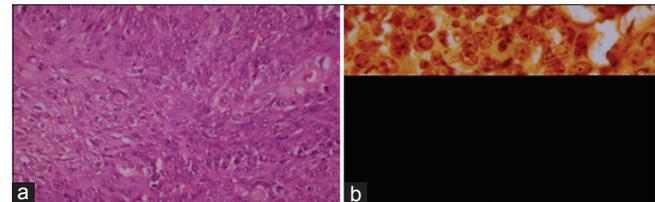


Figure 3: (a) Moderately- differentiated squamous cell carcinoma (H and E, x40), (b) grade “1+” score argyrophilic nucleolar organizer regions (AgNOR) size (AgNOR stain, x100)

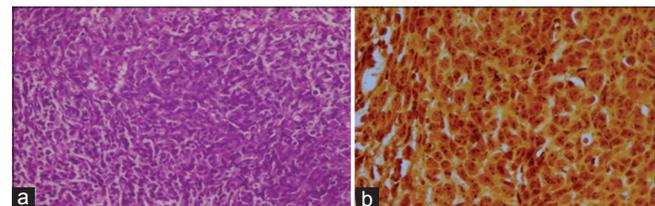


Figure 4: (a) Poorly- differentiated oral squamous cell carcinoma (H and E, x40), (b) great amount and highly stained argyrophilic nucleolar organizer regions (AgNOR) dots (AgNOR stain, x100)

Table 1: Classification of patients according to Broder’s grading

Groups	Number of cases
Group I (WDSCC)	19
Group II (MDSCC)	22
Group III (PDSCC)	9

WDSCC: Well-differentiated squamous cell carcinoma, MDSCC: Moderately-differentiated squamous cell carcinoma, PDSCC: Poorly-differentiated squamous cell carcinoma

routine paraffin sectioning at 3-4 μm thickness. AgNOR staining was performed as described by Ploton *et al.*^{6,10} First, the samples were de-waxed in xylene and then rehydrated through graded ethanols to distilled water. The silver nitrate solution was prepared by mixing two parts of 50% silver nitrate solution with 2 g of gelatin in 100 ml of 1% formic acid in distilled water. The sections are incubated in this solution in dark at room temperature for 60 min and then washed with de-ionized water. This is followed by pair dehydration in graded alcohol solutions, cleared in xylene, and mounted in Canada balsam. AgNORs are seen as distinct intranuclear black dots and are randomly counted manually in 100 nuclei under ×1000 magnification with oil immersion in the three groups. Finally, the mean value and standard deviation of an each case are determined.

AgNORs are seen as distinct intranuclear black dots and were counted manually in 100 epithelial nuclei under ×100 magnifications with oil immersion in different groups. Finally, the mean value and standard deviation of each group are determined and tabulated. One-way ANOVA was used to compare these groups. The mean of AgNOR (mAgNOR) is compared in each group separately using unpaired *t*-test. The data obtained are tabulated in the master charts of the various histological grades/groups in oral SCC. The qualitative assessment of AgNORs based on their size, shape, and the pattern of distribution was processed using frequencies, percentages, and Chi-square test.

The mAgNORs in a different grade of oral SCC per nucleus was 3.3057 ± 0.11 for the well-differentiated group, 5.324 ± 0.43 for the moderately differentiated, and 8.167 ± 0.22 for the poorly differentiated group (Figure 5). According to one-way ANOVA, a significant difference was seen in the number of AgNOR dots between the groups ($P < 0.001$) (Table 2). The second count was the proliferative index (pAgNOR) which is defined as the percentage of nuclei exhibiting five or more AgNOR granules/nucleus/100 cells (Figure 6). This count represents the proliferative activity of tumors cells. High proliferative activity in tumors is considered when there is pAgNOR count of 8% or more (Table 3).¹¹

RESULTS

Clinical data obtained from medical records are compiled according to the tumor site such as 23 cases of the lateral border of tongue, 14 of the base of tongue, 6 of retromolar trigone, and 7 of buccal mucosa. The age of the patients ranged from 31 to 80 years at the time of diagnosis of neoplasm. Regarding the gender, 36 were male and 14 were female. AgNORs were seen through light microscope

Table 2: Distribution based on AgNOR counts (mean and range) in different grades/groups

Broder's grade of oral SCC	Number of subject	mAgNOR count	Standard deviation
WDSCC	19	3.3057	0.11
MDSCC	22	5.3241	0.43
PDSCC	9	8.1677	0.22

SCC: Squamous cell carcinoma, WDSCC: Well-differentiated squamous cell carcinoma, MDSCC: Moderately-differentiated squamous cell carcinoma, PDSCC: Poorly-differentiated squamous cell carcinoma, AgNORs: Argyrophilic nucleolar organizer regions

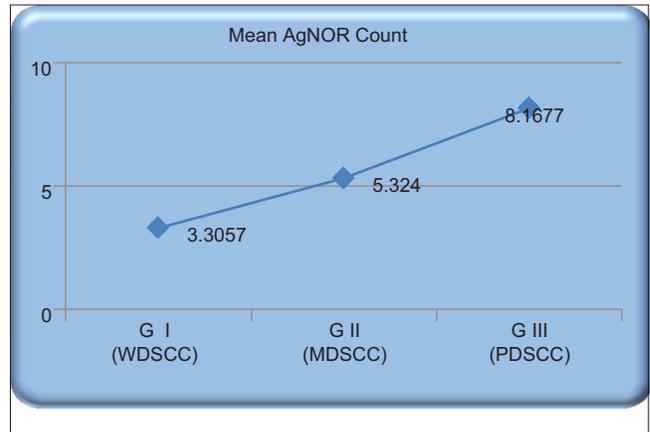


Figure 5: Distribution based on mean argyrophilic nucleolar organizer regions count in different grades of oral squamous cell carcinoma

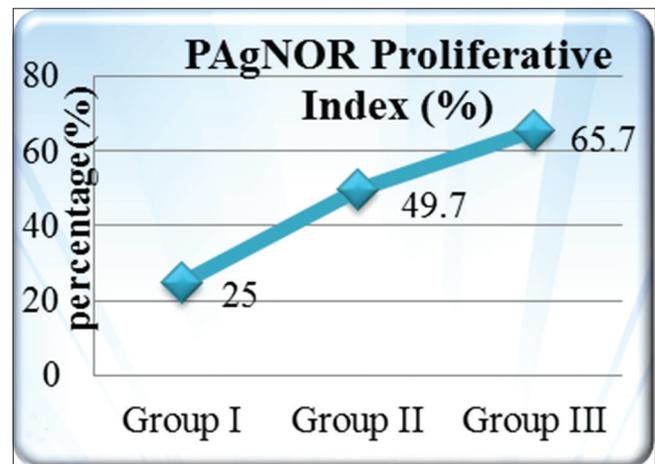


Figure 6: Proliferative index of argyrophilic nucleolar organizer regions count in different grades/groups of oral squamous cell carcinoma

inside the cell nuclei as black to brownish dots as the yellow staining allowed easy visualization of individual NORs. The number and diameter of the NORs, usually round, were variable and either diffusely distributed all over the nuclear area or grouped in a wide, round, and less intensely stained structure. Qualitative assessment was done according to Khan *et al.*⁹ and scores of dot distribution were given

Table 3: Comparison of mAgNOR count, pAgNOR, size, and distribution per cell between different grades/groups of oral squamous cell carcinoma

Grades	Number of cases	mAgNOR count per cell	pAgNOR (percentage of nuclear with >5 AgNOR dots/nuclear)	AgNOR variation in size per cell	AgNOR dispersion per cell
WDSCC	19	3.306	25	0.263	0.263
MDSCC	22	5.324	49.7	0.454	0.41
PDSCC	9	8.167	65.4	1.22	0.88

SCC: Squamous cell carcinoma, WDSCC: Well-differentiated squamous cell carcinoma, MDSCC: Moderately-differentiated squamous cell carcinoma, PDSCC: Poorly-differentiated squamous cell carcinoma, pAgNORs: Proliferative index argyrophilic nucleolar organizer regions, mAgNORs: Mean argyrophilic nucleolar organizer regions

as: 0 - more or less uniform in size; 1+ - two different sizes; 2+ - more than two different sizes (but not those of 3+); 3+ - including all grades and sizes. The grading dots dispersion was performed according to Khan *et al.*⁹ and scores of dispersion of AgNOR dots were given as following: 0 - limited to nucleoli; 1+ - occasional outside nucleoli; 2+ - moderate outside nucleoli; and 3+ - widely throughout the nucleus.

DISCUSSION

Although conventional histological staining with hematoxylin and eosin may be useful in the determination of dysplastic changes in precancerous lesions and grading of SCC, sometimes it is difficult to differentiate these lesions with this staining technique. In such cases, AgNORs staining seems to be useful. The AgNOR counts increase with increased cell ploidy and with increased transcriptional activity in the stages of active cell proliferation.¹² Variations in the size and number of the AgNOR dots may depend on the stage of the cell cycle, the number of NOR-bearing chromosomes in the karyotype, or the transcriptional and metabolic activity of the cell. In a rapidly proliferating cell, AgNOR distribution and the chromosomal remain disorganized with the resultant formation of small, multiple, and dispersed nucleoli. Actively proliferating cells have impaired nucleolar association, and therefore, they exhibit a higher AgNOR count, regardless of the ploidy state of the cell.

In the present study, results of 50 cases were compared according to age, sex, sites of lesions, evaluated quantitative, and qualitative AgNOR counts in the different grades of oral SCC with the study done by other workers, and it was suggested that AgNOR staining can be used to differentiate different grades of oral SCC.

CONCLUSION

The present study shows the importance of AgNORs in the various grades of oral SCC. Although conventional histological staining with hematoxylin and eosin may be useful in the grading of SCC and determination of dysplastic changes in precancerous lesions, sometimes it is

difficult to differentiate these lesions with this conventional staining technique. In such cases, AgNORs staining seems to be beneficial and useful. It has been established that quantification of interphase AgNORs can actually represent a valuable tool for cell kinetics evaluation. The AgNOR counts increase with increased cell ploidy and with increased transcriptional activity in the stages of active cell proliferation.

Of the various newer techniques which were used for assessing the tumor tissue based on nuclear studies, the staining of AgNORs by a silver compound has become popular for its:

- Simplicity than other various techniques
- Ease of use and to carry out
- Low cost of staining
- Good correlation with other proliferative markers of tumors.

Finally, AgNORs (mAgNOR and pAgNOR) counting have a direct relationship with Broder's histopathologic grading, leading us to suggest that AgNOR technique can be used as a biological marker of oral SCC tumor progression.

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Variation in Drainage of Frontal Sinus: A Study on Cadavers

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Abstract

Background: The purpose of this prospective study was to investigate various drainage pathways of the frontal sinus.

Methods: For this, sagittal section of each specimen was made and the frontal sinus was exposed. From the frontal sinus, a probe was passed to demonstrate the opening of the duct into nasal cavity. Photographs were taken.

Results: In 18 cadavers (90%), both the sinuses opened into frontal recess on both the sides. We also found that sinuses were draining to infundibulum, bulla ethmoidalis.

Conclusions: These anatomical variations affect the drainage and ventilation of the paranasal sinus due to infection lead to stasis of secretion cause recurrent and chronic sinusitis.

Key words: Frontal sinus, Middle meatus, Paranasal sinuses

INTRODUCTION

The paranasal sinuses have been recognized from the time of Galen (130-201 AD).¹ There are two groups of paranasal sinuses: Anterior and posterior. Frontal sinus belongs to the anterior group.² The sinuses are divided into several recesses, which communicate with each other through incomplete bony septa. Occasionally, one or both sinuses may be absent.³ Normal average dimensions are height - 3.16 cm, breadth - 2.58 cm, depth - 1.8 cm. Frontal sinuses are drained by the frontonasal duct. The opening of the frontonasal duct is found on the anteromedial aspect of the floor of the sinus. The duct then continues through the ethmoidal labyrinth and enters the ethmoidal groove at the anterior end of the middle meatus. A good knowledge of anatomy will enable the surgeon to operate with more confidence, by improving one's ability to correctly interpret normal variants from abnormal or

pathological conditions, and determine an appropriate surgical treatment plan to reestablish mucociliary flow to the sinus.

METHODS

The protocol was approved by the Ethics Committee of Government Medical College and Hospital (GMCH), Chandigarh, and written informed consent was obtained from each patient. Around 20 adult male cadavers were dissected to see the drainage of the frontal sinus in Department of Anatomy, GMCH, Chandigarh. For this, sagittal section of each specimen was made and frontal sinus was exposed. The middle turbinate was removed. From the frontal sinus, a probe was passed to demonstrate the opening of the duct into nasal cavity.

RESULTS

All subjects had bilateral frontal sinus. In 18 cadavers (90%), both the sinuses opened into frontal recess on both the sides (Figure 1). In one cadaver (5%), the sinus opened into infundibulum on both the sides (Figure 2). In one case (5%), the sinus opened directly to the bulla ethmoidalis on both the sides (Figure 3).

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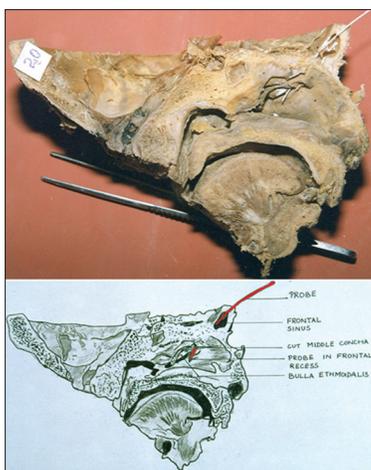


Figure 1: Frontal sinus opened into frontal recess

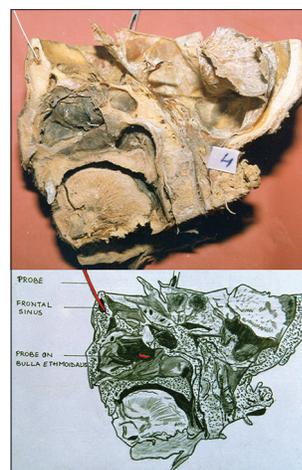


Figure 3: Sinus opened directly to the bulla ethmoidalis

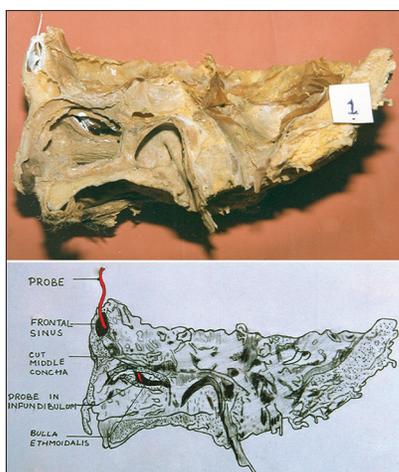


Figure 2: The sinus opened into infundibulum

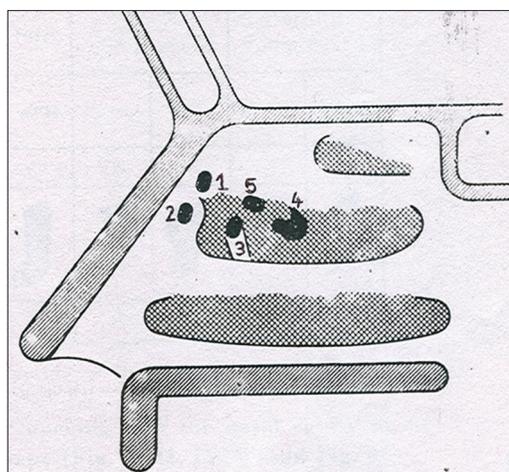


Figure 4: Topography of the opening into middle meatus, according to Laszl'o and Szab'o.

DISCUSSION

The frontal sinus originates as an outgrowth of the cephalic end of the middle meatus in an area termed as frontal recess. Frontal sinus, as well as anterior ethmoidal cells, develops in this area. This area, operculated by the middle turbinate, is identifiable in the late third to the early 4th fetal month. By the age of 6 years, the sinus grows sufficiently large to be just visible in the frontal bone in radiographs. The upward extension continues, with the cell lying at first closer to posterior table before it finally rests in the cancellous bone midway between the two tables. The frontal sinus does not attain its adult size and form until 15-20 years. The frontal sinus and anterior ethmoidal cells develop in this area. At birth, the area has only pits and furrows in the frontal area. It is from one or more furrows that frontal sinus develops. It may develop (1) By direct extension of the whole frontal recess (2) From one or more of the anterior ethmoidal cells, which originate in the frontal furrows or (3) Occasionally, from the ventral end of the ethmoidal infundibulum. In the first instance, there is no true frontonasal duct. Instead,

a wide communication exists with the nasal cavity, anterior and superior to the hiatus semilunaris, which is the most common finding. In the latter two instances, a frontal duct will develop. The tortuosity of the duct will depend on the cells from which the sinus originated and the degree of development and disposition of the neighboring cells. According to Lee variations in the opening of frontal sinus in the middle meatus are (1) Drainage into frontal recess anterior to infundibulum (55%) (2) Drainage above but not into infundibulum (30%) (3) Drainage into infundibulum (14%) (4) Drainage above the bulla (1%).⁴

According to Laszl'o and Szab'o, topography of the opening into middle meatus (50 cases) is as follows: (1) Above the anterior pole of the middle nasal concha in one case (2%) (2) Before the anterior pole of the middle concha opening directly into middle meatus in 2 cases (4%). (3) On the lateral wall of the anterior third of middle meatus in 15 cases (30%) (4) In the middle third of middle meatus together with the orifice of the maxillary sinus, and

a few ethmoidal cells in 2 cases (4%). (5) At the top of the anterior third of middle meatus in 22 cases (44%). (6) Rest of specimens was not included in the study as they showed ossification at the lower end of duct or double orifices (Figure 4).⁵ Basmajian says the most common site of opening is into superior aspect of hiatus semilunar is. In most of the cases of present study, the sinus opened into frontal recess explaining the development of the frontal sinus from the extension of frontal recess.⁶ This is similar to the observations of Lee and Basmajian.^{4,6} In two instances, the frontal sinus appears to have developed either from one or more of the anterior ethmoidal cells, which originate in the frontal furrows or from the ventral end of the ethmoidal infundibulum explaining their opening into infundibulum and onto the bulla ethmoidalis similar to the description given by Lee.⁴

CONCLUSION

We found in 90% of cases, both the sinuses opened into frontal recess on both the sides. In 5% cases, the sinus opened into infundibulum on both the sides. In other 5% cases, the sinus opened directly to the bulla ethmoidalis on

both the sides. It is important for the surgeon to be aware of variations that may predispose patients to increased risk of intraoperative complications and help to avoid these to improve success of management strategies. These anatomical variations affect the drainage and ventilation of paranasal sinus due to infection lead to stasis of secretion cause recurrent and chronic sinusitis. In view of the presence of these significant variations, we reemphasize the need for proper preoperative assessment in every patient to accomplish a safe and effective endoscopic sinus surgery.

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Children with Poor School Performance for Specific Learning Disability

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Abstract

Background: Poor performance of school children has always been a cause of concern. Some students, grasping power may be very poor, some others may speak very slowly and many others may be confused with signs and make careless mistakes. Teachers and parents may know that the child is different, but may not be able to give the reason. Little do they realize that the child is suffering from learning difficulty, which is related to brain development that causes hyperactivity, impulsive behavior, and attention problems. The aim of this study is to identify learning disability in children with poor school performance and to analyze their clinical profile.

Materials and Methods: This is a cross-sectional study over a period of 1-year from July 2013 to June 2014 conducted at Kannur Medical College, Anjarakandy, a total 300 students with poor school performance were selected by their class teacher. To the parents of these children, a questionnaire was given regarding birth history, development history, and questions regarding warning signs of learning disability. The students were later assessed.

Results: Out of the 300 students with poor school performance, parental perception of learning problems was seen in 106 students. Post assessment 39 (13%) students had learning disability. Association was found between low birth weight, preterm birth, language, social and motor developmental delay. Association was also found between learning disability and attention deficit hyperactivity disorder.

Conclusion: Learning disability was identified in a significant number of students. Screening children for learning disability should be there at the kindergarten level so that children can be identified and remedial measures initiated.

Key words: Learning disability, Performance, School

INTRODUCTION

School education is socially and culturally valuable in our world. Good school performance is an indication of future social success. At least one in five students has trouble keeping up academically at some point during school. In recent years, complaints of poor school performance and difficulty in learning have increased in doctor's office.

Poor school performance should be seen as a symptom related to many etiologies. It can be environmental or

individual factors. One of distressed due to persistent failures. Such children require our immediate attention before a youngster develops an aversion to attending school. The aim of this study was to identify learning disability in children with poor school performance and to analyze their clinical profile.

MATERIALS AND METHODS

The study group included children in the age group of 8-12 years studying in third to seventh grade. The study was conducted between July 2013 and June 2014 for 1 year. Students with poor school performance were selected by their class teacher based on their academic and overall performance. Schools included in the study were located in Kannur Medical College, Anjarakandy and rural areas of Kannur district in Kerala state, India. The sample size was 300 students with poor school performance. Consent

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was obtained from the school principal and parents. The study was approved by the Ethical and Research Committee of Our Institute.

For the children included in the study, a questionnaire was given regarding birth history, pre and postnatal events, developmental history, history of any significant medical illness, family history, socio-economic history, question regarding warning signs of learning disability and features of attention deficit hyperactivity disorder (ADHD). The questionnaire was administered in the local language (Malayalam). The questionnaire was piloted before finalization. Back translation was also done. When feasible the interview was directly conducted with the parent and teacher.

A gross assessment of intellectual ability and the individual factor is learning disability. Learning disability is related to problems of acquisition and development of brain function involved in learning such as dyslexia, dyscalculia, and writing disorder. Without recognition and help children with a learning disability become increasingly frustrated and visual motor skills were done using "Good enough Harris draw a man test."¹ A general physical examination was carried out with a notice on dysmorphic features and neurocutaneous markers. Neurological examination was done to look for fine motor abnormalities and soft neurological signs. The audiometric and ophthalmic examination was done to rule out hearing and visual deficits. For school based assessment, Snellen's six-meter test was used for vision. For hearing Rinne and Weber test was done. Assessment of reading, writing, and maths was done by informal method.²

Reading Assessment (Shankarnarayan and Kagan)³

- 1) Letter identification (Children were asked to identify letters of English alphabet presented in upper case and lower case in random order)
- 2) Word recognition (Children were asked to read a list of words)
- 3) Reading text 1 and text 2 (Children were asked to read two texts).

Writing Assessment

Checklist for writing assessment.

No space between words, reverses letters/words, omits letters, add letters, poor punctuation, no or wrong capital letters, poor letter formations, poor slanting, messy, too many cancellations, line quality, holding pen, and placement of paper.

Mathematical Ability

Ability to write the numbers in sequence, ability to do addition, subtraction, multiplication, and division, as

appropriate for age. Children with low IQ for age as assessed by Draw a man test, children with vision/hearing problem were not included for assessment of learning disability.

The diagnosis of co-occurring ADHD was made by ascertaining that the child's specific behavior is meeting the DSM-IV revised criteria.

Data were analyzed using SPSS software version 22; Chi-square test was used to find out the association between various factors and learning disability. $P < 0.05$ was considered statistically significant.

RESULTS

In this study, 300 students with poor school performance, in the age group of 8-12 years were included. From the questionnaire provided to the parents of these children, parental perception of learning problems was seen in 106 students. Out of this, 19 children were excluded from the assessment of learning disability because of poor vision, hearing problems, and lack of intellectual ability by draw a man test. Post assessment learning disability was found in 39 students. Considering clinical profile of these 39 students, 82.05% were boys and 7.18% girls. The majority were 10 years of age. 48.72% belonged to upper middle class; 15.38% belonged to lower middle class, and 5.13% belonged to upper class (modified Kuppaswamy's scale).⁴

Coming to types of learning disability, the majority had difficulty in reading and writing. That is 30.77%. 10.26% had difficulty in reading, writing, and maths. 8.2% had difficulty in reading only. 7.18% had difficulty in writing only, and 2.5% had difficulty in maths.

Children with learning difficulty were compared with other children who were poor in school performance. The following Tables 1-3 shows the parental perception of children with difficulty in reading, language writing, and maths, ($P < 0.05$).

Coming to other associations in the learning disabled group, the following things were found to be statistically significant:

Low birth weight ($P = 0.0085$); pre-term birth ($P = 0.032$); motor developmental delay ($P = 0.0457$); language delay ($P = 0.0002$); and social development ($P = 0.0001$).

Association with ADHD was also found to be statistically significant in the learning disabled group ($P = 0.0067$) neurologi finger agnosia. The association of fine motor abnormality was statistically significant ($P = 0.0001$) in the group with learning disability.

Table 1: Reading and language difficulty (n=106)

Reading and language	No. of children	Learning disability	No learning disability	P value
Dislikes and avoids reading or reads reluctantly	71	33	38	0.003
Has difficulty retelling what has just been said	18	9	9	0.202
Has limited vocabulary	18	7	11	0.839
Demonstrates slow and halting speech	17	8	9	0.338
Uses poor grammar or misuses words in conversation	20	10	10	0.174
Mispronounces words frequently	22	10	12	0.344
Confuses words with others that sounds similar	34	15	19	0.283
Confuses words with others that sounds similar	34	15	19	0.283
Frequently skips paragraphs while reading	38	21	17	0.003
Reverses letter order in words	37	23	14	0.000
Reads slowly	65	34	31	0.000
Has difficulty rhyming	31	16	15	0.069
Confuses similar looking words	31	18	13	0.003
Substitutes or leaves out words while reading	53	26	27	0.008

Table 2: Writing difficulty (n=106)

Writing	Total no. of children	Learning disability present	No learning disability	P value
Writing is messy and incomplete	64	38	26	0.000
Uses uneven spacing between letters and words	53	33	20	0.000
Confuses similar looking letters and numbers	31	18	13	0.004
Grasps pencil awkwardly resulting in poor handwriting	38	25	13	0.000
Dislikes and avoids writing and drawing	44	28	16	0.000

Table 3: Difficulty in math (n=106)

Mathematics	Total no. of children	Learning disability	No learning disability	P value
Difficulty in mastering number knowledge	48	20	28	0.344
Difficulty with learning, basic addition, subtraction, multiplication, and division	57	27	30	0.025
Poorly aligns numbers resulting in computational error	51	28	23	0.000
Has trouble telling time	31	17	14	0.013
Has difficulty counting rapidly or making calculations	61	33	28	0.000

DISCUSSION

Specific learning disabilities are encountered commonly in the school setting in recent years major progress in the understanding of these learning problems has been made. The genetic backgrounds are being unraveled, with advanced neuroimaging techniques, the neurophysiologic mechanism of normal and call abnormalities noted were: Fine motor incoordination, the right to left confusion and abnormal learning are studied. For many parents, pediatrician is becoming their first line of advice.

A necessary framework has been provided by Frith⁵ to work up these cases. The first level is the behavioral level at which the everyday school problems of the child are situated. Here, the school problems are described in detail, problems with math, attention problems, reading problems, copying problems, and so forth. In clinical practice, this is the most important level. Because it is at this level that

intervention should be started and followed. This study has used level one for work up.

About 300 was the total number of children with poor school performance. From the questionnaire provided, parental perception of learning problems was seen in 106 students, i.e., in 35.33% Karande *et al.*⁶ investigated parental knowledge of specific learning disability and evaluated the impact of educational intervention on it. They concluded that parental knowledge of their child's learning disability is inadequate, and this can be improved by the single session education program. A supportive home is one of the factors that can favorably determine the outcome of specific learning disability.

Post assessment 39, i.e., 13% had the learning disability. The occurrence of learning disabilities has been estimated differently in the different countries of the world. The "real" prevalence of learning disability is subject to much

dispute because of the lack of an agreed-on definition of learning disability with objective identification criteria.

A study conducted by Mogasale *et al.*⁷ in South Indian city to measure the prevalence of specific learning disability shows a prevalence of 15.17%.

The lifetime prevalence of learning disabilities in US children is reported to be 9.7%.⁸ Thus, studies conducted for the prevalence of specific learning disability shows variable results.

The present study compared the incidence of learning disabilities in males and females. Schools identified more numbers of males with poor school performance - 259 boys and 41 girls. This could be because boys more often come to attention as a result of disruptive behavioral pattern, and girls often go unnoticed. Our study identified 32 (82.05%) boys and 7 (17.95%) girls with learning disability. The gender difference in learning disabilities has been a subject of debate from a long time.

Shaywitz *et al.*⁹ showed that there was no significant difference in the prevalence of reading disability in research identified girls. They indicated that school identified samples were almost unavoidably subject to a referral bias.

Age group selected was 8-12 years.¹⁰ A conclusive diagnosis of specific learning disabilities should not be made until the child is in the third grade or about 7-8 years old as some children are "normal late developers," and they on their own outgrow their learning problems.

Coming to the socio-economic status, the majority came from upper and lower middle class were 19 (48.72%) and 15 (38.46%), respectively. A study done by Karande *et al.*¹¹ showed that majority came from upper middle class. The poor socio-cultural home environment is one of the causes for children to underperforming but cannot result in learning disability.

Learning problems of children can be classified as dyslexia, dyscalculia after they are analyzed with appropriate neuropsychological test batteries. That is level two of Frith's framework.⁵ This vision also prevents doctors from writing attestation, solely based on their clinical opinion. In this study, the majority 12 (30.72%) had difficulty in reading and writing; 10 (25.64%) children had difficulty in reading, writing, and mathematics; 8 (20.51%) had difficulty in reading only, and 7 (17.95%) and 2 (5.13%) had difficulty in writing and math, respectively.

Study on clinical characteristics of children with learning disorders in Taiwan by Huang *et al.*¹² showed

that percentages of subjects with reading disorders, mathematics disorder, and disorders of written expression only were 11.11%, 7.41%, and 25.93%, respectively. Majority 51.85% had both reading disorders and disorder of written expression.

The questionnaire given to understand the parental perception of learning problems in their children was prepared with questions which commonly children encounter with reading, writing, and math. Problems found to be statistically significant among students detected to have the learning disability is given in Tables 1-3. These can be included in the checklist when screening for learning problems.

Looking into the causal factors of learning disabilities, family history is considered as one of the risk factors. Half of the siblings of dyslexic individuals and half of the parents of dyslexics may have the disorder.¹³ In our study, no one came with a positive history of learning disability. This must be due to lack of awareness. Meister *et al.*¹⁴ in their analysis of 69 children showed that 28 (42%) had a family history of learning disability.

It is known that perinatal complications are associated with an increased prevalence of specific learning disability.¹³ In our study, 4 (10.26%) had antenatal insult, $P = 0.0792$, statistically not significant⁴ and had NICU admission, $P = 0.1147$, statistically not significant. 8 (20.5%) had low birth weight. An extensive screening of children for learning disability conducted by SCIMST,¹⁴ Thiruvananthapuram, showed that children with learning disabilities had the following associations, maternal illness (22.93%), prenatal drug intake (25.68%), birth asphyxia (15.59%), prematurity (5.59%), low birth weight (19.26%), and neonatal seizures (7.33%).

In our study, 5 (12.82%) had motor developmental delay; 12 (30.77%) had language developmental delay, and 11 (28.21%) had social developmental delay. In a study conducted by Karande *et al.*¹¹ had 12 (24%) and 11 (22%) children with delayed walking and delayed talking, respectively. A parental history frequently identifies early subtle language difficulties in dyslexic children. Both prospective and retrospective longitudinal studies indicate that dyslexia is a persistent chronic condition rather than transient development delay.

In this study, 7 (17.95%) had a history consistent with ADHD, which was statistically significant. Meister *et al.*¹⁴ in their analysis of 69 children with learning disability showed that 39.1% of the students had attention deficits. Comorbidity is an important consideration in the assessment of treatment of children with developmental

disabilities. It is important to assess for both disorders in any child and to develop a treatment plan that addresses both disorders when necessary.

The present study sought to identify neurological abnormalities in children with learning disabilities. Neurological abnormalities found were the fine motor incoordination, right to left disorientation, and finger agnosia. Among these, the fine motor in coordination was found to be statistically significant. Johnston *et al.*¹⁵ in their study on the neurological status of language impaired and normal children found that language impaired group was distinguished by less efficient performance in a number of areas, involving the rate of movement and left to right identification. Poor fine motor coordination, mirror movement, right-left disorientation and finger agnosia may occur in otherwise normal children, but these signs occur more often in children with learning or behavior problems.

CONCLUSION

About 13% of children had the learning disability in this study. It was more common in boys. Low birth weight and preterm birth were identified as causal factors. A significant association was found between learning disabilities and developmental delay, fine motor abnormalities, and ADHD.

Children who experienced difficulty in reading, writing, or working with numbers are labeled as lazy, obstinate, dumb and just not interested in studies. Early identification, initiation of appropriate psychoeducational interventions will help these children achieve school grades at a level that is commensurate with their intelligence. This would help prevent not only poor school performance, class retention, and development of behavioral problems

in childhood but also help these children develop into well-adjusted adults.

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Correlation of Central Corneal Thickness and Axial Length in Myopes, Emmetropes, and Hypermetropes

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Abstract

Introduction: The cornea is responsible for approximately two-thirds of optical refraction and its role in myopia has consequently been studied intensely over the years. An emmetropic eye is comparable with a sphere and myopic eye to a prolate spheroid. Myopia is increasing in prevalence among the populations of East Asian origin. Estimates of the proportion of myopia in the young population of South East Asian countries range from 30% to 60%.

Purpose: To determine the correlation between central corneal thickness (CCT) and four variables, namely, the degree of myopia, corneal curvature, axial length, and age of the patient.

Methods: 150 eyes were studied for a prospective observational study done at the Department of Ophthalmology, New Civil Hospital, Surat, Gujarat, India. All patients underwent a complete ophthalmic evaluation. CCT was measured with an ultrasonic pachymeter. Axial length was measured using an A-scan (Echorule2, Biomedix). Corneal curvature was measured using a Keratometer.

Results: Total numbers of 150 eyes were evaluated for the study. 66 were myopes, 51 were emmetropes, and 33 were hypermetropics. The mean CCT was $547.80 \pm 28.6 \mu$. This study showed no statistically significant difference between CCT in myopes, hypermetropes, and emmetropes. There was no correlation between the degree of myopia and CCT ($r = -0.006$, $P = 0.96$). There was a negative correlation ($r = -0.26$) ($P = 0.001$) between CCT and corneal curvature. The correlation was significant at the 0.01 level (2-tailed). There was thinner cornea with increase axial length in our study. There was no statistically significant association between CCT and age or sex.

Conclusion: This study has shown that CCT has no correlation with degree of myopia. CCT was significantly associated with corneal curvature and axial length. There was no association between CCT and age or sex.

Key words: Central corneal thickness, Emmetropia, Hypermetropia, Myopia

INTRODUCTION

Although the exact etiology of myopia is still unknown, approximately two-thirds of optical refraction is due to the cornea and its relation with myopia has been studied since a long time. It mostly affects the posterior segment of the eye such as posterior staphyloma, choroidal atrophy, and thinned retina and sclera, inducing more chances of retinal

detachment. Changes in the anterior segment associated with myopia are still under controversies. The myopic eye is known to be longer than the normal emmetropic eye. If this is the result of general growth, one might expect the cornea to have grown thicker than normal. If instead, the myopic eye is larger due to a mechanism similar to that of a balloon being inflated, one would expect the cornea to be thinner than normal according to physics. An emmetropic eye is comparable to a sphere and a myopic eye to a prolate spheroid. Myopia is increasing in prevalence among the populations of East Asian origin. Estimates of the proportion of myopia in the young population of South East Asian countries range from 30% to 60%. With increasing rates of myopia, refractive surgery such as the laser *in situ* keratomileusis (LASIK) has become popular in

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Asia. When undertaking such surgery to correct refractive error, central corneal thickness (CCT) is an important consideration to prevent the cornea from becoming too thin after treatment. Studies that have attempted to investigate the effect of refractive errors on CCT have reported conflicting results. Some of them have found the cornea to be thinner in more myopic eyes. The purpose of our study was to determine the correlation between CCT and four variables, namely, the degree of myopia, corneal curvature, axial length, and age of the patient.

MATERIALS AND METHODS

In this prospective observational study of 150 patients; 66 were myopic, 33 were hypermetropic, and 51 were emmetropic. They were in the age group of 18-45 years. Subjects with previous ocular surgery, glaucoma, or any disease affecting the corneal thickness were excluded. All patients underwent a complete ophthalmic evaluation. CCT measurement was done with an ultrasonic pachymeter. Axial length was measured using an A-scan (Echorule2, Biomedix). Corneal curvature was measured using a Keratometer (Table 5). Statistical analysis was done using SPSS V.11 and Microsoft Excel. Correlation between CCT and four factors, namely, the degree of myopia, axial length, corneal curvature, and age of the patient was studied using. A probability of 0.05 was considered statistically significant.

RESULTS

Among 150 eyes studied, 66 were myopic, 51 were emmetropic, and 33 were hypermetropic. There were 67 female participants and 54 male participants. Participants in the age group 18-55 years were included in the study. Mean age was 26.88 years (standard deviation [SD] 6.66); median age was 25 years (Table 1). Refractive error splits into groups in Table 2. Table 3 shows the mean of all measured variables of myopia, hypermetropia, and emmetropia.

Correlation between CCT and four variables studied using Karl Pearson’s correlation coefficient. This study showed no statistically significant difference between CCT in myopics ($r = -0.006, P = 0.96$), emmetropics ($r = -0.131, P = 0.360$), and hypermetropics ($r = -0.147, P = 0.626$). Changes in axial length were statistically significant in myopes, emmetropes, and hypermetropics. Changes in the mean of corneal curvature in myopia, emmetropia, and hypermetropia were not statistically significant ($F = 1.48, P = 0.161$). Mean anterior chamber depth and refractive error were directly correlated in the myopic group ($r = 0.357, P = 0.003$), but there was no significant correlation found in emmetropic and hypermetropic groups.

DISCUSSION

The study attempted to determine the relation between CCT and four variables, namely, the degree of myopia, corneal curvature, axial length, and age of the patient. The mean (SD) CCT was $547.80 \pm 28.6 \mu$. Fam *et al.* in a study on 714 Chinese patients had a mean of 534.5μ .¹ Chang’s series had 533μ , whereas Vijaya *et al.* reported it in the rural South Indian population as 505.9μ .² This study showed no statistically significant difference between CCT in myopes, hypermetropics, and emmetropes. There was no correlation between the degree of myopia and CCT ($r = -0.006, P = 0.96$). This result is in agreement with the majority of previous studies (Table 4). There was a negative correlation ($r = -0.26$) ($P = 0.001$) between CCT and corneal curvature. The correlation was significant at the 0.01 level (2-tailed). Similar results were there in Tomidokoro *et al.* in the Tajimi Study from Japan.³ A study was done on Singaporean children showed that the radius of corneal curvature correlated with CCT (Pearson $r = 0.19, P < 0.001$) significantly. There was a thinner cornea in patients having a more axial length in our study. Chang *et al.* and Bueno-Gimeno *et al.*⁴ found similar results, whereas Bhat *et al.* and Chen *et al.*⁵ found no correlation between them. Subgroup analysis by age, gender, and race failed to show an association. There was no statistically significant association between CCT and age. Myopia is increasing in prevalence and may be a growing problem in the future. Consequently, there is a higher rate of refractive surgeries to correct it. With LASIK, there is a general concern that one should ablate the cornea further than a given amount. It is, therefore, necessary to

Table 1: Demographic features of study participants

Total participant	121
Total eyes	150
Myopes	66
Hypermetropes	33
Emmetropes	51
Male	54
Female	67

Table 2: Distribution of participants according to refractive error

Refractive error (diopters)	Number of participants	Percentage
Myopia (n=66) 44%		
2	33	50
>4-6	26	39
>6	7	11
Hypermetropia (n=33) 22%		
2-4	27	82
>4	6	18
Emmetropia (n=51) 34%		
Total	150	

Table 3: Mean of measured variables of myopia, hypermetropia, and emmetropia

Refractive error (diopters)	Number of participants (%)	Mean CCT±SD	Mean AL±SD	Mean K±SD	Mean ACD±SD
Myopia (n=66)		549.16±27.02	24.01±0.88	44.00±1.60	3.19±0.42
2-4	33 (50)	551.51±21.5	23.72±0.69	43.58±1.59	3.09±0.25
>4-6	26 (39)	543.34±27.4	24.25±0.75	43.83±2.08	3.34±0.39
>6	7 (11)	552.51±46.17	24.50±0.79	44.98±1.47	3.53±0.00
Hypermetropia (n=33)		549.84±31.75	21.67±1.30	43.42±1.28	2.88±0.35
2-4	27 (82)	551.44±30.15	21.58±0.39	43.33±1.33	2.82±0.25
>4	6 (18)	542.66±40.62	22.75±2.95	43.81±1.85	3.19±0.44
Emmetropia (n=51)		545.68±27.02	22.37±0.83	44.21±1.59	3.00±0.32
Total	150	547.80±28.665	22.97±1.33	43.87±1.55	3.08±0.39

ACD: Anterior chamber depth, CCT: Central corneal thickness, SD: Standard deviation

Table 4: CCT and degree of refractive error

Authors	Years	Country	Results CCT and myopia
Pedersen <i>et al.</i>	2005	Denmark	No correlation
Kunert <i>et al.</i>	2003	India	Thicker CCT in high myopic
Touzeau <i>et al.</i>	2003	France	Thinner CCT when myopic
Shrivannaboon <i>et al.</i>	2002	Thailand	Thinner CCT when myopic
Chang <i>et al.</i>	2001	Taiwan	No correlation
Liu and Pflugfelder <i>et al.</i>	2000	China	No correlation
Cho and Lam <i>et al.</i>	1999	China	No correlation
Price <i>et al.</i>	1999	USA	No correlation
Tanaka <i>et al.</i>	1996	Brazil	No correlation
Alsbirk <i>et al.</i>	1978	Greenland	Thinner CCT when myopic
Ehlers and Hansen <i>et al.</i>	1976	Denmark	No correlation
Hansen <i>et al.</i>	1971	Denmark	No correlation
Martola and Baum <i>et al.</i>	1968	USA (Boston)	No correlation
Von Bahr <i>et al.</i>	1956	Sweden	Thinner CCT when myopic
Blix <i>et al.</i>	1880	Sweden	No correlation
Present study	2013	India	No correlation

CCT: Central corneal thickness

Table 5: Comparison of correlation between different variables with other studies

Authors	Axial length and CCT	Corneal curvature and CCT	ACD and CCT	Axial length and corneal curvature	Axial length and ACD	ACD and corneal curvature
Lee <i>et al.</i>	Thicker CCT with ↑ AL		Thicker CCT with ↑ ACD		Shallow ACD with ↑ AL	
Chang <i>et al.</i>	Thinner CCT with ↑ AL	No correlation		Flat K with ↑ AL		
Chen <i>et al.</i>	No correlation	No correlation	No correlation	Flat K with ↑ AL	Deep ACD with ↑ AL	Flat K with ↑ ACD
Bueno-Gimenol <i>et al.</i>	Thinner CCT with ↑ AL			Flat K with ↑ AL		
AlMahmoud <i>et al.</i>		Thinner CCT with ↑ K				
Bhat <i>et al.</i>	No correlation	Thinner CCT with ↑ K				
In this study	Thinner CCT with ↑ AL	Thinner CCT with ↑ K	No correlation	Flat K with ↑ AL	Deep ACD with ↑ AL	No correlation

ACD: Anterior chamber depth, CCT: Central corneal thickness, ↑: Increase

measure CCT before surgery. A thin central cornea is a risk factor for the development of glaucoma in patients with ocular hypertension. In the ocular hypertension treatment study, a multivariate model that included intraocular pressure, CCT was an important component of the predictive model.

CONCLUSION

CCT in every person is under genetic control. This study has shown that CCT has no correlation with degree

of myopia. It was significantly associated with corneal curvature and axial length. There was no association between CCT and age or sex.

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Solu, *et al.*: CCT Relations with Axial Length, Myopia, Hypermetropia, and Emmetropia

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Relationship between Employee Empowerment and Organizational Stress: A Research on Hospital Employees

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Abstract

Introduction: In parallel with the increasing importance of human resources, researches carried out on human resources and organizational behavior issues have increased. Issues of from which factors are employees' performance and efficient working affected have become the field of interest of many researchers. Employee empowerment and organizational stress are important concepts affecting the working life.

Purpose: The purpose of this study is to examine the relationship between employees' empowerment and organizational stress with the perspective of hospital employees.

Methods: A questionnaire was applied to 140 employees working in a public hospital in Turkey to accomplish this purpose. Scales used were rated between 1 and 5.

Results: As a result of the research, it was determined that participants' employee empowerment score was at a moderate level (2.717 ± 0.786) and organizational stress score was high (3.420). While employees were affected by "sources of stress regarding the production structure" (3.599 ± 0.863) at the most, they were affected by "sources of stress regarding the cultural structure" (2.923 ± 1.026) at the least. As a result of the correlation analysis performed, negative and significant relationships were found between employee empowerment and sources of stress regarding the duty structure, sources of stress regarding the authority structure, sources of stress regarding the production structure, sources of stress regarding the clustering structure, and sources of stress regarding the cultural structure.

Conclusion: The fact that employees do not have enough components of employee empowerment increases their stress levels. It is a known fact that the increasing stress level has negative impacts on both employees and the organization. Therefore, administrators should be aware of both concepts and try to create the necessary conditions strengthen their employees.

Key words: Empowerment, Hospital employees, Organizational stress

INTRODUCTION

Although it is important for organizations in each period, human resources have become more important especially in recent years. In parallel with the increasing importance of human resources, researches carried out on human resources and organizational behavior issues have

increased. Issues of from which factors are employees' performance and efficient working affected have become the field of interest of many researchers.

The concept of employee empowerment is among the concepts on which great emphasis has been laid in recent years. When the literature was analyzed, employee empowerment was observed to have various definitions. According to Besterfield *et al.*,¹ empowerment is "an environment in which people have the ability, the confidence, and the commitment to take responsibility and ownership to improve the process and initiate the necessary steps to satisfy customer requirements within well-defined boundaries in order to achieve organizational

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values and goals.” According to Koçel,² empowerment refers to “practices and conditions in which employees feel themselves to be motivated, their confidence in knowledge and expertise increases, they feel desire to take action using initiative, they believe they can control events and which allow them to perform business that they find appropriate and meaningful in accordance with the objectives of the organization.”

It is necessary to provide some essential elements for the empowerment of employees in the organization. Teamwork, individual responsibility, directing to common goals, commitment, administration's support, open communication platform, flexibility in the work environment, training and development, giving feedback regarding the performance, praising employees, mutual trust, participation and decision-making authority, decreasing promotion, accessibility of resources, information accessibility, information sharing, innovation, change, motivation, etc., could be ranked among the factors in question.¹⁻⁵

When the literature was analyzed, it was understood that there were significant similarities between employee empowerment and concepts such as job enrichment, delegation of authority, participation. However, there are important differences between these concepts. Empowerment is generally associated with the perceptions of the employee. Reinforced employees can shape their own work and working conditions and thereby can affect the organizational activities. In job enrichment, characteristics of the business come into prominence, unlike the perceptions. In job enrichment, employee has the planning and decision-making powers, but this authority is not too broad to change jobs or working conditions. Besides, employees can feel themselves reinforced without job enrichment.⁵ In the devolution of authority, state of an administrator's temporal devolution of his/her authority to a subordinate is in question. Differently from this, the person who actually works becomes the owner of the business in empowerment.^{6,7} Briefly, the concept of employee empowerment is closely associated with the concepts such as job enrichment, devolution of authority, and participation; however, it includes broader meanings than these concepts.

There are several reasons for the increase in the interests of organizations for employee empowerment in recent years. The most important benefit of employee empowerment is the increase of employee's confidence in the organization. Employees will have opinions about what are valuable in their institutions and the expectations of the administrators from them when they believe and trust in their organization so that employees' role ambiguity and role conflicts will

be reduced.³ Apart from this, employee empowerment has positive effects such as creating freedom in employees' behaviors, thereby increasing cooperation among employees,⁸ ensuring the creation of a customer-focused culture,³ increasing the individual and organizational performance,⁵ improving the quality and speed of services provided.⁹

Another concept associated with the employee empowerment is the stress. Stress is defined as “the fact that the person suffers behavioral and physical changes due to the physical or psychological effects caused by himself or surrounding, the power the psychological and physical effects of which are seen causing organisms to be affected.”¹⁰ Stress can be considered as individual and organizational. Organizationally, experienced stress arises if the employee's some expectations regarding the organization or business are not met. In short, the source of the stress experienced is the business or the business environment.¹¹

Factors causing organizational stress are addressed in various ways. Luthans¹² classified these factors into four groups including organizational policies, structural characteristics of the organization, physical conditions, and organizational processes. According to Price,¹³ role conflict, role ambiguity, and workload cause job stress. In their study carried out in health institutions in Australia, Rickard *et al.*¹⁴ set one of the most comprehensive models regarding the causes of organizational stress. According to this model, stress is a function of the outcomes regarding the business such as the factors outside the organization, structural characteristics of the organization, demands and resources regarding the business, job satisfaction, and employee transfer. As it can be seen, some factors causing organizational stress are among the elements of employee empowerment.

Stress created by the above-mentioned factors leads to various problems in the employee's health, family life, daily life, and business life.¹⁵ Decrease in the performance of employees, deterioration of relations with each other, formation of mental distress and anxiety disorders, and increase in occupational accidents are some of these problems.^{16,17} As the reflection of all these, problems of absenteeism and increase in the institution's staff turnover rate arise.¹⁸⁻²²

Stress is a problem with which employees working in all organizations including private and public face. The possibility of facing with intense stress is very high for employees working in the health sector which is especially a labor-intensive sector and has unique features. Because health sector is directly associated with the human life, it

is obvious that the fact that health workers are affected by this negative situation will have serious consequences.

Stress should be managed well in organizations to avoid such negative consequences mentioned above. Therefore, stress-related factors should be identified, and arrangements should be made in this respect. The aim of this study is to determine the relationship between the empowerment perceptions and organizational stress levels of employees working in the health sector.

MATERIALS AND METHODS

The aim of this study is to examine the relationship between employee empowerment and organizational stress with the perspective of a hospital employee. Healthcare staff and administrative employee working in a public hospital operating in Turkey constituted the population of the research. There were a total of 212 personnel working actually under these titles at the hospital where the research was carried out. The sample was not selected and an attempt to reach all of the employees in question was made. The survey method was used in the collection of data regarding the research 140 of 212 surveys distributed were filled out, and the participation rate was 66% (Table 1).

The survey used consisted of three sections. The first section had the “organizational stress scale,” the reliability and validity studies of which were performed, which was prepared by Pehlivan²³ for the doctoral thesis on “sources of stress in education management.” This survey consisted of 6 dimensions and 35 items including sources of stress regarding the duty structure, authority structure, production structure, clustering structure, role structure, and cultural structure. In the second section of the data collection tool, “employee empowerment scale” with 16 items was included to measure the empowerment levels of hospital employees. A literature review was performed before the creation of the items of the scale, and 16 factors within the scope of employee empowerment were determined. An item was created for each factor. Both scales were rated as 5 point Likert. Questions about the personal and professional characteristics of employees were included in the last section of the survey.

Findings regarding the reliability of the survey used to collect data appear in Table 2. Although alpha reliability coefficient is recommended to be 0.7 and higher in the literature, it is stated that in the literature is a sufficient level to make comparisons between groups when it is 0.5 or higher.²⁴ Cronbach’s alpha coefficients of the dimensions of organizational stress scale used in the research were between 0.68 and 0.85. Cronbach’s alpha coefficient of the overall organizational stress scale and employee

Table 1: Number of personnel at the hospital and level of participation in research

Title	Those working actually	Those participated in the survey	Participation rate (%)
Doctor	32	24	75
Other healthcare staff	148	89	60
Administrative services personnel	32	27	84
Total	212	140	66

Table 2: Reliability of the data collection tool

Scale	Number of Questions	Cronbach's Alpha Value
Employee empowerment scale	16	0.92
Overall organizational stress scale	35	0.92
Stress regarding the duty structure	9	0.71
Stress regarding the authority structure	8	0.85
Stress regarding the production structure	5	0.71
Stress regarding the clustering structure	7	0.82
Stress regarding the role structure	2	0.68
Stress regarding the cultural structure	4	0.79

empowerment scale was 0.92. It is seen that these values are above the acceptability limit. Data collected in accordance with the purpose of the research were analyzed using SPSS program (15.0) and appropriate test methods.

FINDINGS

A total of 140 people participated in the research conducted in a public hospital in Turkey, and the distribution of personal and professional characteristics of participants is given in Table 3.

Regarding the research participants, 17.1% of them were doctors, 63.6% of them were healthcare staff, and 19.3% of them were administrative services employee. 62.9% of the participants were female and 60.0% of them were married. When their ages were analyzed, it was seen that 25.0% of them were aged 25 and below, 35.7% of them were between 26 and 35, and 39.3% of them were aged 36 and above. While the majority of the survey respondents (40.0%) had graduate degree, 18.6% of them graduated from a post-graduate program. When the participants’ working times at the hospital where they were still working were analyzed, it was understood that 57.9% of participants had been working for <6 years at the same place. The majority of survey respondents (57.9%) had working time of 45 h or less per week. The ratio of working in night shift was 38.6%.

Average, standard deviation and levels of participants’ assessments regarding the employee empowerment and

organizational stress scales appear in Table 4. While determining level, first the range coefficient calculated for evaluation range of arithmetic mean ($5-1 = 4$) and then option ranges ($4/5 = 0.80$) were determined. Accordingly, “1.00-1.79” range was leveled as “very low,” “1.80-2.59” range was leveled as “low,” “2.60-3.39” range was leveled

as “moderate,” “3.40-4.19” range was leveled as “high,” and “4.20-5.00” range was leveled as “very high.”

Table 3: Personal and professional characteristics of participants

Variables	n (%)
Profession	
Doctor	24 (17.1)
Healthcare staff (out of doctors)	89 (63.6)
Administrative services personnel	27 (19.3)
Gender	
Female	88 (62.9)
Male	52 (37.1)
Age (years)	
25	35 (25.0)
26-35	50 (35.7)
36+	55 (39.3)
Marital status	
Married	84 (60.0)
Not married	56 (40.0)
Educational status	
High school	27 (19.3)
Associate degree	31 (22.1)
License	56 (40.0)
Post-graduate	26 (18.6)
Service time in the institution (years)	
1-5	81 (57.9)
6-10	29 (20.7)
11-15	17 (12.1)
16 and above	13 (9.3)
Weekly working time (h)	
45 and below	81 (57.9)
46-50	42 (30.0)
51 and above	17 (12.1)
Night work status	
Yes	54 (38.6)
No	86 (61.4)

Table 4: Average standard deviation and levels of participants’ assessments regarding the employee empowerment and organizational stress scales

Variables	Score range	Mean±SD	Level
Employee empowerment	1-5	2.717±0.786	Moderate
Overall organizational stress	1-5	3.420±0.890	High
Stress regarding the duty structure	1-5	3.530±0.710	High
Stress regarding the authority structure	1-5	3.522±0.886	High
Stress regarding the production structure	1-5	3.599±0.863	High
Stress regarding the clustering structure	1-5	3.416±0.904	High
Stress regarding the role structure	1-5	3.079±1.118	Moderate
Stress regarding the cultural structure	1-5	2.923±1.026	Moderate

SD: Standard deviation

According to the findings, participants’ employee empowerment levels are at moderate level (2.717 ± 0.786), and their overall stress levels are high (3.420). When stress factors were analyzed by grouping under dimensions, it was seen that “sources of stress regarding the production structure” affected the participants at the most (3.599 ± 0.863), and “sources of stress regarding the cultural structure” affected them at the least (2.923 ± 1.026).

Comparison of participants’ assessments regarding the employee empowerment and organizational stress scales in terms of gender, marital status, and night work is given in Table 5. Only the sections which were observed to be statistically significant were included in Table 5. Accordingly, female were further affected by the sources of stress regarding the cultural structure; married employees were further affected by the sources of stress regarding the authority structure; unmarried employees were further affected by the sources of stress regarding the cultural structure, and those working in night shifts were further affected by the sources of stress regarding the production structure. Participants’ perceptions on employee empowerment did not show significant differences regarding the above-mentioned variables.

Table 5: Comparison of participants’ assessments regarding the employee empowerment and organizational stress scales in terms of gender, marital status, and night work

Stress scales	Mean±SD	t	P
Sources of stress regarding the cultural structure			
Gender		-3.796	0.000
Male	2.514±1.142		
Female	3.165±0.870		
Sources of stress regarding the authority structure			
Marital status		3.217	0.002
Married	3.713±0.874		
Not married	3.237±0.831		
Sources of stress regarding the cultural structure			
Marital status		-2.493	0.014
Married	2.750±1.028		
Not married	3.183±0.974		
Sources of stress regarding the production structure			
Night work status		2.008	0.047
Yes	3.782±0.757		
No	3.484±0.909		

SD: Standard deviation

Table 6: Comparison of participants' assessments regarding the employee empowerment and organizational stress scales in terms of profession and age

Stress scales	Mean±SD	F	P
Sources of stress regarding the cultural structure			
Profession		13.100	0.000
Doctor	2.115±0.770		
Other healthcare staff	3.199±0.924		
Administrative personnel	2.732±1.143		
Employee empowerment		5.976	0.003
Profession			
Doctor	3.203±0.523		
Other healthcare staff	2.606±0.751		
Administrative personnel	2.651±0.941		
Sources of stress regarding the cultural structure			
Age (years)		3.834	0.024
25 and below	3.293±0.967		
26-35	2.680±1.088		
36 and above	2.909±0.949		

SD: Standard deviation

Table 7: Comparison of participants' assessments regarding the employee empowerment and organizational stress scales in terms of educational status and seniority

Stress scales	Mean±SD	F	P
Sources of stress regarding the cultural structure			
Educational status		4.885	0.003
High school	3.056±0.974		
Associate degree	3.024±1.135		
License	3.112±0.966		
Post-graduate	2.260±0.832		
Employee empowerment		6.535	0.000
Educational status			
High school	2.653±0.761		
Associate degree	2.815±0.891		
License	2.459±0.695		
Post-graduate	3.224±0.618		
Sources of stress regarding the cultural structure			
Service time in the institution (years)		3.698	0.013
1-5	3.437±0.852		
6-10	3.776±0.889		
11-15	3.125±0.931		
16 and above	4.010±0.754		

SD: Standard deviation

Comparison of participants' assessments regarding the employee empowerment and organizational stress scales in terms of profession and age appears in Table 6. Only the sections which were observed to be statistically significant were included in Table 6. Accordingly, other healthcare staff and employees who were aged below 26 were further affected by the sources of stress regarding the cultural structure. In addition, doctors' empowerment perceptions were higher than other employees.

Table 8: Correlation analysis results regarding the employee empowerment and organizational stress relationship

Organizational stress	Employee empowerment	
	r	P
Sources of stress regarding the duty structure	-0.276	0.001
Sources of stress regarding the authority structure	-0.331	0.000
Sources of stress regarding the production structure	-0.230	0.006
Sources of stress regarding the clustering structure	-0.196	0.020
Sources of stress regarding the role structure	-0.122	0.152
Sources of stress regarding the cultural structure	-0.406	0.000

Comparison of participants' assessments regarding the employee empowerment and organizational stress scales in terms of educational status and seniority is presented in Table 7. Only the sections which were observed to be statistically significant were included in Table 7. Accordingly, employees with license degree were further affected by the sources of stress regarding the cultural structure, and employees with 16 years and above service time were further affected by sources of stress regarding the authority structure. In addition, empowerment perceptions of employees with license degree were higher than other employees.

Correlation analysis was performed to examine the relationship between the dimensions of organizational stress and the employee empowerment (Table 8). According to analysis results, there was a negative and low relationship between employee empowerment and sources of stress regarding the duty structure ($r = -0.276$), sources of stress regarding the production structure ($r = -0.230$), and sources of stress regarding the clustering structure ($r = -0.196$). There was a negative and moderate relationship between employee empowerment and sources of stress regarding the authority structure ($r = -0.331$) and sources of stress regarding the cultural structure ($r = -0.406$).

DISCUSSION

This research was carried out to examine the relationship between employee empowerment and organizational stress with the perspective of hospital employees. A questionnaire was applied to 140 staff working in a public hospital in Turkey to accomplish this aim. Scales used were rated between 1 and 5.

According to the findings, participants' overall perceptions regarding the employee empowerment were moderate (2.717 ± 0.786). When the literature was analyzed, it was seen that employee empowerment perceptions of

employees working in hospitals in Turkey were generally at moderate-high level. In this regard, employee empowerment levels were found to be higher in the study carried out in a private hospital in Turkey by Ekiyor and Karagül,²⁵ and in another study carried out in 11 state hospitals in Turkey by Altındış and Özutku.²⁶ In the study carried out in a research and application hospital by Adıgüzel and Altıparmak,²⁷ it was determined that the personnel had empowerment perceptions at moderate level. Similar results were also achieved in various studies conducted in different countries from Turkey.²⁸⁻³⁰

As a result of the research, overall stress point average was found to be 3.420. This result shows that employees' overall stress levels are high. When stress factors were analyzed by grouping under dimensions, it was seen that "sources of stress regarding the production structure" affected the participants at the most (3.599 ± 0.863), and "sources of stress regarding the cultural structure" affected them at the least (2.923 ± 1.026). When studies carried out at hospitals on stress were analyzed, it was seen that stress levels of health care staff were moderate/high. In this regard, parallel results were achieved in the study carried out at 4 hospitals by Özen,³¹ in the study carried out at dental hospital by Kıdak³² and in another study carried out at a training and research hospital by Tekingündüz *et al.*³³

As a result of the correlation analysis performed, negative and significant relationships were found between employee empowerment and sources of stress regarding the duty structure, sources of stress regarding the authority structure, sources of stress regarding the production structure, sources of stress regarding the clustering structure, and sources of stress regarding the cultural structure. Furthermore, various studies carried out in health institutions³⁴⁻³⁷ confirmed that there was a negative and significant relationship between employee empowerment and organizational stress. This situation shows that the results of the present study are consistent with the literature.

CONCLUSION

It can be said that employee empowerment and organizational stress are important concepts affecting the working life. The fact that employees do not have enough components of employee empowerment increases their stress levels. It is a known fact that the increasing stress level has negative impacts on both employees and the organization. Therefore, administrators should be aware of both concepts and try to create the necessary conditions strengthen their employees.

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Targeting Emmetropia in a Pseudophakic Eye: A Prospective Study

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Abstract

Introduction: There are numerous techniques for dealing with astigmatism both during and after cataract surgery. Good uncorrected post-operative distance visual acuity can be obtained for a high percentage of cataract patients with pre-existing corneal astigmatism.

Purpose: To achieve emmetropia in patients undergoing cataract surgery by eliminating corneal astigmatism.

Materials and Methods: A total of 180 patients presenting with cataract underwent phacoemulsification surgery with intraocular lens (IOL) implantation, with procedures like clear corneal incision (neutral astigmatism), incision on steep axis (≤ 0.75 D), limbal relaxing incision (LRI) ($0.75 - \leq 1.50$ D), opposite clear corneal incision (OCCI) ($1.50 - \leq 2.50$ D), foldable toric posterior chamber IOL (PCIOL), and astigmatic keratotomy (AK) (≥ 2.50 D) in their eye, targeting emmetropia.

Results: A total of 30 eyes underwent phacoemulsification cataract surgery with clear corneal temporal incision achieved mean residual astigmatism of 0.24 D and standard deviation (SD) of 0.22. About 30 eyes with an incision on steep axis had mean residual astigmatism of 0.18 D and SD was 0.21. Around 30 eyes with LRI procedure with cataract surgery, mean residual astigmatism was 0.18 D and SD achieved was 0.21 with $P < 0.05$. 30 eyes with OCCI and phacoemulsification with clear corneal temporal incision achieved mean residual astigmatism of 0.37 D and SD of 0.27 with $P < 0.05$. 30 eyes which underwent foldable toric PCIOL procedure had mean residual astigmatism of 0.71 D and SD was 0.12 with $P < 0.05$. 30 eyes which were subjected to AK procedure had mean residual astigmatism of 0.41 D and SD of 0.38 with $P = 0.02$.

Conclusions: If right modality to tackle pre-operative astigmatism along with cataract is considered, the patient can be given 20/20 vision and can enjoy life with no dependence on spectacles and also patient may not require another refractive surgery to tackle the residual astigmatism.

Key words: Clear corneal incision, Foldable toric posterior chamber intraocular lens and astigmatic keratotomy, Incision on steep axis, Limbal relaxing incision, Opposite clear corneal incision, Phacoemulsification

INTRODUCTION

Naturally occurring (idiopathic) astigmatism is frequent with up to 95% of eyes having detectable astigmatism. It is estimated that approximately 70% of the general cataract population has at least 1.00 D of astigmatism, and

approximately 33% of patients undergoing cataract surgery are eligible for the treatment of pre-existing astigmatism.^{1,2}

Today, cataract surgery is regarded as a refractive surgery, aiming pseudophakic emmetropia, which makes eliminating corneal astigmatism critical.³⁻⁵ Ferrer-Blasco *et al.*, studied the prevalence of corneal astigmatism before cataract surgery and found that; in 13.2% of eyes no corneal astigmatism was present; in 64.4%, corneal astigmatism was between 0.25 and 1.25 diopters (D) and in 22.2%, it was 1.50 D or higher.⁶

When planning a surgery, both the spherical and the astigmatic components should be taken into account to

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achieve post-operative outcomes as close to emmetropia as possible. Due to new developments in phaco tips, changes in operation techniques and the use of small incisions in cataract surgery which reduce the operation-induced astigmatism or make an inconsiderable change in the existing corneal astigmatism, the general aim of cataract surgery has gone from simple cataract extraction to ensuring the best visual acuity and quality without spectacle dependence.

The most important and critical step in treating the astigmatism is to find out the exact source, magnitude and axis of astigmatism and making the decision about which technique is appropriate for that patient. The cylindrical component is evaluated by automated and/or manifest refraction, placido ring reflections, keratometry and/or corneal topography primarily, but other factors need to be taken into account, such as age of the patient and the corneal characteristics of both eyes. To quantify the discrepancy between corneal and refractive astigmatism measurements, the corneal astigmatism value measured by topography or keratometry is subtracted from the refractive cylinder measured by wave front or manifest refraction and the vectorial difference is known as the ocular residual astigmatism, which is expressed in diopters.⁷⁻⁹ Corneal topography provides a qualitative and quantitative image map based on an evaluation of the corneal curvature, also measure the power and astigmatism of the posterior corneal surface, which may improve the correlation.

With the refractive astigmatism,^{10,11} Lucciola reported the first cases of non-penetrating corneal incisions, in 1886, where he also attempted to reduce astigmatism by flattening the steep corneal meridian in ten patients.¹²

Lans first appreciated that the flattening that occurs in a corneal meridian after placing a transverse incision was associated with steepening in the opposite meridian. He also demonstrated that the deeper and the longer incisions had more effect.¹³

In the 1940s, Sato began his work on radial and astigmatic keratotomy (AK).¹⁴

Nordan proposed a relatively simple method of straight transverse keratotomy, with target corrections in the range on 1-4 diopters.¹⁵

Consequently, Troutman and Swinger also discussed the benefits of corneal relaxing incisions to decrease residual astigmatism.¹⁶

Thornton's technique involved making paired arcuate incisions placed at the 7.0 mm and 8.0 mm optical zones,

following a curve on the cornea, while Chavez *et al.*, recommended optical zone sizes as small as 5.0 mm.^{17,18}

Nichamin developed an extensive nomogram for AK at the time of cataract surgery; "Intralimbal relaxing incision nomogram for modern phaco surgery," which has age adjustments for correction of against-the-rule astigmatism and with-the-rule astigmatism. It utilizes an empiric blade depth setting of 600 μm .¹⁹⁻²²

Corneal astigmatism occurs due to unequal curvature along the two principal meridians of the anterior cornea and internal astigmatism due to factors such as the toricity of the posterior surface of the cornea, unequal curvatures of the front and back surfaces of the crystalline lens, or tilting of the crystalline lens with respect to the optic axis of the cornea. The aim of this study was to achieve neutral astigmatism in a pseudophakic eye and optimizing them for a different degree of astigmatism and to study the effect of different modalities used for correcting astigmatism in our study and rating them in their order of effectiveness.

MATERIALS AND METHODS

This was a general free hospital-based prospective study (Table 1). About 180 patients were included in this study. All patients visiting the outpatients' clinic and indoor patients diagnosed with cataract during the course of investigations were recruited after a due informed written consent in this study (Table 2). Pre-determined inclusion and exclusion criteria (as described below) were applied to all patients before a patient was accepted into the study to get 180 completed patients after an attrition rate of 10%. The study was started from May 2012 and was completed by May 2014. Recruitment phase was 2 year's follow-up phase 6 weeks post-operative for every patient (Figure 1).

Pre-operative cataract evaluation included: Cycloplegic refraction to rule out lenticular and corneal astigmatism (Figure 2). Corneal astigmatism by manual keratometry and corneal topography, the latter also ruled out conditions such as keratoconus and peripheral corneal degenerations. Pachymetry was done preoperatively. In the case of limbal relaxing incision (LRI) just inside the limbus, and at 7 mm optical zone for AK. A scan was done by SRKT formula for intraocular lens (IOL) power. IOP was measured in all cases by applanation tonometer. Slit lamp examination for cataract grading and funduscopy to r/o retinal pathology. Written informed (W/I) consent of the patient taken before recruitment into the study.

Inclusion Criteria

1. All patients with established cataract on V/A of <6/18 and S/L changes

Table 1: Gender distribution

Type of incision	Male	Female
	Count (%)	Count (%)
Clear corneal temporal incision with neutral axis	15 (50)	15 (50)
Incision on steep axis	11 (36.67)	19 (63.33)
Temporal incision with LRI	9 (30)	21 (70)
Incision on steep axis with OCCI	12 (40)	18 (60)
Clear corneal temporal with toric lens	13 (43.33)	17 (56.67)
Incision on steep with AK	10 (33.33)	20 (66.67)

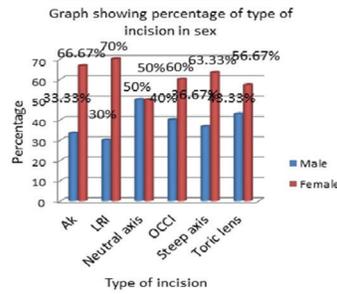


Table 2: Type of incision with respect to eye

Type of incision	Left eye	Right eye
	Count (%)	Count (%)
Clear corneal temporal incision with neutral axis	13 (43.33)	17 (56.67)
Incision on steep axis	12 (40)	18 (60)
Temporal incision with LRI	14 (46.66)	16 (53.33)
Incision on steep axis with OCCI	15 (50)	15 (50)
Clear corneal temporal with toric lens	13 (43.33)	17 (56.66)
Incision on steep with AK	20 (66.67)	10 (33.33)

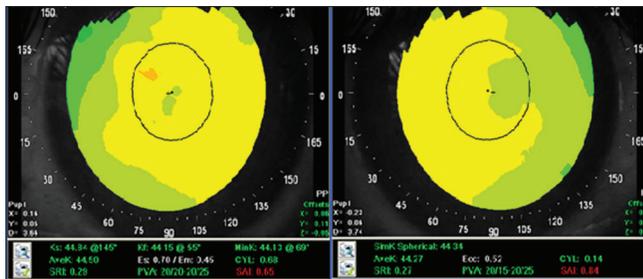
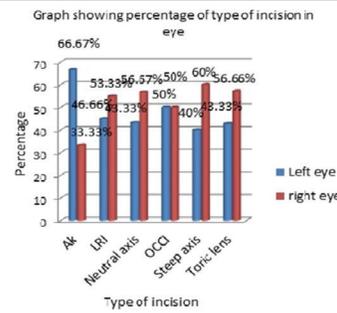


Figure 1: Clear corneal incision on the steep axis pre-operative and post-operative topography

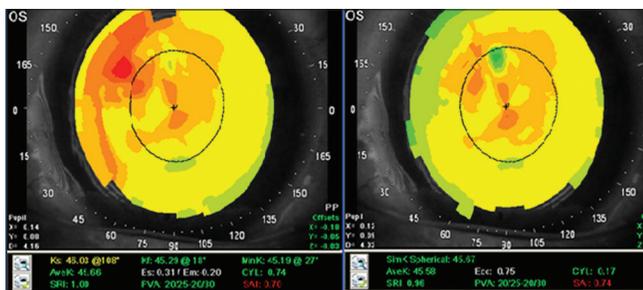


Figure 2: Clear corneal incision on the steep axis (superior incision). This is reflected in the incision on the steep axis (superior incision) where approx 0.6 D is getting corrected to give an astigmatic neutral incision

2. Age >18 years were chosen as FDA guidelines for corneal refractive surgery comments an age of at least

- 18 years
3. Sex - No criteria
4. Pre-operative astigmatism of nil to ≤ 6 diopters
5. Patent sac
6. No dry eye which could hamper wound healing and no retinal disease hampering V/A improvement
7. IOP: 14-19 mm Hg with C/D ratio < 0.5
8. Grade of cataract: $< \text{grade } 3$
9. Systemic diseases controlled.

Exclusion Criteria

1. Non-complaint patient
2. Systemic diseases such as hypertension, diabetes mellitus, collagen vascular disease
3. Cataract like Grade 4 or 5 brown cataract (high phaco power needed may cause wound burn), subluxated cataract, pseudoexfoliated cataract, congenital cataract
4. Cornea: Keratoconus and central corneal thickness of $< 500 \mu$ with a corresponding weak peripheral corneal thickness.

Methodology

Incision chart is stuck on the OT Wall to guide the operating surgeon. It has the eye marked with the steep meridian, along with the corneal topography photograph. W/I consent is taken from the patient before the initiation of surgery, peribulbar anesthesia given (however topical anesthesia was preferred before LRI and AK procedure), parts painted and draped, eye exposed with wire eye speculum (Figure 6). The incision was taken according to the keratometry and corneal topographic values of that particular eye (Figures 7,8).

- a. Clear corneal temporal incision was used in cases with neutral astigmatism. A 2.8 mm keratometer was used and a triplanar clear corneal entry is made.
- b. Incision on steep axis was used in cases with astigmatism of < 0.75 D (Figure 9). A 2.8 mm keratome was used and a triplanar entry is made on the steep axis, and the surgery is performed from that incision (Figure 10).
- c. LRI was used in cases with astigmatism of 0.75 D to 1.5 D according to keratometric, corneal topographic, and pachymetric values. LRI was made according to the Gills and Nichamin nomogram depending on the degree of astigmatism. Axis marking was done preoperatively on the slit lamp. The proper incision depth for LRIs was approximately 90% of the thinnest corneal depth around the limbus (Figure 3).²³ The cutting depth of the empiric blade was normally set to 550-600 μm (Figure 11). LRI was done before phacoemulsification procedure on topical anesthesia. The Clear corneal incision was made and a triplanar entry with a 2.8 mm keratome is done. Whole of the surgery was done from the temporal incision.

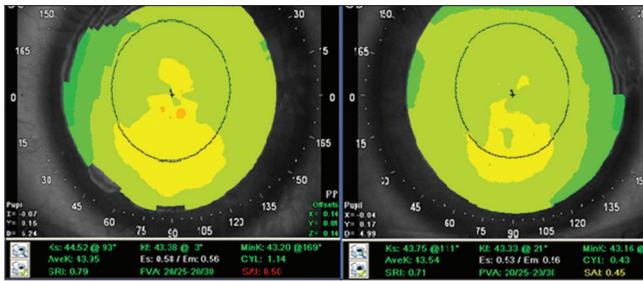


Figure 3: Temporal 3 mm clear corneal incision with limbal relaxing incision at 6 o'clock position. Correction achieved is approx 0.75 D (A11)

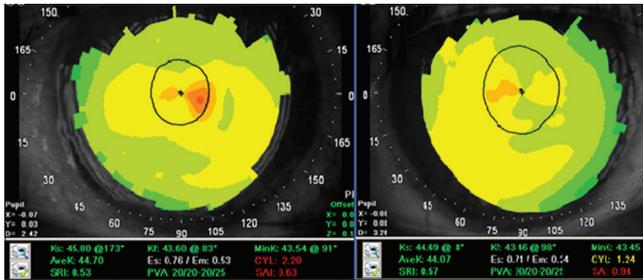


Figure 4: Astigmatism was >2 but <2.4 so a clear corneal temporal incision done and diagonally opposite clear corneal incision done at the end of the surgery. The correction achieved was 0.96

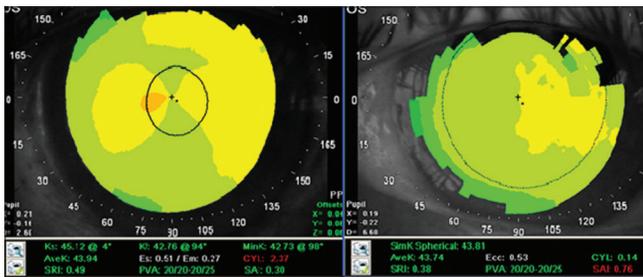


Figure 5: Temporal clear corneal incision with an AK in the superior and inferior quadrant 7 mm from the optical center, Arcuate in nature and 1 clock h in dimension. Correction achieved was approx 2.2 D

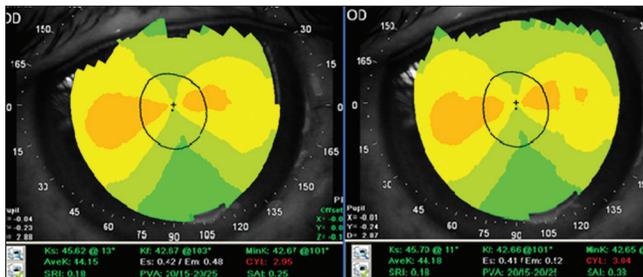


Figure 6: Pre-operative and post-operative corneal topography remains almost same yet patient is 20/20 as astigmatism is internally compensated by the toric IOL

d. Opposite clear corneal incision (OCCI) was used in cases with astigmatism of 1.5 D to 2.5 D according to corneal topographic, keratometric and pachymetric



Figure 7: Reference marking at 0° and 180° and reference marking for axis of placement



Figure 8: Reference marking on axis in upright position to avoid cyclotorsion

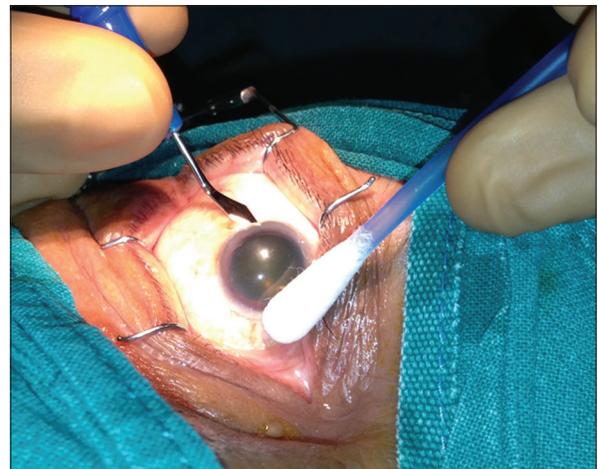


Figure 9: Clear corneal temporal incision

values (Table 5). Incision was made on the steep axis and triplanar entry with 2.8 mm keratome was made and surgery was performed from the same entry. Before insertion of the lens a similar OCCI was made (i.e., opposite to the main incision) and entry in the cornea was done with a 2.8 mm keratome. No instrumentation or surgical procedure was done from this entry.

e. Foldable toric posterior chamber IOL (PCIOL) are put in cases with astigmatism of more than 2.5 D (Figure 5). Pre-operative corneal reference marking was done on the slit lamp with patient sitting in the upright position to avoid cyclotorsion (Figure 12). On table, the desired axis was marked. Toric lens was inserted and positioned 10° degrees before the desired axis marking. Viscoelastic substance (VES) was aspirated out which

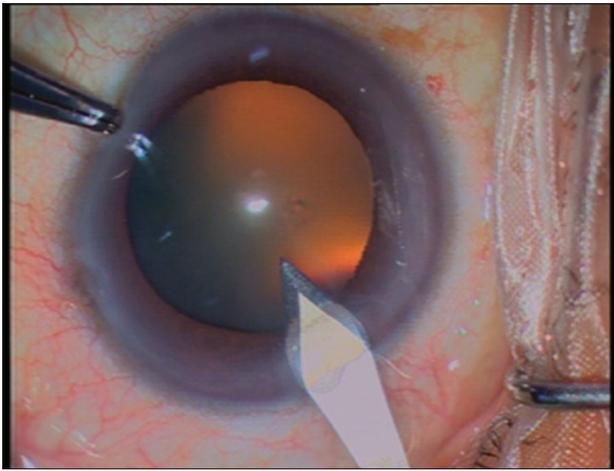


Figure 10: Incision on steep axis

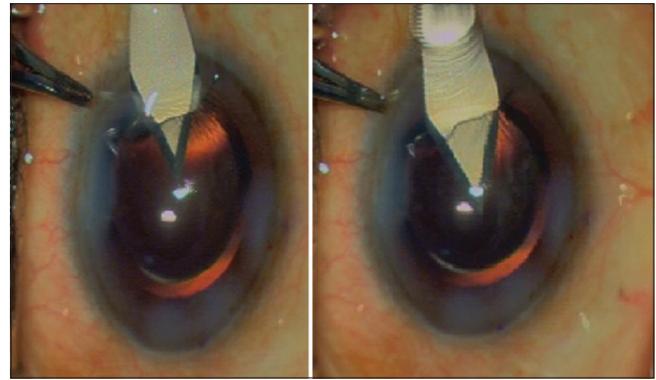


Figure 12: Opposite clear corneal incision

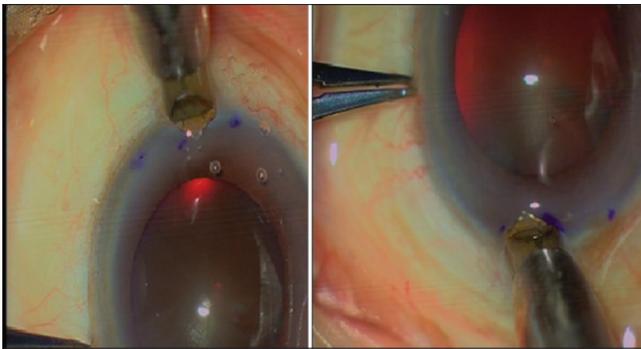


Figure 11: Limbal relaxing incision

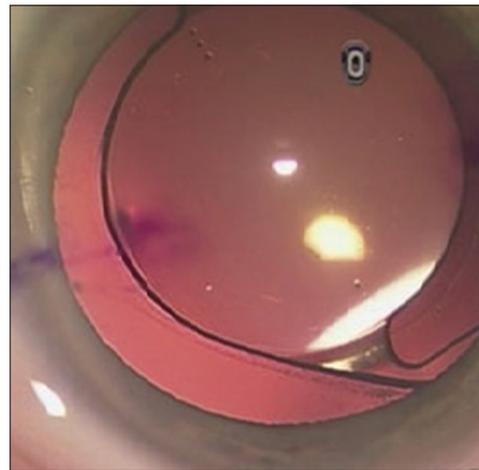


Figure 13: Toric lens insertion on axis

caused certain degree to clockwise forward rotation of the lens and the remaining rotation till the desired axis was done manually with the help of a dialler.

- f. AK was an alternative cheaper option in patients with astigmatism of more than 2.5 D (Figure 13). Axis marking was done preoperatively on the slit lamp. Before starting of the surgery preferably under topical anesthesia, single or paired arcuate incision on the cornea was made depending on nomogram and degree of astigmatism.

Surgery was performed by making clear corneal temporal incision with a 2.8 mm keratome and the whole procedure was done from this entry (Figure 6). Side port made at 90° from main incision, VES injected in anterior chamber, capsulorhexis done with no. 26 bent needle/cystitome. Hydrodissection done, phaco 1 used and trenching done, nucleus divided into 2, phaco 2 used and nucleus emulsified by stop and chop method, cortex I/A done, polishing of posterior capsule done, VES injected, foldable hydrophilic PCIOL inserted in the bag or a foldable Toric PCIOL at the desired axis, air bubble injected. Stromal hydration of all parts and main wound done with 0.1% intracameral moxifloxacin, e/d septidine, e/d predmet and e/oint chlorappticap put, eye patching done.

RESULTS

About 30 eyes underwent phacoemulsification cataract surgery with clear corneal temporal incision that had no pre-operative astigmatism. As shown in Table 1, We achieved mean residual astigmatism of 0.24 D and standard deviation (SD) of 0.22.

Whereas studies conducted by Ozkut, Nikola Susic and Mohammad Pakravan^{24,25} achieved mean residual astigmatism of 0.88 D, 1.06 D, 0.73 D, respectively, and their SD achieved was 0.82, 0.83 and 0.46, respectively, in their studies has been shown in Table 1. We had chosen eyes with neutral astigmatism for this procedure.

Around 30 eyes underwent cataract surgery with incision on steep axis who had pre-operative astigmatism of ≤ 0.75 D. In our study, mean residual astigmatism was 0.18 D and SD was 0.21 as shown in Table 2. This study conducted by Gonçalves and Rodrigues²⁶ had mean residual astigmatism of 0.89 D and SD of 0.80.

30 eyes which underwent LRI procedure with phacoemulsification by clear corneal incision had

astigmatism between 0.75 and 1.50 D in our study. The mean residual astigmatism was 0.18 D and SD achieved was 0.21 with $P < 0.05$ in our study. In a similar study conducted by Carvalho *et al.*, and Bayramlar *et al.*,^{27,28} they achieved a mean residual astigmatism of 1.02 D and 1.59 D respectively with the SD of 0.6 and 1.28 with a $P < 0.05$ and <0.001 , respectively, as been shown in Table 3.

We preferred with patients with astigmatism of 1.50 D-2.50 D to undergo OCCI procedure as the previous studies conducted had suggested a good result with this procedure with above astigmatism.

30 eyes which were subjected to OCCI with phacoemulsification with clear corneal temporal incision achieved mean residual astigmatism of 0.37 D and SD of 0.27 with $P < 0.05$ (Table 8).

As been documented in Table 4, studies conducted by Khokhar *et al.*, Bazzazi *et al.*, and Qammar and Mullaney²⁹⁻³² mean residual astigmatism documented was 0.91 D, 1.19 D, 2.02 D and SD was 0.54, 0.64 and 1.04, respectively (Table 7).

Table 3: Age distribution

Age	Type of Incision					
	Neutral axis	Steep axis	LRI	OCCI	Toric lens	AK
	Count (%)	Count (%)	Count (%)	Count (%)	Count (%)	Count (%)
26-40	2 (6.67)	2 (6.67)	4 (13.33)	0 (0)	0 (0)	0 (0)
41-55	9 (30)	7 (23.33)	6 (20)	14 (40)	5 (16.66)	10 (33.33)
55-75	18 (60)	21 (70)	20 (66.66)	16 (60)	25 (83.33)	10 (33.33)
>75	1 (3.33)	0 (0)	0 (0)	0 (0)	0 (0)	10 (33.33)

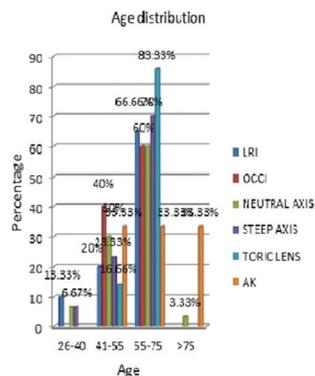
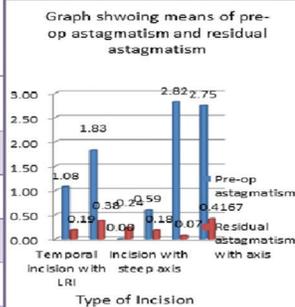


Table 4: Comparison of pre-operative astigmatism and residual astigmatism with axis

Type of Incision	Pre-op astigmatism		Residual astigmatism with axis		t-value	P-value
	Mean	Std	Mean	Std		
Clear corneal temporal incision with neutral axis	0.00	0.00	0.24	0.222	5.95	<0.05
Incision with steep axis	0.59	0.17	0.38	0.217	7.52	<0.05
Temporal incision with LRI	1.0	0.21	0.18	0.212	11.38	<0.05
Incision on steep axis with OCCI	1.8	0.26	0.37	0.270	17.75	<0.05
Temporal incision with toric lens	2.8	0.23	0.71	0.121	22.54	<0.05
Incision on steep axis AK	2.7	0.25	0.41	0.381	7.00	<0.05



Foldable toric IOL are a better modality than AK procedure; we performed AK on 30 patients and 30 patients underwent clear corneal temporal incision with toric lens implantation on desired axis. AK is a cheap and easy procedure to perform as compared to foldable toric PCIOL which cost more, but we preferred toric lenses over AK on the basis of better outcome, lesser pain, reliability, and safety.

30 eyes which underwent foldable toric PCIOL procedure had mean residual astigmatism of 0.71 D and SD was 0.12 with $P < 0.05$. Mendicute *et al.*,^{33,34} in their study had mean residual astigmatism of 0.62 D and SD of 0.46 with $P < 0.01$, as shown in Table 9.

30 eyes which were subjected to AK procedure had mean residual astigmatism of 0.41 D and SD of 0.38 with $P = 0.02$. Titiyal *et al.*,^{35,36} in their study had got mean residual astigmatism of 1.26 D and SD of 0.54 with $P = 0.067$, as shown in Table 10.

DISCUSSION

There are numerous techniques for dealing with astigmatism both during and after cataract surgery. Good uncorrected postoperative distance visual acuity can be obtained for a high percentage of cataract patients with pre-existing corneal astigmatism. Corneal astigmatism can be treated effectively at the time of cataract surgery with either

Table 5: Comparison of clear corneal temporal incision with other studies

Study comparison	Pre-op astigmatism		Residual astigmatism with axis		P-value
	Mean	Std	Mean	Std	
Our Study	0	0	0.24	0.224	<0.05
Yelda Ozkut, Gurkan Erdogan	0.74	0.45	0.88	0.82	
Borasio E, Mehta JS	0.78	0.51	0.74	0.68	
Nikola susic, Jasevka Brajkovic	0.72	0.57	1.06	0.83	
Mohammad pakavan, atom ayoun	0.63	0.48	0.73	0.46	<0.001

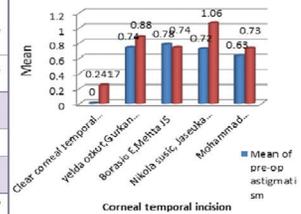


Table 6: Comparison of incision on the steep axis

Our Study	Pre-op astigmatism		Residual astigmatism with axis		p-value
	Mean	Std	Mean	Std	
Incision with steep axis	0.5917	0.1796	0.1833	0.21709	<0.05
Goncalves FP, Rodrigues AC	1.06	0.65	0.89	0.8	

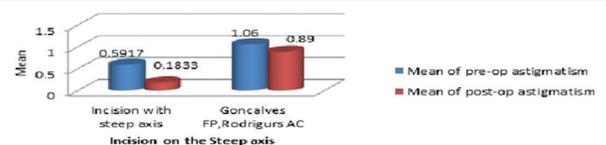


Table 7: Comparison of limbal relaxing incision on steep meridian with temporal clear corneal incision

	Pre op astigmatism		Residual astigmatism with axis		p-value
	Mean	Std	Mean	Std	
Our Study					
Temporal incision with LRI	1.075	0.21613	0.1875	0.21267	<0.05
Carvalho MJ,Suzuki SH	1.93	0.58	1.02	0.6	<0.05
Rayamlar,Borazan M	3.31	1.5	1.59	1.28	<0.001

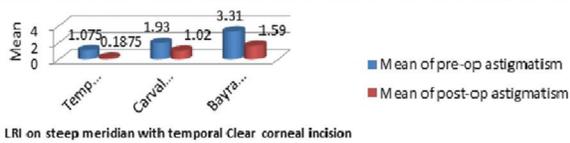
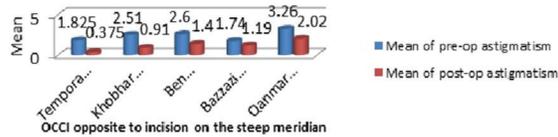


Table 8: Comparison of opposite clear corneal incision opposite to incision on the steep meridian

	Pre-op astigmatism		Residual astigmatism with axis		p-value
	Mean	Std	Mean	Std	
Temporal incision with OCCI					
Temporal incision with OCCI	1.825	0.26484	0.375	0.27003	<0.05
Khobhar S,Lohiya P	2.51	0.92	0.91	0.51	
Ben simon GJ,Desatnik H	2.6		1.4	-	
Bazzazi N. Barazandeh B	1.74	0.86	1.19	0.64	0.009
Qanbar A, Mullaney	3.26	1.03	2.02	1.04	



foldable toric PCIOLs, corneal or LRI or OCCI or AK or combination of all. There are advantages and disadvantages to each method. The appropriate patient-based plan of either one or a combination of these different surgical techniques can provide a greater ability to correct cylindrical errors intra-operatively, achieving improved visual acuity, and visual quality independent of spectacles. Many studies have demonstrated that temporal incision induces least astigmatism, the value of 0.28 D to 0.50 D post-operative,^{37,38} probably be due to the fact that the temporal limbus is farther from the visual axis than the superior limbus.²⁴ It is effective to create a clear corneal incision at the steep corneal axis, whether superiorly, temporally, or obliquely, to profit the flattening effect of the incision which can help to reduce astigmatism along that axis. This approach is usually sufficient for most of the eyes.^{39,25,26}

CONCLUSION

It should be kept in mind that postoperative keratorefractive surgery may also be available to enhance the condition of

Table 9: Comparison of toric intraocular lens

	Pre-op astigmatism		Residual astigmatism with axis		p-value
	Mean	Std	Mean	Std	
Incision with Toric lens					
Incision with Toric lens	2.8214	0.23780	0.0714	0.12199	<0.05
Mendicute ,Migoyen,Ruiz	-1.75	0.71	-0.62	0.46	<0.01
Mendicute ,Migoyen	-2.34	1.28	-0.72	0.43	<0.01

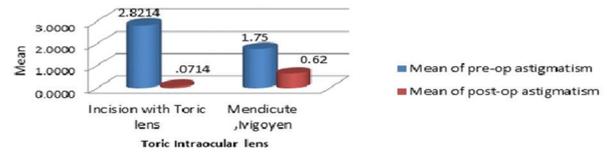
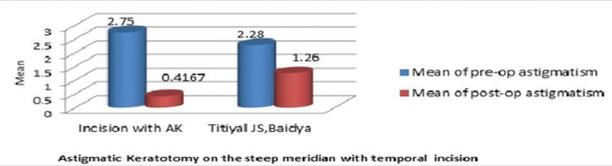


Table 10: Comparison of astigmatic keratotomy on the steep meridian with temporal incision

	Pre-op astigmatism		Residual astigmatism with axis		p-value
	Mean	Std	Mean	Std	
Incision with AK					
Incision with AK	2.75	0.25	0.4167	0.38188	0.02
Titiyal JS,Baidya	2.28	0.89	1.26	0.54	0.067
Kulkarni A, Matafatsi A	2.88		1.89		



patients who achieve less-than-optimal astigmatic results. A small 2.8 mm corneal incision in phacoemulsification induces on average very small corneal refractive change, but differences were detected depending on the location of the incision.

SIA of the operating surgeon in our study was 0.30 D.

In our study, we compared our results to other studies which were done in the past which used similar modalities to tackle pre-operative astigmatism during cataract surgery.

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Comparative Study of Role of Fentanyl and Dexmedetomidine as an Adjuvant to Bupivacaine in Controlling Post-operative Pain

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Abstract

Background: Neural anesthesia is becoming popular because of its ease of practice and multiple advantages. The addition of adjuvants such as fentanyl and dexmedetomidine to drugs like bupivacaine can improve the outcome. However, lack of knowledge limits its acceptance. Various amendments have been done in the technique to curtail the undesirable events and increase the efficiency in a precise direction.

Aim: The aim of the present study was to compare the effect of intrathecal fentanyl and dexmedetomidine as an adjuvant to hyperbaric bupivacaine in the patients admitted for lower abdominal surgeries.

Materials and Methods: The observational study was conducted in the Department of Anesthesiology at Teerthanker Mahaveer Medical College, Moradabad from August 2015 to January 2016. The patients were randomized and divided into two groups each containing 50 members. In Group 1, 2.5 mL of 0.5% hyperbaric bupivacaine was given along with 25 g fentanyl intrathecally. In Group 2, 5 g dexmedetomidine was added to 2.5 mL of 0.5% hyperbaric bupivacaine and given intrathecally. Onset of sensory and motor blockade, duration of analgesia and side effects were noted in both groups.

Results: The combination of dexmedetomidine (5 g) and 0.5% bupivacaine, prolongs the duration of analgesia, decreases total analgesic dose necessity in first 24 h post-operative with unwavering hemodynamic parameters and is also not associated with side effects like pruritus as observed in fentanyl group, hence can be an attractive alternative for being used as the adjuvant to bupivacaine in controlling post-operative pain.

Conclusion: The good post-operative analgesia is to produce a long lasting, continuous effective analgesia with minimum side effects. These requirements are fulfilled by the dexmedetomidine better as compared to fentanyl.

Key words: Adjuvant, Analgesia, Bupivacaine, Dexmedetomidine, Fentanyl

INTRODUCTION

Neural anesthesia is nowadays becoming popular because of its ease of practice and multiple advantages. However, the high failure rate of block, other side effects and lack of knowledge limits its acceptance. Various

amendments have been done in the technique to curtail the undesirable events and increase the efficiency in a precise direction.¹ The addition of adjuvants such as fentanyl and dexmedetomidine to drugs like bupivacaine is one of the alterations, which can improve the outcome.²

The blockage of opioid receptors in the spinal cord plays an important role in improving perioperative analgesia. Along with this, the identification of these receptors has also reduced the other supraspinal side effects of systemic steroids such as sedation and respiratory depression.²

The opioids which have a rapid mode of onset, slow and steady clearance from cerebrospinal fluid and decreased the

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risk of delayed side effects such as respiratory depression are preferred. Thus lipophilic opioids are more ideal to be used intrathecally as compared to morphine.³ Various studies^{2,4,5} suggest that when the anesthetic drugs such as lidocaine or bupivacaine are given along with the adjuvant fentanyl (15-25 mcg), the drastic improvement is seen in the quality of intra as well as post-operative blocks. However, some studies^{1,3} suggest that although fentanyl is one of the most beneficial spinal anesthesia adjuvants, but it is associated with certain side effects such as nausea, pruritus, and retention of urine.

In recent literature,⁶ some other drugs such as clonidine and alpha-2 agonist-like dexmedetomidine are becoming popular as adjuvants for spinal anesthesia. These drugs have good sedative, analgesic, and hemodynamic stabilizing property with fewer side effects. They are being used in veterinary anesthesia for several years. Recent literature^{5,7} suggests that dexmedetomidine is more specific alpha-2 adrenoceptor agonist with almost eight times more empathy for alpha-2 adrenoceptor as compared to clonidine. Dexmedetomidine has 1:1620 ratio for alpha-2 receptor binding selectivity as paralleled to 1:220 for clonidine. Besides this, this drug also provides good quality intra and post-operative analgesia, stable hemodynamic parameters and nominal side effects. So, this drug can also be considered as adjuvant in spinal anesthesia in humans.

The aim of the present study was to compare the effect of intrathecal fentanyl and dexmedetomidine as the adjuvant to hyperbaric bupivacaine in the patients admitted for lower abdominal surgeries. The important parameters such as the onset of sensory blockade, duration of analgesic effect, dose requirement in first 24 h after surgery, and various side effects of the drug will help in comparing the two drugs.

MATERIALS AND METHODS

It is an observational study which is randomized and prospective. The study was conducted in the Department of Anesthesiology at Teerthanker Mahaveer Medical College, Moradabad from August 2015 to January 2016. The written consent was taken from all the patients, and the study was passed through the Ethical Committee. The sample size was 100 including males and females which were admitted for elective lower abdominal surgeries under spinal anesthesia. The age group ranged from 20 to 50 years. The patients of body weight more than 100 kg, height <140 cm, having any cardiac or respiratory abnormalities, taking medications such as alpha 2 receptor antagonists, calcium channel

blocker, and angiotensin converting enzyme inhibitors, allergic to drug, having psychiatric illness or neurological disorder were excluded from the study. The patients were randomized and divided into two groups each containing 50 members. In Group 1 ($n = 50$), 2.5 mL of 0.5% hyperbaric bupivacaine was given along with 25 µg fentanyl intrathecally. In Group 2 ($n = 50$), 5 µg dexmedetomidine (dexmedetomidine 100 µg/mL was diluted in 10 ml of normal saline) was added to 2.5 mL of 0.5% hyperbaric bupivacaine and given intrathecally. Pre-anesthetic check-up of the patients was done to assess respiratory tract and spine. Other investigations such as complete hemogram, blood grouping, urine microscopy, blood urea, creatinine, electrocardiogram (ECG), and chest X-ray were done.

In the pre-operative preparation, the patient was kept nil per orally for 6 h before surgery. Tablet alprazolam 0.5 mg and tablet ranitidine 150 mg were given in night before surgery. 500 ml of Ringer lactate solution was preloaded intravenously half an hour before the surgery. Preoperatively, all the vitals were recorded.

Proper sterilization was maintained. The patient in lateral decubitus was positioned, and the skin was cleaned with the help of iodine, spirit and was draped properly. A 25 G Quincke spinal needle was introduced into the L2-L3 or L3-L4 intervertebral space until it enters the subarachnoid space which is confirmed by the dripping of cerebrospinal fluid. 2.5 ml of 0.5% hyperbaric bupivacaine with 0.5 ml (25 µg) of fentanyl or 2.5 ml of 0.5% hyperbaric bupivacaine with 0.5 ml (5 µg) of dexmedetomidine was injected in Groups 1 and 2, respectively, at the rate of 0.25 ml/s. The patient was turned supine after withdrawing the needle. 100% oxygen via face mask (at the rate of 4 L/min) was administered.

Hemodynamic checking was done by measuring various parameters such as heart rate (HR), systolic blood pressure (SBP) diastolic blood pressure, mean arterial pressure (MAP), ECG and SpO₂ intraoperatively and postoperatively.

Hypotension

The decrease in SBP more than 30% of baseline is defined as hypotension. The treatment includes giving intravenous fluids and if required injection mephentermine 6 mg.⁸

Bradycardia

The decrease in HR to 60/min is called as bradycardia. Injection atropine 0.6 mg IV is given to treat it.⁸

The following parameters were measured:

- a. Onset of sensory blockade
- b. Onset of motor blockade
- c. Duration of analgesia
- d. Side effects if present.

Onset of Sensory Blockade

It is the duration in between the time of injection and absence of sensation of pinprick at tenth thoracic level.⁸

Duration of Analgesia

It is defined as the interval in between the time of injection and rescue analgesic in the post-operative period.⁸

Duration of Sensory Blockade

It is defined as the duration between the time of injection and the presence of sensations at S1 dermatome.⁸

Duration of Motor Blockade

It is defined as time duration in between the time of injection and complete recovery of motor functions.⁸

All the side effects intra and postoperatively were recorded. The vitals (pulse, blood pressure, respiratory rate, and oxygen saturation) were recorded. After evaluating the sensory and motor functions clinically, the patient was transferred to post-operative room.

RESULTS

The least age in Group 1 is 20 years and in Group 2 is 21 years. 50 years are the maximum age in both the groups. The mean age in Group 1 and 2 are 38.74 ± 10.6 and 37.17 ± 10.8 years, respectively. There is no statistical difference between the two ($P > 0.05$).

The mean time of sensory blockade onset in Group 1 is 1.88 ± 0.62 min while in Group 2 is 1.71 ± 0.61 min. There is no statistical significance between Group 1 and Group 2 regarding mean time taken for onset of sensory blockade, with $P = 0.170$ ($P > 0.05$) (Table 1).

The mean duration of analgesia is 172.64 ± 16.2 min in Group 1 and 285.35 ± 32.6 min in Group 2. There is a statistically highly significant difference between Group 1 and Group 2 ($P < 0.05$) (Table 2).

In the Group 1, the basal value of mean HR is 78 ± 7.01 bpm and we observed a decrease in mean HR which is maximum of 6 bpm from basal value at 50th min, whereas in the Group 2 the basal value of mean HR is 78 ± 7.2 bpm and we observed a decrease in mean HR which is maximum of 7 bpm from basal value at 60th min. The greater decrease

in mean HR is seen in Group 2, but there is no statistically significant difference between the two groups (Table 3).

In the Group 1, the basal value of mean MAP is 96.68 ± 2.76 mmHg, and we detected a drop in MAP, which is maximum of 9.99 mmHg from mean basal MAP at 20th min. In the Group 2, the basal value of mean MAP is 96.56 ± 2.88 mmHg, and we found a reduction in MAP, which is maximum of 13.34 mmHg from mean basal MAP at 20th min. The mean MAP from basal to 20th min recording is statistically not significant between the two groups. The mean MAP from 20th to 60th min recording is statistically highly significant between Groups 1 and 2 (Table 4).

Table 1: Time taken for onset of sensory blockade (min)

Group	Mean±SD	Maximum	Minimum
1	1.88±0.62	3	1
2	1.71±0.61	3	1

SD: Standard deviation

Table 2: Duration of analgesia in both the groups (min)

Group	Mean±SD	Maximum	Minimum
1	172.64±16.2	205	140
2	285.35±32.6	410	260

SD: Standard deviation

Table 3: Mean HR (beats per min) in two groups at various intervals

HR (min)	Group	Mean±SD	P value	Significance
Basal	1	78±7.01	1.0	Not significant
	2	78±7.2		
5	1	80±6.84	1.0	Not significant
	2	80±6.55		
10	1	78±7.3	0.171	Not significant
	2	76±7.21		
15	1	77±7.16	0.487	Not significant
	2	76±7.2		
20	1	76±7.8	0.192	Not significant
	2	74±7.45		
30	1	76±6.86	0.133	Not significant
	2	74±6.34		
40	1	74±5.28	0.572	Not significant
	2	72±5.11		
50	1	72±6.95	1.0	Not significant
	2	72±6.78		
60	1	72±7.19	0.488	Not significant
	2	71±7.2		
90	1	74±5.7	0.399	Not significant
	2	73±6.1		
120	1	76±7.27	0.167	Not significant
	2	74±7.12		

HR: Heart rate, SD: Standard deviation

Table 4: MAP (mmHg) in two groups at various intervals

MAP (min)	Group	Mean±SD	P value	Significance
Basal	1	96.68±2.76	0.832	Not significant
	2	96.56±2.88		
5	1	94.62±3.12	0.143	Not significant
	2	93.64±3.52		
10	1	88.54±4.11	0.455	Not significant
	2	87.92±4.16		
15	1	90.68±2.98	0.55	Not significant
	2	91.00±2.32		
20	1	86.69±3.75	<0.0001	Significant
	2	83.22±2.99		
30	1	91.00±3.94	0.004	Significant
	2	88.92±3.23		
40	1	92.45±4.94	<0.0001	Significant
	2	87.93±3.75		
50	1	91.79±2.42	<0.0001	Significant
	2	89.19±2.99		
60	1	92.85±3.1	<0.0001	Significant
	2	89.94±2.22		
90	1	94.79±5.1	0.361	Not significant
	2	93.88±4.82		
120	1	96.46±3.93	0.906	Not significant
	2	96.55±3.67		

MAP: Mean arterial pressure, SD: Standard deviation

In Group 1, 3 out of 50 and in Group 2, 5 out of 50 patients established hypotension which is statistically not significant ($P > 0.05$). Intravenous fluids and vasopressor were used to treat these patients (Figure 1).

In Group 1, 4 out of 50 and in Group 2, 6 out of 50 patients developed bradycardia which is statistically not significant ($P > 0.05$). A single dose of 0.6 mg of atropine was given to cure them (Figure 2).

In Group 1, 6 out of 50 patients, i.e., 18% of patients had developed pruritus, whereas in Group 2 pruritus was absent in all patients. There is a statistically highly significant difference in the incidence of pruritus between the two groups ($P < 0.05$) (Figure 3).

DISCUSSION

The good post-operative analgesia is the basic requirement of any surgical intervention. Ideally, the post-operative analgesia should be continuous, long lasting, and with least adverse effects. Nowadays in India, the most commonly used intrathecal local anesthetics are lignocaine and bupivacaine. The post-operative analgesia action of these drugs is limited. Continuous epidural analgesia is used in some places for prolonging the duration of analgesia, but this method is costly and technically difficult. Thus, local anesthetics additives prove to be a better and cheaper method of prolonging analgesic effect.⁹

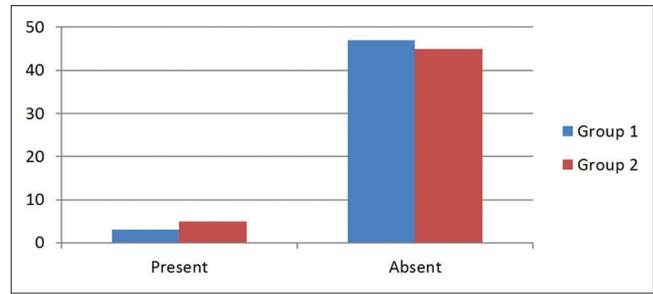


Figure 1: Incidence of hypotension in two groups

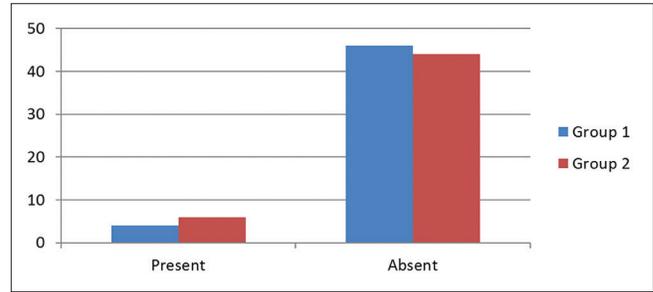


Figure 2: Incidence of bradycardia in two groups

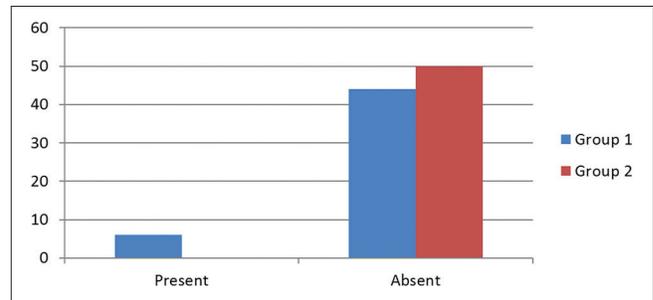


Figure 3: Incidence of pruritus in two groups

The most commonly used drugs for this purpose are opioids like fentanyl, which is a lipophilic receptor agonist. Fentanyl blocks the opioid receptors present in the dorsal horn of spinal cord.¹⁰

Dexmedetomidine is an adrenergic-2 receptor agonist which has been recently approved by the FDA in 1999 for analgesia in humans. The mechanism of action of sensory and motor blockade of alpha-2 adrenoceptors is not clear. They bind to the presynaptic C fibers and decrease the release of C-fiber transmitters. Intrathecal 2-receptor agonists have been found to have antinociceptive action for both somatic and visceral pain.⁸

This study was conducted to weigh and relate the effects of adding fentanyl versus dexmedetomidine with intrathecal hyperbaric 0.5% bupivacaine in elective lower abdominal surgeries. In the study, it was hypothesized that intrathecal bupivacaine and dexmedetomidine mixture provides

prolonged sensory blockade and better analgesia than the intrathecal bupivacaine and fentanyl.

In regard to onset of sensory blockade, no statistically significant difference was found in between fentanyl group and the dexmedetomidine group. The mean duration of analgesia in our study is 172.64 ± 16.2 min in Group 1 (fentanyl) and 285.35 ± 32.6 min in Group 2 (dexmedetomidine group). There is a statistically highly significant difference between the two groups. ($P < 0.05$) In studies conducted by Tarbeeh *et al.*,¹¹ Gupta *et al.*,⁹ and Eid and Shafie¹⁰ authors observed that mean duration of analgesia is more in dexmedetomidine as compared to fentanyl.

In the Group 1, the basal value of mean MAP is 96.68 ± 2.76 mmHg, and we detected a drop in MAP, which is maximum of 9.99 mmHg from mean basal MAP at 20th min. In the Group 2, the basal value of mean MAP is 96.56 ± 2.88 mmHg, and we found a reduction in MAP, which is maximum of 13.34 mmHg from mean basal MAP at 20th min. The MAP from basal to 20th min recording is statistically not significant between the two groups. However, the mean MAP from 20th to 60th min recording is statistically highly significant between Groups 1 and 2. In a study piloted by Tarbeeh *et al.*,¹¹ authors witnessed no significant difference between the two groups in MAP at 120 min but significantly lower when equated with the basal values, which coincides with our study outcomes.

The greater decrease in mean HR was seen in Group 2, but there is no statistically significant difference between the two groups (1 and 2). Similar findings were also witnessed by other studies such as Al-Ghanem *et al.*,¹² and Tarbeeh *et al.*¹¹ who found no significant difference in mean value of HR throughout the intraoperative and post-operative period.

In a study conducted by Al-Ghanem *et al.*,¹² authors observed that the hypotension was present in only 10.5% of patients in fentanyl group, whereas this percentage was 23.7% in fentanyl group, but it did not reach a significant difference. Similarly, Tarbeeh *et al.*¹¹ observed 15% incidence of hypotension in both the groups. In our study, the incidence of hypotension was three out of 50 (6%) in Group 1 and in Group 2, 5 out of 50 patients (10%) established hypotension which is statistically not significant ($P > 0.05$).

In our study, none of the patients developed other side effects such as nausea, vomiting, and respiratory depression. Other complaints such as backache, pain in buttock or leg, and any neurological deficit were also not reported.

Pruritus in fentanyl group is a common side effect, although it is mild in nature and requires no treatment.¹³ A study was conducted on spinal anesthesia for ambulatory knee arthroscopy in which the combination of bupivacaine with fentanyl was used resulting in pruritus ranging from 48 to 75% compared with the group getting only bupivacaine.¹⁴ Ackerman *et al.*¹⁵ have also reported that opioids that stimulated-receptors following epidural administration exhibited significantly less pruritus than pure-receptor opioids administered similarly.

CONCLUSION

The combination of dexmedetomidine (5 g) and 0.5% bupivacaine, prolongs the duration of analgesia, decreases total analgesic dose necessity in first 24 h post-operative with unwavering hemodynamic parameters and is also not associated with side effects like pruritus as observed in fentanyl group, hence can be an attractive alternative for being used as an adjuvant to bupivacaine in controlling post-operative pain.

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Outcome of Modified Papineau Technique with Vacuum-assisted Closer System in the Treatment of Chronic Osteomyelitis and Infected Nonunion of Tibia

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Abstract

Introduction: Infection of bone is either hematogenous or direct in the case of open fractures and is very difficult to eradicate. However, a combination of age-old Papineau technique and modern vacuum-assisted closer (VAC) system may be used for successful eradication of bone infection. Sometimes, soft tissue cover may be added if required.

Materials and Methods: We treated 24 consecutive patients between July 2013 and August 2015 using modified Papineau technique, who were suffering from chronic osteomyelitis tibia - 10 patients and infected nonunion of tibia - 14 patients. Among them, 18 were male and 06 were female. After initial debridement, VAC system was applied in all cases. 2-3 weeks later when healthy granulation became apparent, cancellous/corticocancellous bone grafting was done. VAC still continued until the wound healed completely or wound was covered by split skin grafting or musculocutaneous flap.

Results: Mean follow-up for the study group was 6 months ranging from 5 to 24 months. In approximately 80% of the cases, we were able to eradicate the bone infection completely and achieve good union in cases of infected nonunion of fracture tibia. There were no signs of relapse of infection clinically, radiologically, and hematologically. All patients returned to preinfection status and their routine activity.

Aims of Study: Evaluation of results of modified Papineau technique with VAC system, in the treatment of chronic osteomyelitis and infected nonunion of the tibia.

Conclusion: We can conclude on the basis of the results of our study that Papineau technique combined with modern VAC system of soft tissue coverage is a useful tool in the management of chronic recurrent osteomyelitis and infected nonunion cases of extremity bones. In our opinion, extensive bone and soft tissue debridement are the key to successful eradication of bone infection. Removal of necrotic avascular bone, scarred soft tissue, and musculature is absolutely necessary.

Key words: Chronic osteomyelitis, Infected nonunion, Papineau technique, Vacuum-assisted closer system

INTRODUCTION

In spite of various advancements in the field of medical science including high-class antibiotics, various surgical implants and fixator, cases of chronic osteomyelitis and infected nonunion after the trauma is still a challenge to the orthopedic fraternity.

High energy trauma leads to significant soft tissue damage leading to the avascularity of bone which gets infected in case of open fractures which requires multiple repeated debridement of necrotic tissue and effective fracture stabilization, usually with the external fixator. Many patients require early soft tissue cover with local muscle flap or muscle transfer.^{1,2}

Many techniques have been described like-cancellous bone grafting,³ open cancellous bone grafting (Papineau technique),⁴ or bone transport using the ilizarov fixator⁵ and sometimes vascular fibular graft to cover bony defects.⁶

Papineau technique⁷⁻⁹ involves thorough curettage or removal of the necrotic bone and unhealthy granulation in chronic osteomyelitis or infected nonunion of long bones

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followed by cortical and corticocancellous bone grafts in recipient bed.^{10,11} Soft tissue cover may be added if required.

In the present study, we have used the modified Papineau technique-where vacuum-assisted closer (VAC) system has been applied along with the open bone grafting to eradicate the infection from the infected nonunion site or patients of hematogenous chronic osteomyelitis of tibia.

Aims of Study

Evaluation of results of modified Papineau technique with VAC system in the treatment of chronic osteomyelitis and infected nonunion of the tibia.

MATERIALS AND METHODS

We treated 24 consecutive patients between July 2013 and August 2015, using modified Papineau technique, 14 male and 10 female, aged between 10 and 55 years. 10 case of chronic osteomyelitis tibia with discharging sinus and 14 patients of the infected nonunion - tibia. Original injury was (Gustilo-Anderson classification Grade-I - Grade-III) open fractures in all infected nonunion cases.

Mode of injury was road traffic accidents in 10 patients, 4 had an injury due to fall from height. Remaining 10 patients had osteomyelitis due to hematogenous infection.

According to classification by Cierny and Mader¹² and Cierny,¹³ infection was diffuse in 16 cases, localized in 5, medullary in 2, and superficial in 1.

Initial management had been done by external fixation in 8 cases, intramedullary nailing/pin fixation in 4 cases and plate fixation in 2 cases soon after the trauma.

When these patients were admitted to SRMS-IMS, Bareilly, all had discharging pus from wound site in the leg and septic skin necrosis. Osteomyelitis of tibia was located in proximal 1/3rd in 8 patients, middle 1/3rd in 11 patients, and lower 1/3rd in 5 patients. Donor site for corticocancellous/cancellous bone grafts was same side iliac crest in 18 patients and opposite side in 6 patients.

Blood investigations included-blood cell count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and hemoglobin% (Hb%). Pus culture sensitivity and X-ray leg AP and lateral view were taken in all patients, before starting the treatment and repeated after every 4 weeks interval. An appropriate antibiotic therapy was initiated soon after culture sensitivity report.

Definitive surgery included removal of intramedullary implant or plate, stabilization of fracture by external fixator

AO type/Jess fixator/Rail fixator. Excision of necrotic bone and soft tissue or saucerization was done in cases of chronic hematogenous osteomyelitis.

All cases were applied VAC system after definitive surgery. VAC dressing was changed after every 4-5 days and continued till healthy granulation appeared in the bed. It took 2-3 weeks. Corticocancellous bone grafting was done using Papineau technique and VAC applied again.

Intravenous (I/V) antibiotics were given for initial 10-15 days and later oral therapy was continued for 6 weeks.

Surgical Techniques

Debridement

Our first step was the removal of intramedullary implants or plate, non-viable soft tissues, and bone. Avascular sclerotic bone was excised till the healthy bleeding margins were noted on the osseous bed. Culture specimen was taken from the infected area, and the extremity was stabilized by either external fixator AO type/Jess or rail fixator. Antibiotics were given as per culture sensitivity report till the blood cell count, ESR, and CRP returned to normal. VAC system was applied soon after surgery in all cases.

After 2-3 weeks wound showing healthy granulation tissue was followed by corticocancellous bone grafting in the osseous bed taken from the outer table of iliac wing and crest. We required fasciocutaneous or musculocutaneous flap to cover the bone in 8 patients. The wound was allowed to heal by secondary intention in 12 patients. In 4 cases, we required split thickness skin graft to cover the wound, later.

After 2 weeks of I/V antibiotic therapy, we switched over to oral antibiotic which were continued for 6 weeks.

RESULTS

Mean follow-up for the study group was 8 months, ranging from 5 months to 24 months, and in 80% of the cases, we were able to achieve bony union and complete eradication of infection. All patients were followed every 4 weeks. Radiographs were taken after every 4 weeks and blood investigations were also repeated every 4 weeks. There were no signs of relapse of infection clinically or radiologically (Figure 1a and b), and blood reports also were showing all parameters of chronic infection such as - total leukocyte count, differential leukocyte count, Hb%, ESR, and CRP, normal. The external fixator was removed at a mean period of 16 weeks after union (range 14-24 weeks). All patients returned to their normal routine work.

Staphylococcus was isolated in 18 patients, and Gram-negative bacilli were reported in 6 patients. Most of the patients had

already taken multiple courses of various broad spectrum antibiotics. In most of our patients, we used amoxiclav, ceftriaxone, ceftazidime, and sometimes clindamycin.

In 3 patients, we required local muscle flap/rotational muscle flap to cover the wound and exposed bone. These patients were kept non-weight bearing for 6-8 weeks. Later, they were allowed partial weight bearing when signs of the union were apparent radiologically. Full weight bearing was allowed only after an average of 16 weeks period, in nonunion cases.

5 patients required more than one debridement before bone grafting. Mean period from bone grafting to skin coverage was 8-10 weeks. Time to bony union and eradication of infection was on an average 22 weeks - range 16-40 weeks (Figure 2a-c).

1 patient lost to follow-up after 12 weeks. In 3 patients, we required to excise the infected bony fragment up to the length of 2-3 cm, where we used ilizarov ring fixator for compression-distraction histogenesis to achieve the union and bone length.

Pin tract infection was observed in 5 patients, and it was managed successfully by the local care and systemic antibiotics. One of our patients landed in below knee amputation because of malignant change in the ulcer.

DISCUSSION

In the management of chronic osteomyelitis and infected nonunion of long bones of the lower extremity, our aim is to achieve the perfect control of infection and bony union. Favorable outcome may be expected by use of a combination of age-old Papineau technique of open corticocancellous bone grafting and modern technique of wound healing by VAC. In these patients, the presence of necrotic bone or scarred tissue with poor blood supply is responsible for non-eradication of the infection.¹² After removal of necrotic bone, a dead space is created, the ablation of dead space may be achieved by the bone grafting.¹²⁻¹⁴

Adequate antibiotic therapy, appropriate and timely soft tissue cover plays an important role in eradication of infection of the bone.¹⁵

Papineau technique was developed to assist the management of bony defect and post-traumatic osteomyelitis. Papineau and others have reported high rates of successful management in eradicating bone infection.^{7,8,10,16,17}

Ilizarov ring fixator and AO type external fixator are also good options because they can allow the correction of axial translation and angular deformities and simultaneously

maintain mobility and weight bearing. Tissue dissection and periosteal stripping as with the internal fixation are also avoided.^{5,9,18}

In the present study, we have reviewed our clinical results in lower extremity open fractures of the tibia which led to infected nonunion - 14 patients and 10 patients who had chronic osteomyelitis of hematogenous origin.

In all cases, Papineau technique was used. The first stage included aggressive debridement of necrotic tissues, meticulous local wound care, and application of VAC system followed by corticocancellous open bone grafting and skin cover in some cases. Repeated check of parameters of infection-like ESR, CRP, Blood counts was done.



Figure 1: (a) Chronic osteomyelitis tibia - 12-year-old male patient treated by modified Papineau technique, (b) chronic osteomyelitis tibia in 12 years male patient. Wound healed within 18 weeks



Figure 2: (a) Infected nonunion tibia earlier treated by fibula grafting and hybrid fixator, (b) hybrid fixator removed and vacuum-assisted closer (VAC) applied after thorough debridement, (c) fracture united after corticocancellous bone grafting (Papineau technique) and VAC application-12 weeks post-operative

In our series, we encountered few complications. 5 patients developed pin tract infection which was managed conservatively, and 1 of our patient landed into below knee amputation. All patients had fully developed infected nonunion with multiple surgeries or full-fledged chronic osteomyelitis. Papineau technique combined with the VAC system has resulted in salvaging the difficult cases.¹⁹

CONCLUSION

As regards, the management of complicated infected nonunion of long bones of extremities and hematogenous chronic osteomyelitis, use of Papineau technique combined with the VAC application, is an important modality to control infection and achieve the bony union.

In our opinion, extensive surgical debridement is the most important part of the management of infection of bones regardless of the size of the defect created. Removal of the necrotic bone, soft tissue, avascular periosteum, scarred sub cutaneous tissue, and muscle is a must for the successful outcome. Patient's compliance and physiotherapy also play an important role in the overall functional outcome of the patient.

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Knowledge, Attitude, and Practices on Vaccination among Mothers of under-5 Children, Attending Immunization Out Patients Department at Gwalior, Madhya Pradesh

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Abstract

Introduction: Immunization is one of the most cost-effective interventions to prevent the suffering that comes from avoidable sickness, disability, and death. India still accounts for the largest number of children who are not immunized, approximately 7.4 million. This underlines the need for further improvement.

Purpose: This study aimed to assess the vaccination status of children and also the knowledge and attitude of mothers, in relation to vaccination.

Methodology: It was a cross-sectional observational study. The study was conducted on 150 mothers of reproductive age group attending immunization Out Patients Department of JAH group of hospitals, over a period of 90 days.

Results: Out of 150 mothers, 123 (82%) mothers knew about the benefits of immunization, whereas 27 (18%) mothers did not know about benefits of the same. Moreover, out of 150 respondents, 86% (129) had completed their child's immunization on time, whereas 14% (21) had delayed immunization or incomplete immunization.

Conclusion: The present study findings concluded that 86% immunization coverage is prevalent with 82% awareness level of participants in the study.

Key words: Attitude, Cost-effective, Cross-sectional, Immunization, Knowledge, Observational

INTRODUCTION

Immunization is one of the most cost-effective interventions to prevent the suffering that comes from avoidable sickness, disability, and death. The benefits of immunization are not restricted to improvements in health and life expectancy but also have a social and economic impact at both community and national levels.

Universal immunization program (UIP), launched by the government of India in 1985¹, with a mission to achieve immunization coverage of all infants and pregnant women, targets to reduce the burden of vaccine-preventable diseases (VPDs). It became a part of child survival and safe motherhood program in 1992 and remained one of the key areas under national rural health mission since 2005.

A VPD is an infectious disease for which an effective preventive vaccine exists. If a person acquires a VPD and dies from it, the death is considered a vaccine-preventable death.

The program consists of vaccination for seven diseases²: Tuberculosis, diphtheria, pertussis (whooping cough), tetanus, poliomyelitis, measles, and hepatitis B. Hepatitis B

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was added to the UIP in 2007. Thus, UIP had 7 VPDs in the program.

On 2014, it was announced that four vaccines will be added to the program, namely rotavirus, rubella, and Japanese encephalitis, as well as the injectable polio vaccine.

India has the largest number of births in the world - more than 26 million a year - and also accounts for more than 20% of child mortality worldwide. Nine million immunization sessions are organized each year to target these infants and 30 million pregnant women for routine immunization.

It is among the most financially effective public health interventions since it provides direct and effective protection against preventable morbidity and mortality. It has been a major contributor in the decline of under-5 mortality rate in last five decades in India. Despite the improvement, the country still accounts for the largest number of children who are not immunized, approx 7.4 million. This underlines the need for further improvement.

An effective, evenly targeted immunization program and its ability to reduce the burden of VPDs will greatly contribute to achieving the Millennium Development Goal 4 that aimed for a two-third reduction in child mortality by 2015, which has not been achieved yet. Therefore, this study aimed to assess the vaccination status of children and also the knowledge and attitude of mothers, in relation to vaccination.

Aims and Objectives

1. To assess knowledge regarding immunization status and its sources
2. To assess immunization status and practices among mothers.
3. To assess the vaccination status among children of participant mothers.

METHODOLOGY

It is a cross-sectional observational study. The study was conducted on 150 mothers of reproductive age group attending immunization Out Patients Department (OPD) of JAH group of hospitals.

The collection and analysis of data were done with the help of a questionnaire assessing the immunization status of children and awareness about immunization among mothers. The study was conducted over a period of 90 days during the OPD hours of JAH group of hospitals (Table 1).

Out of 150 mothers, 123 (82%) mothers knew about the benefits of immunization, whereas 27 (18%) mothers did not know about benefits of the same.

Out of 150 mothers, 87.3% (131) mothers knew that vaccine is available for polio; 75.3% (113) mothers knew that for measles, the vaccine is available, whereas 60.6% (91) mothers knew that vaccine is present for the whooping cough. 52% (70) had knowledge about booster doses, whereas 48% (80) knew nothing about booster doses of vaccination (Table 2).

Out of 150 mothers, 86% (129) of participants had completed their child's immunization on time, whereas 14% (21) had delayed immunization or incomplete immunization. Out of 21 participants with delayed or incomplete immunization, 53% (11) were ignorant about immunization; 33% (7) were unaware about immunization, whereas 14% (3) participants had incomplete immunization due to lack of medical facilities (Table 3). Out of 150 mothers, 94% (141) mothers had their children vaccinated for polio at the time of birth; 77.3% (116) for hepatitis B, whereas 65.3% (98) had Bacillus Calmette - Guerin vaccines at birth (Table 4).

Table 1: Knowledge about benefits of immunization, vaccine-preventable diseases and about booster doses

Diseases	Yes (%)	No (%)
Benefits of immunization	123 (82)	27 (18)
Polio	131 (87.3)	19 (12.7)
Measles	113 (75.3)	37 (24.7)
Whooping cough	91 (60.6)	59 (39.4)
Rabies	50 (33.3)	100 (66.7)
Booster doses	70 (52)	80 (48)

Table 2: Status of full immunization of children

Full immunization (%)	Delayed/incomplete immunization (%)
129 (86)	21 (14)

Table 3: Vaccine administered at the time of birth

Disease	n (%)
Polio	141 (94)
Hepatitis B	116 (77.3)
BCG	98 (65.3)

BCG: Bacillus Calmette - Guerin

Table 4: Vitamin A along with measles

Vitamin A given	91 (60.6%)
Vitamin A not given	59 (40.4%)

Out of 150 mothers, children of 60.6% (91) mothers were given Vitamin A along with measles, whereas 40.4% (59) were not given.

DISCUSSION

In the present study, the immunization coverage found by this study (86%) was a little higher as compared to a hospital based study of S.R.T.R. Medical College, Ambejogai conducted by Chaudhary *et al.*,^{5,6} where the percentage of fully immunized children was found to be 61.9%.

About 82% participants knew about benefits of immunization, of which the major source of information was doctors and nurses (45%). This contradicts with the findings of Angadi *et al.*^{4,5} according to whom relatives and friends serve as major source of information (42.48%) followed by health care workers such as auxiliary nurse midwives, and doctors.

At the time of birth; maximum coverage is of polio vaccine (94%). The main reason for delayed or incomplete immunization among remaining families (14%) was ignorance. Only 61% children received Vitamin A supplements along with measles. A similar study was conducted by Kadri *et al.*^{3,4} in urban slums of Ahmedabad where only 47.8% children had received Vitamin A supplement at the time of measles vaccination.

The study also shows that 64% participants have suffered from some sort of adverse effect after vaccination and most of them developed fever. Some of them also experienced diarrhea and rashes. The similar study was also conducted by Das⁶.

CONCLUSION

The present study findings concluded that 86% immunization coverage is prevalent with 90% awareness level of participants in the study. This needs to be increased to reach maximum coverage of vaccination.

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Comparison of Bolus Bupivacaine, Fentanyl, and Mixture of Bupivacaine with Fentanyl in Thoracic Epidural Analgesia for Upper Abdominal Surgery

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Abstract

Introduction: Thoracic segmental epidural analgesia despite its technical difficulty and time consumption provides better analgesia and has a beneficial effect on the post-operative pulmonary and metabolic function; immunological and stress response.

Aims and Objectives: To study the efficacy of fentanyl for pain relief of inpatients after upper abdominal procedures and compare with bupivacaine alone and with bupivacaine and fentanyl combination (1) To find out the synergistic effect of bupivacaine with fentanyl. (2) Assessment of severity of pain at rest and during function, intensity of post-operative pain relief, duration of post-operative pain relief, and the incidence of side effects.

Materials and Methods: After institutional approval, patients were allocated into three groups of 30 patients each. Group A patients receiving 10 ml of 0.25% bupivacaine epidurally; Group B patients receiving 10 ml of fentanyl 50 µg epidurally, and Group C patients receiving 10 ml of 0.25% bupivacaine with fentanyl 50 epidurally. Required parameters were assessed.

Result: Combination of bupivacaine with fentanyl in thoracic epidural analgesia after upper abdominal surgery, showed better analgesic efficacy, synergistic effect, short onset of action, and longer duration of action (ranges from 150 to 280 min) with minimal side effects.

Conclusion: The thoracic epidural is strongly recommended technique for post-operative pain relief after upper abdomen surgery.

Key words: Analgesia, Bupivacaine, Epidural, Fentanyl

INTRODUCTION

The pathophysiologic consequences of upper abdominal surgery are intimately associated with severe post-operative pain and resultant higher incidence of post-operative complication and increased morbidity. Conventional methods of narcotic analgesia not only provide inadequate pain relief but are also associated with deleterious systemic side effects.

Intermittent doses of bupivacaine (0.25-0.5%) provides adequate neural blockade for effective post-operative analgesia. It provides undesirable motor blockade in some patients in the post-operative period. Hence, a search was on to find a suitable drug, which would provide adequate sensory block without affecting motor neurons.

The discovery of opioid receptors in the brain and spinal cord¹ raised exciting new possibilities in the management of severe pain. Opioids are known for the production of profound analgesia without loss of other sensations, minimal or nil central nervous system depression, and devoid of unpleasant consequences of the autonomic blockade.

Epidural opioids have been widely used for facilitation of central neuraxial blockade and post-operative analgesia.

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Although they may be used alone in this regard, multiple studies have shown that analgesia is more effective when they are combined with local anesthetics.²⁻⁴

Extradural opioids are preferred to subarachnoid because of lower rate of infection, the lack of a post-spinal headache, and low incidence of side effects, further incremental doses can be given through an indwelling catheter to increase the duration of action and minimize the side effects.

Ideal opioids for extradural use should fulfill the following criteria;

- High lipid solubility including fast diffusion into neural tissues
- Lowest systemic absorption with minimal side effects
- Strong receptor binding protein producing prolonged effects
- High molecular weight
- Intense and prolonged intrinsic activity.

Fentanyl, a new synthetic opioid, fulfills almost all these criteria.

Given the unique pharmacologic properties of each opioid and studies that show different rates of accumulation in the cerebrospinal fluid, there is biologic plausibility for differences in the side effect profiles and analgesia among different opioids.⁵⁻⁸

Fentanyl also has a remarkable safety profile. The near absence of respiratory depression with fentanyl (with permissible doses) and better pulmonary spirometric function (forced vital capacity and forced expiratory volume in 1 s) as reported by Guinard *et al.* and shorter hospitalization makes it an ideal drug for extradural use.⁹

For optimal analgesia, the thoracic epidural route should be used for pain relief after upper abdominal surgery.¹⁰

In this study, an attempt was made to compare bolus bupivacaine, fentanyl, and mixture of bupivacaine with fentanyl in thoracic epidural analgesia for upper abdominal surgery.

Aims and Objectives

The present study was undertaken with the following aims and objectives:

1. To study the efficacy of fentanyl for pain relief of in-patients after upper abdominal procedures and compare with bupivacaine alone and with bupivacaine and fentanyl combination
2. To find out the synergistic effect of bupivacaine with fentanyl

3. Assessment of severity of pain at rest and during function
4. Assessment of the intensity of post-operative pain relief
5. Assessment of the duration of post-operative pain relief
6. Assessment of the incidence of side effects.

MATERIALS AND METHODS

The present study was carried out in the Department of Anesthesiology, N.S.C.B. Medical College, Jabalpur, Madhya Pradesh.

After institutional approval, a total number of 90 patients of ASA Grades I, II, and III of either sex, aged 20-60 years were included in this study. Patients scheduled for elective and emergency upper abdominal surgeries. The name, age, sex, and body weight of the patients noted, and all the patients were assessed before the surgery and judged fitness for the study. A detailed history was taken and thorough physical examination was done. Routine investigation and essential evaluation according to the requirement of the case were done before the operation.

For the purpose of the study, the patients were randomly allocated into three groups of 30 patients each.

Group A: Patients receiving 10 ml of 0.25% bupivacaine epidurally

Group B: Patients receiving 10 ml of fentanyl 50 µg epidurally

Group C: Patients receiving 10 ml of 0.25% bupivacaine with fentanyl 50 µg epidurally.

In case of routine surgery, a thoracic epidural block was performed in sitting position before induction of general anesthesia, while in case of emergency surgery, the block was performed in lateral decubitus after the completion of surgical procedure under general anesthesia and patients were still under general anesthesia and intubated, at interspace between T7 and T10 depending on level of surgical incision with taking all aseptic precautions.

After recovery room where they kept and received post-operative analgesia as decided by the random numbers.

Preparation of the Drugs

Group A ($n = 30$): 0.25% bupivacaine 10 ml

Group B ($n = 30$): 50 µg of fentanyl (1 ml fentanyl ± 9 ml of normal saline).

Group C ($n = 30$): 50 µg of fentanyl ± 0.25% bupivacaine (10 ml) (1 ml fentanyl ± 9 ml of 0.25% bupivacaine).

When the score on visual analog scale (VAS) was ≥ 25 , the solution of local anesthetic and/or opioid injected into the epidural space.

Time taken for pain relief, i.e. onset of analgesia. Time of reappearance of pain, i.e. duration of analgesia and side effects of the drugs were noted.

Following parameters - pulse rate, blood pressure, respiration, intensity, and duration of analgesia was monitored during the post-operative period every 15 min for first 30 min, and thereafter 1 h for 5 h.

The intensity of pain was assessed by VAS.

RESULTS

About 90 patients of ASA Grades I-III from both sexes who were to undergo upper abdominal surgeries under general anesthesia were chosen for this study. Patients who already received analgesics preoperatively were excluded from the study.

The patients were randomly allocated into three equal groups of thirty each.

Group A: 30 patients (only bupivacaine)

Group B: 30 patients (only fentanyl)

Group C: 30 patients (bupivacaine with fentanyl)

The onset and duration of analgesia, changes in blood pressure, pulse rate respiration, and side effects, if any, were noted for each group.

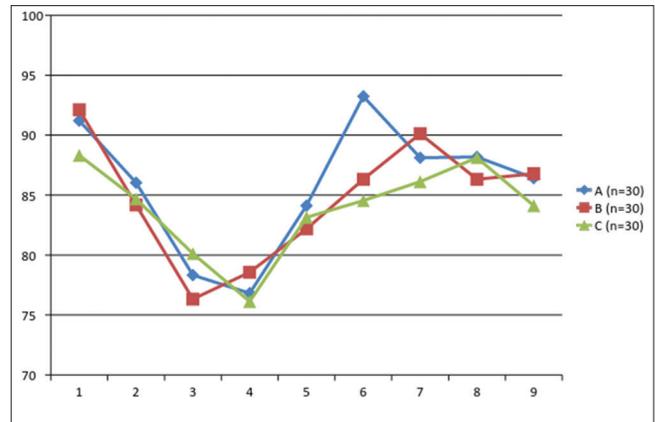
The study population was similar with respect to age, sex, and weight.

A fall in pulse rate was observed after 15 min in all the groups. However, the mean pulse rate returned to pre-operative values subsequently (Graph 1).

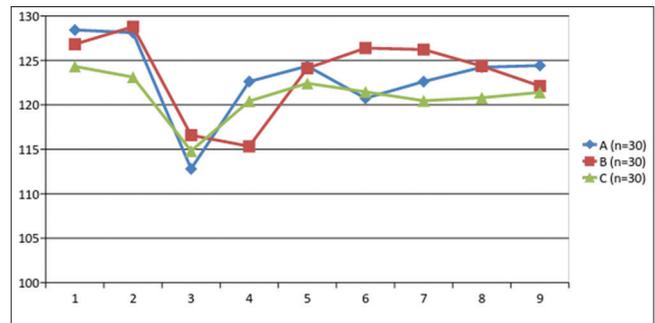
A change in mean systolic pressure was recorded at 15 min, 30 min, and 1 h thereafter. Mean of the values recorded has been shown in Graph 2.

A fall in blood pressure was observed to be more in Groups A and B, as compared to Group C (Graph 3).

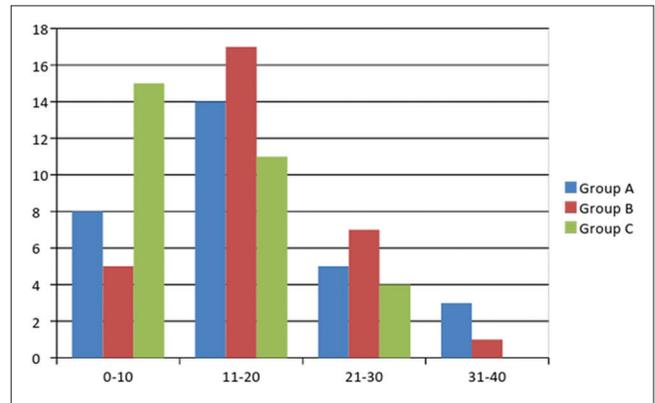
The change in mean respiratory rate among the three groups has been depicted in Graph 4. In the post-operative period 15 min after the drug administration, there was a transient but not significant decrease in respiratory rate. This may be due to the relief of pain by the drug administered. Later on, there was a gradual increase to pre-operative values.



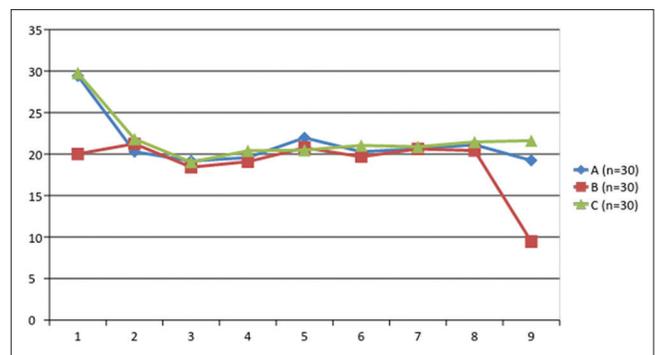
Graph 1: Change in mean pulse rate ± standard deviation



Graph 2: Change in mean systolic blood pressure (mmHg) ± standard deviation



Graph 3: Fall of blood pressure (systolic) (%)



Graph 4: Change in mean respiratory rate ± standard deviation

Mean time of onset of analgesia was 13.42 ± 4.60 min in Group A, 6.06 ± 2.43 min in Group B, and 4.46 ± 2.38 min in Group C (Table 1).

Mean duration of analgesia was 132.63 ± 34.78 min in Group A, 166.30 ± 24.64 min in Group B, and 192.84 ± 18.72 min in Group C (Table 2).

A comparison of mean pain score has been shown in Graph 5. While the maximum pain score (score-4) was seen in Groups A, B, and C at about 3 h, 4 h, and 5 h, respectively (Table 3).

Most of the patients of Groups A, B, and C needed supplementation in between 2 and 3 h (70%), 3-4 h (76.6%), and 4-5 h (70%), respectively. It is clear from these data that the subsequent repeat of drug administration is least in the case of fentanyl with bupivacaine group in comparison to only bupivacaine and fentanyl alone group (Table 4).

The incidence of side effects was minimal as depicted in Table 5.

DISCUSSION

An ideal analgesic should provide relief of pain without change of consciousness and should permit the early return of normal function. It should have its effect localized to where analgesia is required and should not produce a systemic side effect.

A safe and effective post-operative analgesia should induce a maximal analgesic response without any appreciable effects on the respiratory and cardiovascular systems or any tendency to produce post-operative complications.

The benign side effect profile of fentanyl despite good analgesic activity is thought to be due to its lipophilicity which restricts its fast rostral spread, thus limiting its ill effects such as respiratory depression, and pruritus. Its lipophilic nature also contributes to its shorter duration of action but used for continuous epidural analgesia. It is preferred over other hydrophilic compounds because of its rapid onset; it becomes much easier to observe the desired effects and thus titrate the dosage, to an optimal analgesic level.¹¹ There are a few studies regarding its effect in continuous epidural analgesia.¹²

In this clinical study, patients aged more than 60 years and <20 years of age were excluded to circumvent the variables at the extremes of age. Patients belonging to ASA I-III subjected to routine and emergency surgical procedures were taken for the study. Patients who received analgesics before surgery were excluded from the study. In this study, fentanyl was given in two different forms; 50 µg s only in Group B and 50 µg s in Group C with 0.25% bupivacaine. A study by Torda *et al.*¹³ have shown that fentanyl 50 µg administered epidurally is effective for post-operative pain relief. As the intravenous dose of fentanyl for analgesia is 1-2 µg/kg, a dose of 50 µg was considered safe for epidural use.

Table 1: Mean onset of analgesia (minutes±SD)

Groups (n=30)	Onset in minutes	Range in minutes
A	13.42±4.60	8.4-18.2
B	6.06±2.43	4.2-10.2
C	4.46±2.38	3.6-8.4

SD: Standard deviation

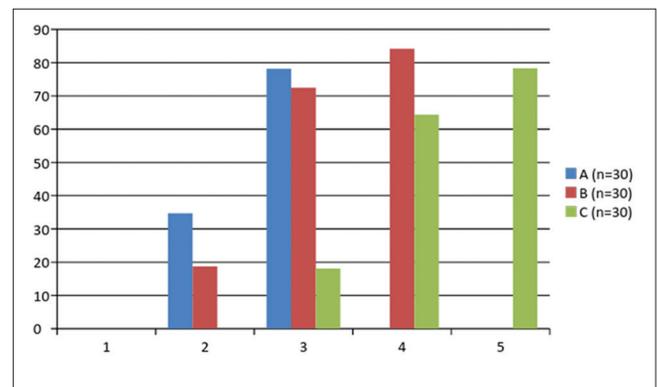
Table 2: Mean duration of analgesia (minutes±SD)

Groups (n=30)	Duration in minutes	Range in minutes
A	132.63±34.78	96-170
B	166.30±24.64	124-210
C	192.84±18.72	150-280

SD: Standard deviation

Table 3: Five level paint score

Group (n=30)	0-1		1-2		2-3		3-4		4-5	
	Paint (%)	Score	Paint (%)	Score	Paint (%)	Score	Paint (%)	Score	Paint (%)	Score
A	53	0	68	2	46	3	100	4	-	-
B	100	0	85	1	80	2	80	3	100	4
C	100	0	93	0	84	2	86	3	63	4



Graph 5: Comparison of mean pain score (± standard deviation)

Table 4: Number of patients requiring supplementation (post-operative)

Groups (n=30)	Hours after operation (%)			
	1-2	2-3	3-4	4-5
A	6 (20)	21 (70)	3 (10)	-
B	0	4 (13.3)	23 (76.6)	3 (10)
C	0	3 (10.3)	6 (19.6)	21 (70)

Table 5: Incidence of side effects

Side effects	Group A (%)	Group B (%)	Group C (%)
Hypotension	5 (16.67)	5 (16.67)	6 (23.3)
Nausea and vomiting	2 (6.67)	4 (13.3)	4 (13.3)
Sedation	2 (6.67)	3 (10)	3 (10)
Pruritus	0	4 (13.3)	5 (16.67)
Respiratory depression	0	1 (3.33)	0
Motor weakness	1 (3.33)	0	0

In our study, it was observed that there was an initial decrease in the pulse rate in all the three groups 15 min after drug administration and, later on, rise back to pre-operative value. This is more marked in Groups A and B and less in Group C. This observation is similar to the observation of Torda *et al.*¹³ that the effects on heart rate are not significantly different between the studies.

It was also seen that there was an initial fall in mean systolic blood pressure, 15 min after the epidural drug administration. The fall in systolic blood pressure was more in Group A and Group B as compared Group C. This observation also corroborates with the observations of Torda *et al.*¹³ This fall of systolic blood pressure was followed by a gradual rise in all the three groups to pre-operative values at about 1 h.

We also recorded a fall in systolic blood pressure in this study. For most of the patients in any group, the fall was within 20 mmHg. However, in Group C, the fall was within 10 mmHg in 50% patients.

Graph 4 shows the changes in mean respiratory rate in the post-operative period compared before and after drug administration. Hence, it can be inferred from these finding that epidural fentanyl and bupivacaine combination can provide post-operative analgesia without early or delayed clinical respiratory depression. This corroborates with the findings of Torda *et al.*¹³

The mean onset of analgesia in Groups A, B, and C, were 13.42 ± 4.60 , 6.06 ± 2.43 , and 4.46 ± 2.38 min, respectively. The difference between Groups A and Group C was found to be highly significant. This confirms with the findings of George *et al.*¹⁰ that fentanyl had an onset of action within 4-10 min and was superior compared to bupivacaine.

The mean duration of analgesia (minutes) in Groups A, B, and C was 132.63 ± 34.78 , 166.30 ± 24.64 , and 192.84 ± 18.72 , respectively. The difference between the three groups in different combinations was found to be statistically significant. It is observed that Group C (bupivacaine and fentanyl) produced prolonged analgesia in comparison to Group A and Group B. This is similar to the findings reported by Cooper and Turner.¹⁴ They have found that combination of fentanyl with bupivacaine is more effective for post-operative pain relief.

In our study, the mean pain score during the post-operative period was highest for Group A at 2-3 h. In the Group B, it peaked at 3-4 h while in Group C it was highest during 4-5 h. From these findings, it is clear that combination of fentanyl and bupivacaine provided longer duration of analgesia than only fentanyl (50 µg) and bupivacaine alone. This corroborates with the findings of George *et al.*¹⁰

Most of the patients of Groups A, B, and C needed supplementation in between 2 and 3 h (70%), 3-4 h (76.6%), and 4-5 h (70%), respectively. It is clear from these data that the subsequent repeat of drug administration is least in the case of fentanyl with bupivacaine group in comparison to only bupivacaine and fentanyl alone group.

There were no significant changes in the vital parameters. Mild hypotension was found in 5 patients of Group A, 5 patients of Group B, and 6 patients of Group C, easily corrected with crystalloid infusion (Table 5).

The incidence of side effects was remarkably minimal. The most common side effects found in this study were hypotension, nausea and vomiting, pruritus, sedation, respiratory depression, and motor weakness.

Nausea and vomiting have been observed following epidural administration of all currently employed opioids and also local anesthetics. The incidence of nausea is dependent on many factors such as age, sex, and type of operation. In the present study, the incidence was 2 patients in Group A and 4 patients in Groups B and C, each. In this study, the incidence is almost equal in all the three groups, i.e. 13.3%. This corroborates with the findings of Torda *et al.*¹³

Pruritus was seen in 13.3% patients in Group B and 16.6% of patients of Group C. Respiratory depression was seen in only one patient of group B, easily managed by oxygen supplementation using the face mask.

Motor weakness was seen in 1 patient in Group A that is thought to be due to some motor blocking action of

bupivacaine. Opioid lack this effect and hence the choice for post-operative pain relief.

Remarkably no complication was noted in our study regarding the technique of epidural puncture or catheter insertion or removal. Only in three patients epidural failure (lack of post-operative analgesia) were seen and they were excluded from the study.

In our study, we also found that the post-operative epidural analgesia was satisfactory.

SUMMARY AND CONCLUSION

It is concluded from observations and results that combination of bupivacaine with fentanyl in thoracic epidural analgesia after upper abdominal surgery, comparatively showed the:

1. Better analgesic efficacy
2. Synergistic effect, short onset of action, longer duration of action (ranges from 150 to 280 min) with minimal side effects
3. Intensity of pain was least, associated with low pain scores and severity was also minimal at rest and during function (five level pain score)
4. The incidence of side effect which occurred was remarkably minimal.

The thoracic epidural is strongly recommended the technique for post-operative pain relief after upper abdomen surgery as it is highly beneficial for the patient, highly accepted by the surgeon also, and epidural fentanyl with bupivacaine provides effective, prolonged analgesia in comparison to either fentanyl or bupivacaine alone.

However, the present study invites positive criticism and hopes for further studies.

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Observation on Effects of Lumbar Epidural Analgesia for Painless Labor

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Abstract

Objective: To study the effects of epidural analgesia during labor on the mother and newborn. To find out the effects of epidural analgesia on the course of labor. To compare the epidural analgesia deliveries with those deliveries where no pain relief method is used.

Materials and Methods: This is a prospective observational study. A total of 50 primipara patients in labor were studied, and a comparative study was done with 50 deliveries as control during August 2007 to August 2009 in Choithram Hospital and Research Center, Indore.

Result: The Result of this study suggests that: (1) The progress of labor was not hampered in epidural group. (2) There was no significant difference in instrumental and caesarian section rate. (3) There was no serious complication, and there was no side effect of drugs applied or the technique itself. (4) There were good pain relief and high satisfaction in epidural groups.

Conclusion: The epidural analgesia does not affect the duration of labor and no bad effect on the fetus, and there was no increase in instrumental and operative procedures. Hence, this procedure is quite safe, well-accepted, and tolerated by patients.

Key words: Analgesia, Labor, Patients

INTRODUCTION

The distress and pain which women often endure while they are struggling through a difficult labor are beyond description.

We can change the perception of labor pain with the introduction of labor analgesia. Attempts to alleviate labor pain on demand have been made since the 18th century when analgesic drugs such as morphine and pethidine were used.

The credit of introducing the obstetrical anesthesia goes to three eminent physicians:

- James Young Simpson of Scotland

- John Snow of England
- Water Changing of USA.

In 1885, coring performed the first epidural block for relief of pain and the drug used was cocaine.

Epidural analgesia provides complete analgesia in the majority of laboring woman.¹

In a survey of 1000 consecutive patients who choose a verity of analgesic technique for labor and vaginal delivery, pain relief and overall satisfaction with birth experience were grater in patients who received epidural analgesia.²

According to ACOG and The ASA - "In the absence of a medical contraindication, maternal request is sufficient medical indication for pain relief during labor."³

MATERIALS AND METHODS

The patients included for study were those admitted in labor ward of Choithram Hospital and Research Center, Indore, from August 2007 to August 2009.

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My study was prospective observational study, and data collection was done by observing patients in labor room.

A total of 50 cases were studied in this series, and a comparative study was made with 50 deliveries as control during the same period. Inclusion and exclusion criteria which taken into account were as the following section.

Inclusion Criteria

- Primipara at term (in labor)
- Single fetus in cephalic presentation
- Cervical dilatation of more them 2-3 cm
- No contraindication to administration of epidural analgesia.

Exclusion Criteria

- Patients were excluded if they received an opioid drug preceding epidural analgesia
- Patients with H/O coagulation disorder
- Patients with malpresentation and multiple pregnancy
- Patients with major degree of CPD.

A detailed history was taken and a thorough general physical and obstetrical examination was done and patient's consent was taken before giving epidural analgesia. Epidural analgesia was given only when labor was well established, and cervix was at least 3-4 cm dilated. In epidural analgesia, small doses of medicine introduced into lower back spine into epidural space (L3-4) using 18 G epidural catheter. Initially, 8 ml bolus (0.125% of bupivacaine with 50 mg fentanyl) was given followed by infusion of 0.0625% bupivacaine +2 mg/ml fentanyl at 6-8 ml/h.

Once the baby is delivered the infusion was stopped and catheter was removed once episiotomy is sutured. Close watch on blood pressure, pulse, respiration was given.

RESULT

In this study, we have shown in Tables 1-5.

Figure 1 shows that there was no significant difference between epidural and control groups.

One lower segment cesarean section (LSCS) was required in epidural group because of non-progress of labor, where in control Group 4 cases underwent LSCS one because of non-progress of labor and 3 because of fetal distress.

There was no fetal mortality in any group.

Around 43 cases of the epidural group were completely relieved of pain and 7 cases were partially relieved, whereas no one was relieved of pain in control QMP.

Patients satisfaction: About 45 patients of epidural group were fully satisfied and 5 patients were partially satisfied. Whereas no patient was fully satisfied in control group, but 4 patients to were satisfied even without any pain relief (Figures 2-5).

DISCUSSION

Painless labor with epidural analgesia has various advantages which includes the following section.

- Absolute pain relief
- Patient remains conscious and cooperative
- Depressant drugs are avoided

Table 1: Average duration of second stage of labor

Group	Average duration of 2 nd stage of labor (min)	Maximum duration of 2 nd stage of labor
Epidural group	39 min	1 h 10 min
Control group	43 min	1 h

P>0.1, *Z*=1.47

Table 2: Mode of delivery

Type of delivery	Epidural group (%)	Control group (%)
Spontaneous	36 (72)	37 (74)
Forceps	02 (04)	02 (04)
Ventouse	11 (22)	07 (14)
LSCS	01 (02)	04 (08)

P>0.05, means no significant sufferance in both groups, LSCS: Lower segment cesarean section

Table 3: Maternal morbidity and mortality

Type of trauma	Epidural group (50) (%)	Control group (50) (%)
Hypotension	03 (06)	Nil
Episiotomy	46 (92)	44 (88)
Perineal laceration	03 (06)	05 (10)
PPH	02 (04)	04 (08)
Urinary retention	12 (24)	01 (02)
Pruritus	04 (08)	Nil

Table 4: Fetal morbidity and mortality

APGAR score	Epidural group (%)	Control group (%)
1 min (<7)	12 (24)	10 (20)
7-10	38 (76)	40 (80)
5 min (<7)	0 (0)	0 (0)
7-10	50 (100)	50 (100)

Table 5: Comparison of degree of pain relief

Pain relief	Epidural group (%)	Control group (%)
Complete	43 (86)	Nil (06)
Partial	07 (14)	Nil (06)

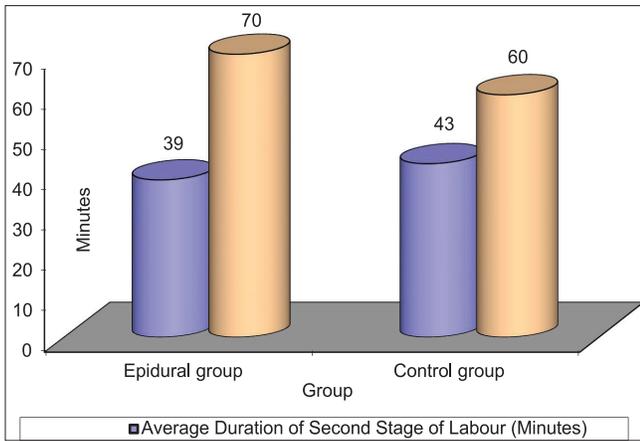


Figure 1: Comparison of duration of second stage of labor in epidural and control group

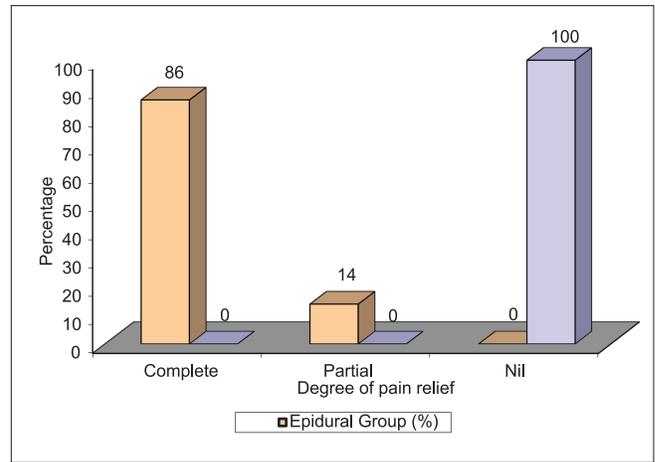


Figure 4: Degree of pain relief

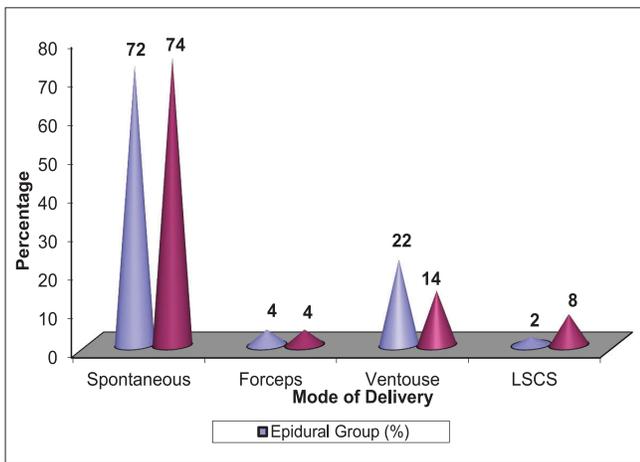


Figure 2: Comparison of mode of delivery

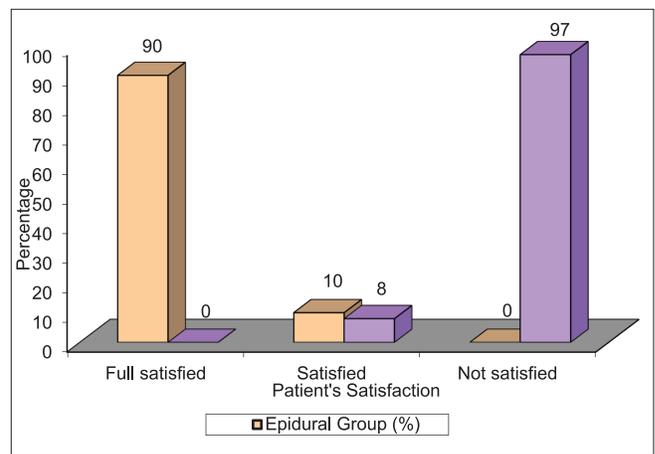


Figure 5: Comparison of patient's satisfaction

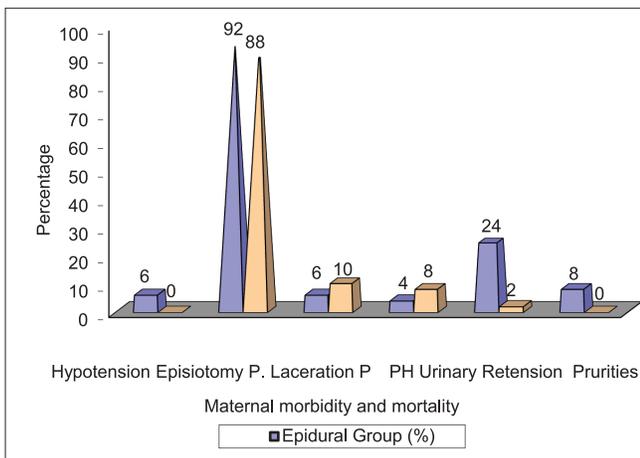


Figure 3: Maternal morbidity and mortality

- Operative delivery can be carried out whenever required without general anesthesia and its attendant risks

- Relaxation of pelvic floor and cervix results in minimal injury to the soft tissues
- Episiotomy and its repair can be carried out without delay
- The third stage is shortened, manual removal of the placenta can be accomplished without general anesthesia a blood loss is reduced.

In 1965, bupivacaine was used in instead of Lidocain because this drug had very minimal motor block effect. It causes more sensory block and its duration of action is more than Lidocain.

There is prolongation of the 2nd stage of labor as shown in various studies^{4,5} but prolongation of second stage is not itself harmful to the fetus as long as maternal and fetal well-being preserved.

A retrospective study by Cohen *et al.*⁶ on 4403 primipara found “no relationship between Apgar and duration of the second stage of labor.”

There is no significant prolongation of second stage of labor in the epidural group in our study.

In this study, there is no significant prolongation of second stage of labor in both epidural and control group.

In this study, it is seen that there is no increase of instrumental and operative delivery in the epidural group. This finding is supported by various studies example:

Bailey *et al.*⁷ and Doughty⁸ had earlier reported that the patterns of obstetric intervention both before and after the establishment of epidural services were similar.

Impey *et al.* in a retrospective analysis of 1000 pregnancies found that increased use of epidural had no effect on operative delivery rate.⁹

There was no serious complication and there were no side effect of drugs applied or the technique itself.

Few side effects commonly seen in epidural group are as follows:

- Urinary retention
- Pruritus
- Hypotension.

These side effects are managed easily with the encouragement of frequent voiding, antiallergic, and prophylactic hydration. Epidural analgesia does not decrease uterine flow even after temporary hypotension.

Careful patient evaluation, meticulous technique during epidural catheter placement, appropriate doses of medication and close monitoring minimize the risk of serious complication.

CONCLUSION

In our country, pain relief during labor is still in infancy. Mass awareness and public illiteracy and shortage of trained personnel could be the main reasons. The conclusion of our study was that the epidural analgesia does not affect the duration of labor and is not associated with any adverse effect on the fetus; there was no bad effect on third stage of labor, no significant prolongation of the second stage of labor, no significant incidence of instrumental and operative delivery and it gave the excellent pain relief with full consciousness. Almost all patients viewed this experience as luxurious labor. On the whole, it can be said that in this study there was no effect seen on fetus and mother, procedure is quite safe, well tolerated and accepted by patients and it carries a special place in modern obstetrics and is going to be a very popular technique in our country as well in future.

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Effects of Deviated Nasal Septum on Sinus Mucosa: A Cadaveric Study

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Abstract

Introduction: A role of deviated nasal septum in nasal obstruction may result into recurrent or chronic sinus infection (sinusitis), as it may block openings of paranasal air sinuses.

Materials and Methods: In this study, we have taken one control group (cadavers with midline septum) and one study group (cadavers with deviated nasal septum). From both groups, mucosa of maxillary sinus was taken.

Results: It was found that in the control group, there were no changes in mucosa or submucosa, but in this study, group findings were suggestive of acute and chronic inflammation.

Conclusion: This proves a strong correlation between deviated nasal septum and chronic sinusitis.

Key words: Chronic sinusitis, Deviated nasal septum, Maxillary ostium, Maxillary sinus mucosa

INTRODUCTION

The nasal septum plays a major role in both formation and function of the nose. Deviation of the nasal septum is extremely common. Theile¹ was first to calculate the frequency (22%) of nasal septum deviation. McKenzie² studied over 2000 European skulls and found that only 23% had a straight septum. Septal deviation has an unfavorable influence on sinus ventilation and drainage. Ganjian *et al.*³ observed that ostial patency is essential to the function of the maxillary sinus. Normally, all paranasal air sinuses open into the lateral wall of the nasal cavity by various small ostia. A deviated nasal septum can obstruct these ostia and may trap fluid in a sinus causing recurrent or chronic sinusitis. Elahi and Frenkiel⁴ found an increased incidence and severity of bilateral chronic sinus disease with increasing septal deviation.

This study was done in cadavers to study the septal deviation and its role as a cause for chronic sinus disease.

MATERIALS AND METHODS

This study was conducted in the Department of Anatomy at Himalayan institute of Medical Sciences, Jolly Grant, Dehradun, Uttarakhand and Shri Guru Ram Rai Institute of Medical and Health Sciences, Dehradun, Uttarakhand. We have divided this study into two groups.

Group - A (Control): It comprised 15 cadavers with a midline nasal septum.

Group - B (Study): It comprised 15 cadavers with a deviated nasal septum.

Total we have taken 30 cadavers. Cadavers with gross external nasal deformity, abnormal mass, or polyps in the nasal cavities were excluded from the study. The head and face regions were cut sagittally just to the right of the midline. The cadavers were examined for midline or deviated nasal septum and associated paranasal sinus involvement.

We observed the following parameters:

- I. Nose:
 - The nasal septum was examined to find out whether in midline or deviated. If deviated:
 1. Side - right or left
 2. Shape - C-shaped or S-shaped
 3. Deformity in cartilaginous part or bony part or both.

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II. Paranasal sinuses:

In this study, only maxillary sinus was taken into account because of all paranasal sinuses - maxillary sinuses are most constant in shape and size, and also most commonly involved in chronic sinusitis.⁵

We observed the following parameters:

1. Patency and size of maxillary ostium - it was done with the help of probes of different sizes and were measured with the help of sliding caliper
2. The volume of maxillary sinus - it was measured with the help of mustard seeds, funnel, and volumetric jar. Mustard seeds being more or less circular leave no interseed space when fully packed and also cost-effective. These were filled in volumetric jar up to a measured level. The sinuses were filled through the ostia by means of a funnel with mustard seeds⁶
3. Histological study of mucosa is taken from maxillary sinus - it was fixed in 10% formalin and further processed for paraffin sections and were stained by Hematoxylin and Eosin method.

The results were compared between two groups.

RESULTS

I. Nasal septum:

1. Side Incidence - In Group B, it was observed that right sided deviation found in 47% cases while left-sided deviation was in 53%
2. In 80% cases, C-shaped deviation on both sides was found while S-shaped deviation was much less in comparison to C-shaped (Figure 1)
3. Incidence of deviation of the cartilaginous part was much more (80%) than bony part (20%).

II. Maxillary sinus:

1. Patency and size of maxillary ostium - The reading observed in Group B was statistically significant ($P < 0.01$, Figure 2)
2. Volume of maxillary sinus - The reading observed in Group B was statistically significant ($P < 0.001$, Figure 3)
3. Histological Examination - On microscopic examination of mucosa is taken from cadavers of both groups, it was observed as follows:

Group A - Most of the cadavers (73.4%) had normal mucosa (pseudostratified ciliated columnar epithelial lining without erosion) (Figure 4).

Group B - Findings suggestive of acute (20% cadavers) as well as chronic inflammation (80%) were found.

- Acute inflammation: There was epithelial erosion, congested, and dilated blood vessels with infiltration of polymorphs (Figure 5)

- Chronic inflammation: Glands were seen hyperplastic along with eroded epithelium. Edema was seen in submucosa beneath the epithelium (Figure 6). Infiltration of lymphocytes and polymorphs is also seen (Figure 7).

DISCUSSION

In this study, the incidence of left-sided nasal septal deviation was found to be more (53.3%) than that of right side which was seen in 46.7% cadavers. The c-shaped

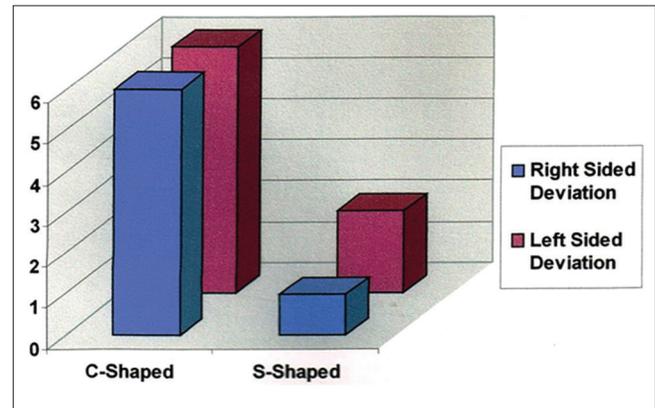


Figure 1: Incidence of right and left sided deviation according to shape of nasal septal deviation in Group B

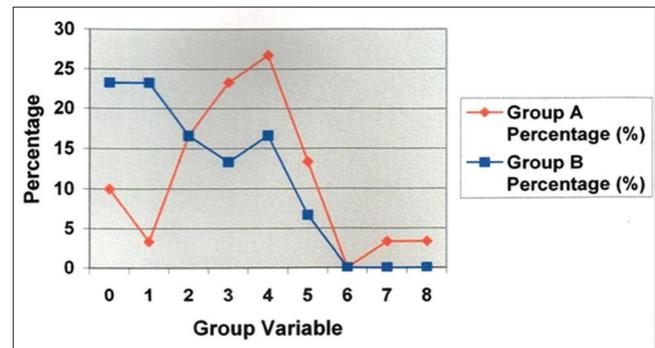


Figure 2: Comparison of incidence of number of cadavers in different group variables of size of ostium in both groups

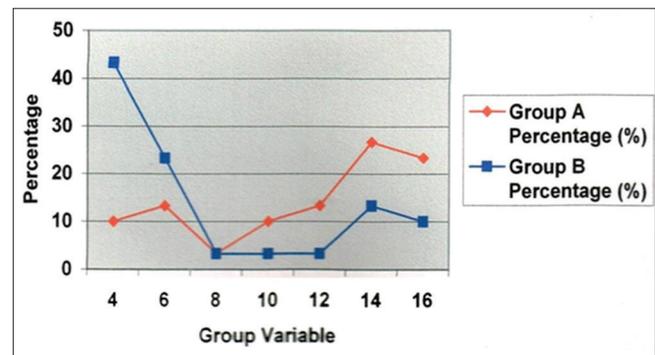


Figure 3: Comparison of incidence of number of cadavers in different group variables of volume of maxillary sinuses in both groups

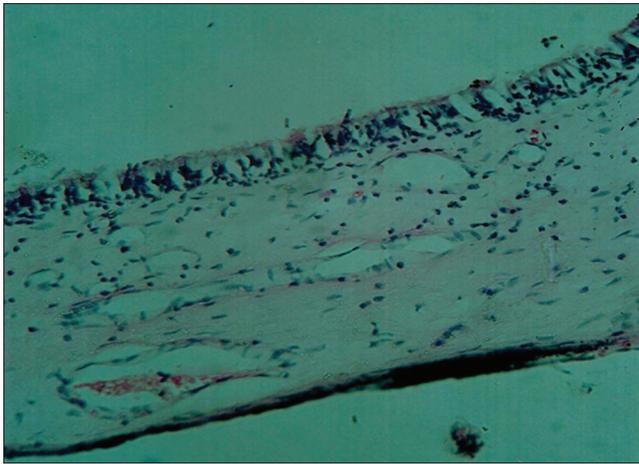


Figure 4: Normal histology of maxillary sinus mucosa of midline septum cadaver showing pseudostratified ciliated columnar epithelium, (H and E, ×200)

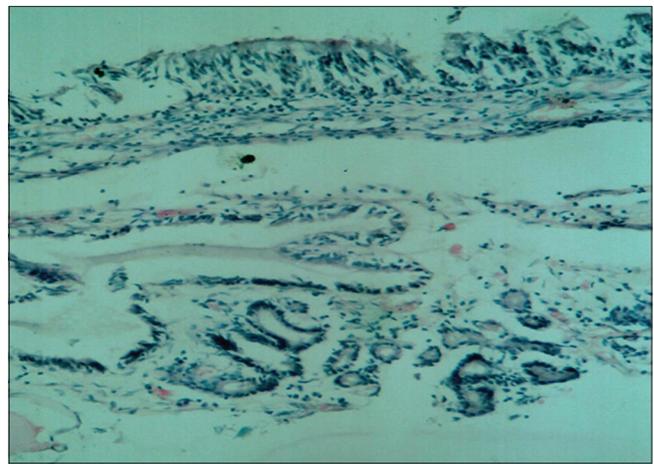


Figure 6: Sinus mucosa of deviated septum cadaver showing chronic inflammation. Epithelial erosion is seen along with edema in submucosa. Gland is too much enlarged and hyperplastic in nature, (H and E, ×200)

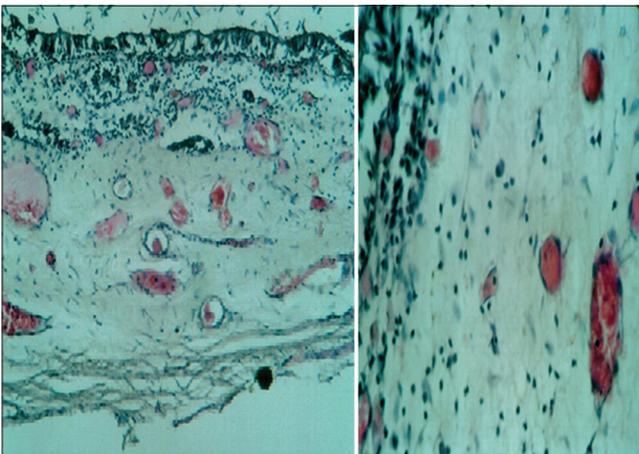


Figure 5: Sinus mucosa of deviated septum cadaver showing acute inflammation dilated and congested blood vessels are seen with infiltration of polymorphs (H and E ×200), (H and E, ×400)

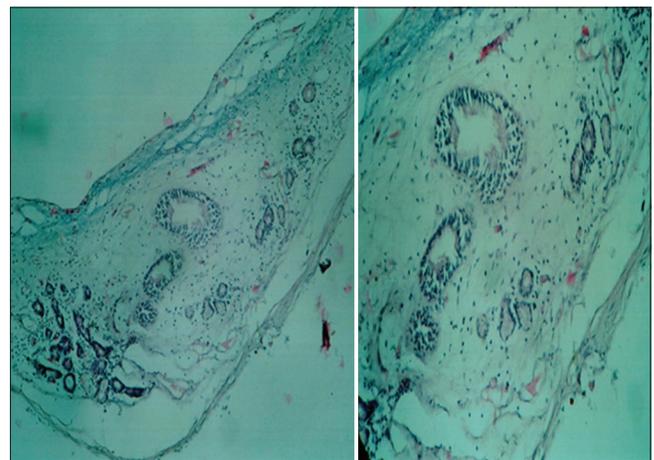


Figure 7: Sinus mucosa of deviated septum cadaver showing chronic inflammation. Epithelium not well marked. Edema and cellular predominance in submucosa. Glands are exceedingly numerous and hyperplastic, (H and E, ×100), (H and E, ×200)

deviation was more common than S-shaped deviation. Sinha and Maheshwari⁷ also reported this in anatomical study on skulls (879) from different provinces; they found 25% incidence of deviation of bony septum. They also found left sided deviation more common than the right side.

In Group A, the average size of ostium was 3.65 mm while in Group B it was 2.15 mm. Statistically this difference was found to be highly significant ($P < 0.01$). In previous studies, Francis and Mathew⁸ found that ostium size averages 2.4 mm but can vary from 1-17 mm, whereas Saijo *et al.*⁹ found it to be 6.8 mm (range 3.7-14.5). Less diameter of the maxillary ostium of Group B signifies that edema of mucosa surrounding it can markedly reduce the size of the ostium.

In this study, the average volume of maxillary sinus was 10.16 cc (range 3-16 cc) in Group A while in Group B it was 6.13 cc (range 2-16 cc). Thus, it was less in Group B than Group A ($P < 0.001$). This finding correlated well with the size of ostium. In previous computed tomography research studies, Sanchez *et al.*¹⁰ found that volume of maxillary sinus was 13.07 cm³ while according to Francis and Mathew⁸ it was 15 ml.

In this study, we observed that most of the cadavers had normal mucosa in Group A while cadavers in Group B had marked changes in the mucosa of maxillary sinus like acute as well as chronic inflammation. In both these groups, there was correlation of histological findings with other measurements like size of ostia and volume of the sinuses.

All these findings suggestive of inflammatory changes of sinus mucosa were more marked in cadavers of Group B.

In this study, it was found that all cases of chronic maxillary sinusitis were associated with anatomical variations and most common was deviated nasal septum.

CONCLUSION

In this study, histopathology of maxillary sinus mucosa was done which proves a strong correlation of deviated nasal septum with chronic sinusitis. It is, therefore, necessary that the management of chronic maxillary sinusitis should include simultaneous treatment of deviated nasal septum.

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Effect of Oral Awareness Intervention on Dental Caries Prevalence among 3-6 Years Old School Children in Mumbai City

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Abstract

Introduction: Dental caries is the predominant cause of tooth loss in children and young adults. It is still a major oral health problem in most industrialized areas affecting 60-90% of school children and vast majority of adults. Although the disease most commonly affects the crown of the tooth, caries of the tooth root is also prevalent. The localized prevalence data is essential not only to understand the disease but also plays a vital role in prevention and treatment planning.

Aim: To investigate the effectiveness of oral awareness to reduce the prevalence of caries.

Materials and Methods: The present study was a cross-sectional analytical study conducted among school going children in two government schools, one at Dadar and the other at Bandra in Mumbai City, Maharashtra in the month of July - August 2015. These two schools were selected so as to establish similar socio-economic status of the study population. In one of the schools, i.e., at Bandra, there was an already ongoing oral health awareness program conducted on a yearly basis wherein all school going children are given oral health talk and made aware of practicing oral hygiene techniques. Comparison of (number of teeth) between the schools was done by Chi-square test.

Results: The number of children found to be brushing in Dadar was 24 and in Bandra were 259. It was found that the most common type of decay occurring was occlusal caries and the least common is root piece variety. The most commonly affected is primary left lower second molar and the least commonly affected tooth is primary right lower canine.

Conclusion: From the present study, it can be concluded that oral awareness and its implementation in daily life leads to significant decrease in caries prevalence.

Key words: Awareness, Dental Caries, Rampant caries, School children

INTRODUCTION

Shafer (1993) had defined dental caries as¹ an irreversible microbial disease of the calcified tissues of the teeth, characterized by demineralization of the inorganic portion and destruction of the organic substance of the tooth which often leads to cavitation.¹ Dental caries is the predominant cause of tooth loss in children and young

adults. It is still a major oral health problem in most industrialized areas affecting 60-90% of school children and vast majority of adults. Although the disease most commonly affects the crown of the tooth, caries of the tooth root is also prevalent. It interferes with the normal nutrition intake, speech, self-esteem, and daily routine activities of the children.³ The principal causative agents are a group of streptococcal species. However in the past decade, rapid changes have been taking place and significant improvements in oral health statuses due to factors, such as changing patterns of sugar consumption, improved oral hygiene, effective use of fluorides,² changing lifestyles and standard of living, establishment of school based preventive programs, and effective use of oral health services, are seen. At 3-6 years of age, all the primary teeth would have erupted. It is also one of the index ages

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for oral health assessment suggested by the WHO.² The localized prevalence data is essential not only to understand the disease but also plays a vital role in prevention and treatment planning.

Aim

To investigate the effectiveness of oral awareness to reduce the prevalence of caries.

MATERIALS AND METHODS

The present study was a cross-sectional analytical study conducted among school going children in two government schools, one at Dadar and the other at Bandra in Mumbai city, Maharashtra in the month of July-August 2015.

These two schools were selected so as to establish similar socio-economic status of the study population. In one of the schools that are at Bandra, there was an already ongoing oral health awareness program conducted on a yearly basis wherein all school going children are given oral health talk and made aware of practicing oral hygiene techniques that are brushing by a team of dental experts. Before the start of the study, all necessary permissions were taken from Y. M. T. Dental College Ethical Board. Examination of all study subjects was done in a dental camp where in study subjects were randomly selected, and American Dental Association Type 3 examination was done. Each child was examined using diagnostic tools and the number of tooth surfaces and the type of decay was noted. The age was taken from the school records the sex of the child was also recorded. The study was conducted by experienced dental students in their last year of dentistry. The clinical examination was conducted under natural light. Permission to carry out such kind of examination was taken from the principal of the respective schools. Study subject was such selected that an equal representation of the sample was achieved pertaining to independent variable like age. Sample size determination was done before the start of the study using a single proportion formula where assuming that the disease level (dental caries) to be at 50%. Thus, a sample size of 384 per school was taken as the minimum sample size. However, 400 students from each school aged 3-6 years were included in the present study. A standard recording performa was used in the present study which was designed by consulting experts in the field. The performa also had a question asking about brushing after meals. The decayed teeth were recorded taking into account (the number of teeth decayed and the number of surfaces along with the type of decay).

Statistical Analysis

The recording sheets were serially numbered, data obtained were compiled onto MS Office excel sheet version 2010.

Results are expressed as % and frequency between the schools using statistical package for social sciences (SPSSV.22.0, 1BM).

RESULTS

A total of 800 questionnaires were distributed among two government schools located in Bandra and Dadar, respectively. They were collected and assessed. The age group for the survey was taken between 3 and 6 years. In Dadar, 231 males and 169 females were examined, whereas in Bandra 226 males and 174 females were examined. In this study, it was found that 4% of the children brushed twice in Dadar and 72.2% of children brushed in Bandra. The number of children found to be brushing in Dadar was 24 and in Bandra were 259. From the next question, it was found that the most common type of decay occurring was occlusal caries 49.6% in Dadar and 27.6% in Bandra and the least common is root surface caries that is 0.3% in Dadar and 0% in Bandra. Proximal caries were 28.3% and 16.3% in Dadar and Bandra, respectively. Smooth surface caries were 13.7% and 14.3% in Dadar and Bandra, respectively, and grossly decayed were 7% and 6.6% (Figure 1). The most commonly affected is primary left lower second molar and the least commonly affected tooth is primary right lower canine. There are 14 numbers of rampant caries cases present out of 800 and 16 number of nursing bottle caries cases out of 800.

DISCUSSION

The rise in the prevalence of dental caries among the people of developing countries is a cause for concern. In the current study, it is found that 42.5% of children in Bandra and 69.75% of children in Dadar have one or the other form of caries. According to a study conducted in

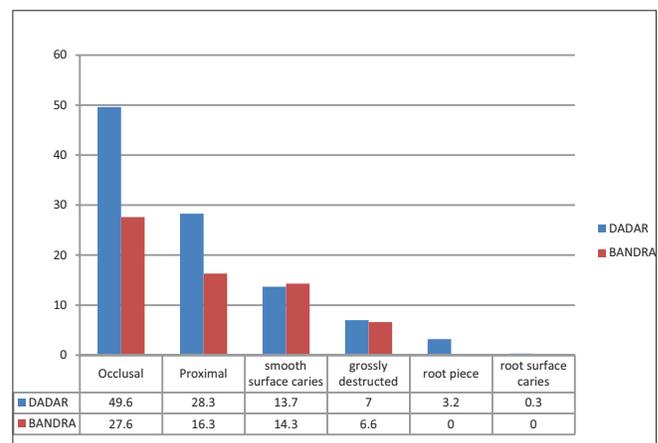


Figure 1: Comparison of caries prevalence in Dadar School and Dandra School

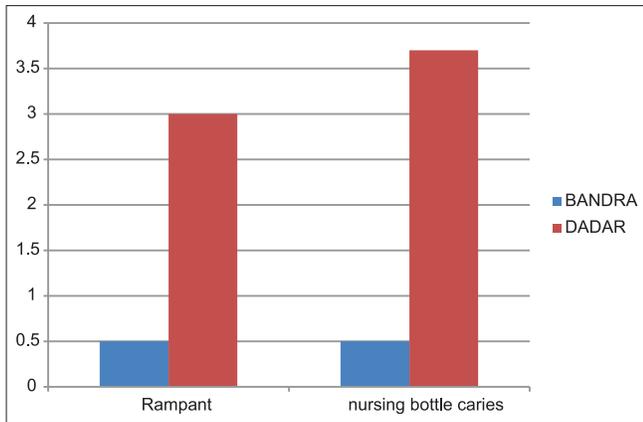


Figure 2: Comparison of rampant and nursing bottle caries in Dadar and Bandra schools

Northern Palestine², 76% of the children of 4-5 years of age have caries. When compared to other countries like Pakistan, it is revealed that caries prevalence in pre-school children is about 50-60% which is similar to the findings of the current study. In United Arab Emirates,² a high prevalence of caries among pre-school children has been registered to be about 70-80%. In the United Kingdom,⁴ the numbers are 40-60%. While in Brisbane,⁶ it is around 66% (4-6 years) and in Sweden⁵ 69% of 3-year-old pre-school children have caries. Tooth affected with dental caries is like a one-way street, once in there is no going back. The only option is to get the necessary treatments done which in turn diminish the natural strength and vitality of the tooth. Another way is to prevent the entry of caries itself which can be done mainly through oral awareness.

People need to be made aware of the types of decay, how they occur, how they can be prevented from infecting the tooth by adopting basic measures such as brushing twice regularly, stoppage of in-between meal snacks, flossing, and using mouthwashes. The present study was conducted among school going children between the ages of 3-6 to measure the effectiveness of oral awareness to reduce the prevalence of caries. The age Groups 3-6 were selected to study the caries status of the primary dentition. In this study, it was found that 4% of the children brushed twice in Dadar and 72.2% of children brushed in Bandra. As to whether, there is any difference in the prevalence of caries among boys and girls cannot be judged accurately due to the limited sample size of 400 each from both the schools.

The most common type of decay is the occlusal type as seen on the data chart present in both schools. 49.6% of the decay in Dadar and 27.6% in Bandra were found to be of the occlusal type. The least occurrence of the type of decay was found to be of the root caries variety. The most common tooth to be affected is the mandibular left deciduous second molar with 23.8% decay seen in Bandra and 29% seen in Dadar. It is also seen that deciduous molars and centrals are the most commonly affected teeth. The cause for this could be a number of reasons ranging from oral hygiene practices to patterns of sugar consumption. Hence, care must be taken and preventive measures such as applying preventive resin restoration, sealants, and must be undertaken. The study also included cases involving rampant and nursing bottle caries. It was found that Bandra recorded fewer cases of rampant/nursing bottle caries as compared to Dadar (Figure 2). Such Difference in the findings between the two schools could be attributed to higher awareness among children of Bandra of oral hygiene. By comparing both the areas, it can be seen that Bandra shows relatively fewer caries incidence as compared to Dadar.

CONCLUSION

From the present study, it can be concluded that oral awareness and its implementation in daily life leads to significant decrease in caries prevalence.

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Incidence of Infectious Complications in Central Venous Catheterization: Internal Jugular versus Subclavian Route

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Abstract

Introduction: Central venous catheters (CVC) are increasingly becoming an essential component of modern critical care. Despite their utility, placement of CVCs is often associated with mechanical, infectious, and thromboembolic complications.

Purpose: The present study was designed to compare the incidence of infectious complications in CVC by landmark technique between two routes (internal jugular and subclavian).

Materials and Methods: After approval from the Hospital Ethical Committee, the present study was conducted in 100 patients admitted to the medical intensive care unit (ICU)/surgical ICU of Shri Ram Murti Smarak Institute of Medical Sciences who underwent CVC for various reasons. Patients were divided into two groups: Group A - Internal jugular vein (IJV) and Group B - Subclavian vein with 50 patients in each group.

Results: The incidence of infectious complications in our study was 12% (exit site infections 7%, catheter tip infections 3%, and catheter-related bloodstream infection [CRBSI] 2%). The incidence of infectious complications in the internal jugular group (exit site and catheter tip) was more as compared to the subclavian group. The incidence of infection in IJV group can be attributed to its proximity to the oral cavity where the presence of oral secretions can result in infection at this site. The incidence of CRBSI was similar in both groups (2%). The *P* value obtained after application of Z-test to these proportions gave a value which was more than 0.05 showing that this difference was statistically insignificant.

Conclusion: Internal jugular route was associated with higher incidence of infectious complications as compared to the subclavian route of CVC, but statistically the difference was found to be insignificant.

Key words: Catheter tip infections, Catheter-related bloodstream infections, Central venous catheterization, Exit site infections, Internal jugular vein, Subclavian vein

INTRODUCTION

Central venous catheters (CVCs) are increasingly becoming an essential component of modern critical care.¹ CVCs are commonly inserted for hemodynamic monitoring, volume monitoring, administration of medications, long-term total

parenteral nutrition, access for renal replacement therapy, cardiopulmonary resuscitation, and difficult peripheral catheterization.²

Despite their utility, placement of CVCs is often associated with mechanical, infectious, and thromboembolic complications.¹

Hospital-acquired infection is a serious problem in the intensive care unit (ICU), the susceptibility of patients in the ICU, combined with the risk factors associated with the invasive treatments and monitoring that they may be receiving, and the ICU environment itself, contribute to the increased risk of infection in this patient group.³

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There has been very little data reported from adult Indian ICU on the rates of infectious complications associated with CVC insertions.⁴

Hence, in the present study, the incidence of infectious complications during CVC by landmark technique was studied, and comparison of two routes - internal jugular and subclavian routes were done.

MATERIALS AND METHODS

After approval by Hospital Ethical Committee, the study on CVC insertions by landmark technique was conducted in the ICU on 100 patients in Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly.

Informed consent was obtained either from the patient or his or her relative. Baseline data on each patient such as name, age, sex, admission number (I.P No.), body mass index, primary diagnosis, need for CVC insertion, site of CVC insertion, were recorded.

Patients were divided into two groups alternately: Group A - Internal jugular vein (IJV) and Group B - Subclavian vein (SCV) with 50 patients in each group.

Inclusion Criteria

About 100 patients admitted to medical ICU (MICU)/surgical ICU (SICU) of SRMS-IMS needing insertion of CVC for various reasons.

Exclusion Criteria

1. Patients with infections at puncture site
2. Deranged coagulation profile
3. Contralateral pneumothorax
4. Trauma to clavicle and upper ribs
5. Distorted anatomy of neck of clavicle
6. Cervical spine trauma
7. Post-surgical/radiotherapy.

Painting and Draping

Complete sterile-barrier precautions were followed for all CVC insertions. Strict hand washing was followed by person inserting central venous line and assisting nurse with 2% chlorhexidine for skin disinfection and wore masks, gloves, surgical gowns, and hair covers. After anatomical landmarks were visualized, the skin was prepared with chlorhexidine and draped. Lidocaine (1%) was used for local anesthesia, and the patient was sedated at the discretion of the operator.

Procedure

All cannulations were performed either by an ICU consultant or by 3rd year registrar (with a minimum prior experience

of at least 25 CVC insertions), under the supervision of a consultant. Each CVC insertion attempt was considered a new attempt, and if a cannulation attempt failed and was subsequently performed by another operator, these were considered as separate insertion events. By protocol, all catheters were inserted via a modification of the original Seldinger technique.

Post Procedure

Once the CVC was inserted, it was sutured into place with 2-0 silk sutures and covered with a sterile dressing. Catheter position was preliminarily confirmed by return of blood and free flow of fluid through all ports.

Procedure characteristics were the date of insertion, site of insertion, time of procedure (day defined as 8 am to 8 pm, night as 8 pm to 8 am), number of percutaneous punctures, and whether the procedure was emergent or elective.

The procedure was defined as emergent if the operator judged that 1-h delay would be harmful. Later caring of CVP line was done by trained ICU nurse.

Follow-up

All patients were followed-up daily, and the central venous insertion site was examined for purulence or soiling. If an exit site infection was suspected, exit site swabs were sent for microbiological analysis.

If catheter tip colonization/infection or catheter-related bloodstream infection (CRBSI) were suspected, the CVC was removed and the tip of the catheter along with two sets of blood was sent for culture analysis. CVC was inspected for the presence of infection until day 7 of catheter insertion.

1. Exit site infection - Erythema, tenderness, induration, or purulence within 2 cm of skin at the insertion site of catheter along with microbiological growth on culture of the purulent exudates
2. Catheter tip colonization - Growth of more than 15 colony forming units on culture of the distal segment of the CVC with clinical signs of infection
3. CRBSI - Isolation of the same organism from the catheter tip culture and at least one of two blood cultures, along with signs and symptoms of infection.

Statistical Analysis

Data were entered using Microsoft Excel 2010 and statistical analysis was done using IBM SPSS v 20.0.0. Categorical variables were analyzed using proportions and percentages. The absence of selection bias was ascertained using Chi-square test in the demographic distribution table and the difference between proportions was analyzed using Z-test for proportions. $P < 0.05$ was considered statistically significant.

RESULTS

The proportion of infectious complications was higher when CVCs were inserted by internal jugular venous route (8%) as compared to the subclavian venous route (4%). The difference in proportions was tested using Z-test for proportions which gave a *P* value of more than 0.05 showing that the difference is statistically not significant (Graph 1).

The incidence of exit site infection was found to be more in IJV cannulations (10%) as compared to subclavian cannulations (4%). Z-test was applied to test the proportions which gave a *P* value of more than 0.05 showing that the difference is statistically not significant (Table 1 and Graph 2).

The incidence of taking two or more attempts at CVC insertion was found to be higher in internal jugular CVC (12%) and subclavian venous catheterization (10%). Z-test for proportions was applied to test the proportions which gave a *P* value of more than 0.05 showing that this difference is statistically not significant (Graph 3).

The incidence of catheter tip infection was found to be more in IJV cannulation (4%) in comparison to subclavian

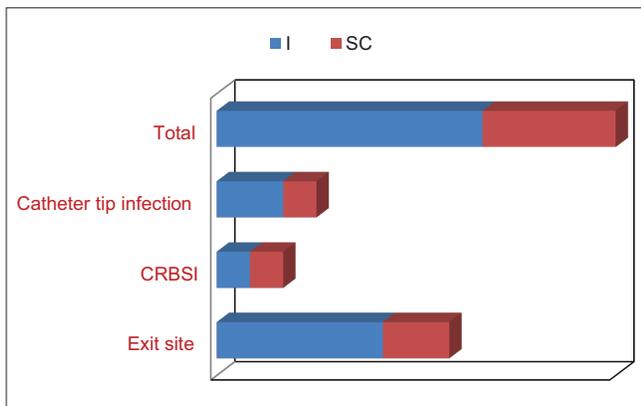
cannulation (2%). Z-test was applied to test the proportions which gave a *P* value of more than 0.05 showing that this difference is statistically not significant and could be by chance (Table 2 and Graph 4).

The proportion of CRBSI was found to be similar in both IJV and SCV groups (2%), and the *P* value obtained after application of Z-test to these proportions gave a value which was more than 0.05 showing that this difference is statistically not significant (Table 3 and Graph 5).

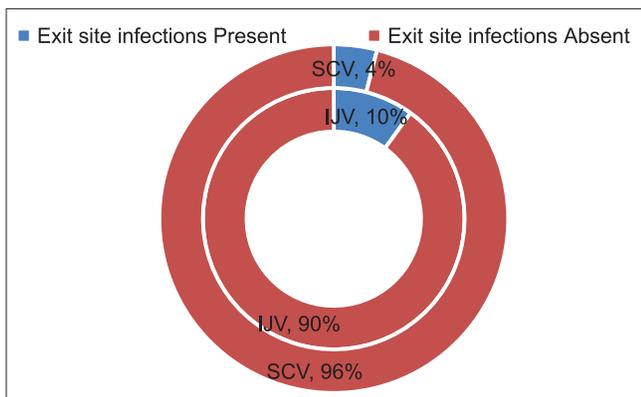
DISCUSSION

Complications associated with CVCs had a major impact on the hospital course of patients admitted to the ICU due to the morbidity, mortality, and increased healthcare costs associated with them.⁴

The present study was designed to compare the incidence of infectious complications in central venous cannulation by landmark technique between two routes (internal jugular and subclavian). After approval from the hospital ethical committee, the present study was conducted in 100 patients admitted in MICU/SICU who underwent central venous



Graph 1: Incidence of infectious complications



Graph 2: Incidence of exit site infections in IJV and SCV

Table 1: Incidence of exit site infections in IJV and SCV

Incidence of exit site infections in IJV and SCV	Site of insertion, N (%)		Total
	IJV	SCV	
Exit site infections			
Present	5 (10.0)	2 (4.0)	7
Absent	45 (90.0)	48 (96.0)	93
Total	50 (100.0)	50 (100.0)	100

IJV: Internal jugular vein, SCV: Subclavian vein

Table 2: Incidence of catheter tip infections in IJV and SCV

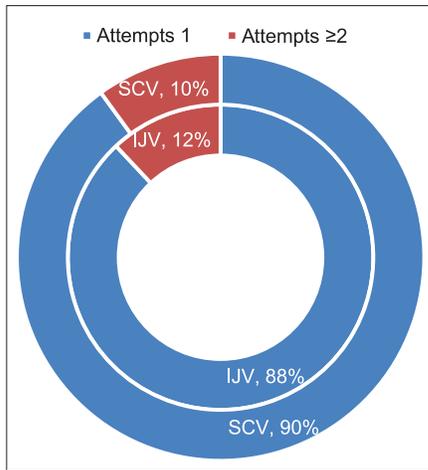
Incidence of catheter tip infections in IJV and SCV	Site of insertion, N (%)		Total
	IJV	SCV	
Catheter tip infections			
Present	2 (4.0)	1 (2.0)	3
Absent	48 (96.0)	49 (98.0)	97
Total	50 (100.0)	50 (100.0)	100

IJV: Internal jugular vein, SCV: Subclavian vein

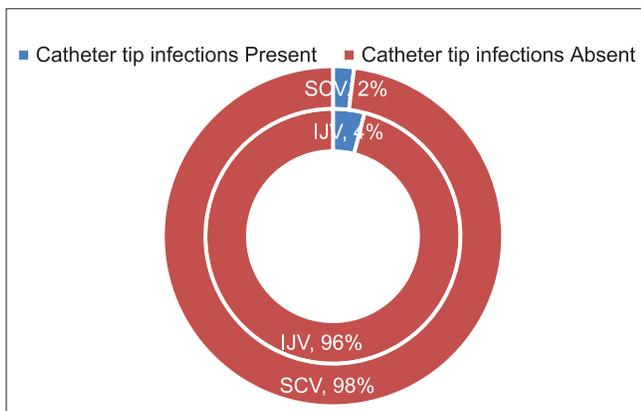
Table 3: Incidence of CRBSI in IJV and SCV

Incidence of CRBSI in IJV and SCV	Site of insertion, N (%)		Total
	IJV	SCV	
CRBSI			
Present	1 (2.0)	1 (2.0)	2
Absent	49 (98.0)	49 (98.0)	98
Total	50 (100.0)	50 (100.0)	100

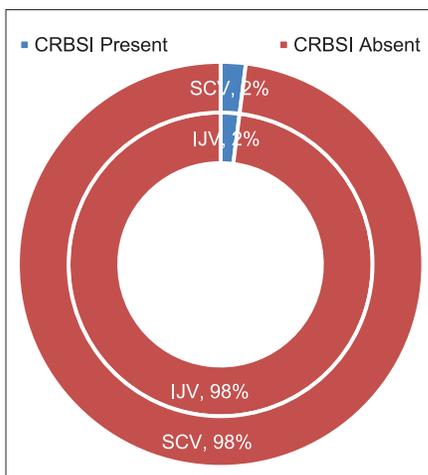
CRBSI: Catheter-related bloodstream infection, IJV: Internal jugular vein, SCV: Subclavian vein



Graph 3: Number of attempts during cannulation



Graph 4: Incidence of catheter tip infections in IJV and SCV



Graph 5: Incidence of CRBSI in IJV and SCV

cannulation for various reasons. Patients were divided into two groups: Group A - IJV and Group B - Subclavian with 50 patients in each group.

The incidence of infectious complications in our study was 12% (exit site infections 7%, catheter tip infections 3%,

and CRBSI 2%) (Graph 1). The incidence of infectious complications in the internal jugular group (exit site and catheter tip) was more as compared to the subclavian group. The incidence of infection in IJV group can be attributed to its proximity to the oral cavity where the presence of oral secretions can result in infection at this site. The incidence of CRBSI was similar in both groups (2%) (Table 3 and Graph 5). The *P* value obtained after application of Z-test to these proportions gave a value which was more than 0.05 showing that this difference is statistically insignificant.

Seven patients were found to have exit site infection in our study out of which 5 were in group-IJV and 2 in Group-SCV (Table 1). The CVCs were removed in all these patients and were sent for culture analysis. Out of these patients, only 3 CVCs had the presence of organisms on catheter tip. The other catheter tip cultures remaining sterile. The organisms that were isolated from the catheter tip were *Acinetobacter* and *Pseudomonas*. *Staphylococcus aureus* was found most commonly at the exit site which can be attributed due to its presence as a skin commensal and in the external environment.

The presence of CRBSI was confirmed only in two patients. *Acinetobacter* was isolated in these two patients. In the present study, the presence of infection was inspected till day 7 from the day of catheter insertion. The incidence of infection was found to be statistically insignificant which can explain by the conclusion drawn from various studies conducted that found that infection rates were low in CVC *in situ* for <7 days.

Richet *et al.*⁵ Conducted a multicenter trial to determine the incidence rate of complications associated with vascular catheters in ICU patients and to analyze risk factors for a positive vascular culture.

Siqueria *et al.*⁶ in their prospective, descriptive, and comparative study of 114 CVCs placed in 96 patients admitted to the surgical wards of a tertiary care hospital compared the catheter-associated bloodstream infections between subclavian and jugular access. They found that the CABS rate was higher in the SCV than in the internal jugular vein access (odds ratio 11.2, 95% confidence interval 1.4-90.8; *P* = 0.023). They found that the internal jugular vein access has a lesser incidence of CABS than SCV access in patients admitted to surgical wards. They explained this by the fact that ward patients do not present the difficult clinical problems seen in ICU patients.

They also concluded that infection in the jugular access compared to the subclavian access remains under investigation. It is probably due to two factors: (1) Proximity to the oral cavity; (2) higher density of the local bacterial

flora due to the high local temperature and difficulty of keeping occlusive bandages. The limitation of all studies is that they were carried out in the ICU setting, with sicker patients with fever, some of them on ventilatory support with an endotracheal tube or tracheostomy and difficulty to clear oral secretions. Thus, from this study, they concluded that their results showed the superiority of the jugular access over the subclavian access regarding the incidence of CABSIs in settings other than the ICU.

Kaur *et al.*⁴ in their study on 480 CVCs found that the risks of infectious complications increased significantly if the CVC was *in situ* for longer than 7 days ($P = 0.009$), especially with IJV cannulae. They explained these findings due to the proximity of the IJV insertion site to the mouth and the oropharyngeal secretion, the higher density of local skin flora due to the higher local skin temperature and the difficulties in maintaining occlusive dressings. The risk of infectious complications with CVCs has also been reported to be more with increased duration of use.

Marik *et al.*⁷ in their study on the risk of CRBSI with femoral venous catheters as compared to subclavian and internal jugular venous catheters: A systematic review of the literature and meta-analysis in which they included two randomized controlled trials (1006 catheters) and 8 cohorts (16,370 catheters) studies.

There was no significant difference in the risk of CRBSIs between the femoral and subclavian/internal jugular sites in the two randomized controlled trials. There was no significant difference in the risk of CRBSI between the subclavian and internal jugular sites. These results were consistent with the present study.

In 2005, Lorente *et al.*⁸ evaluated 2595 catheters and found a statistically significant difference of infection rate between three sites: Femoral access was associated with higher incidence of infection compared to the other accesses, and the jugular access was associated with a significantly higher incidence of infection, compared to the subclavian access (risk ratio: 3.1; $P = 0.005$).

Sadoyama and Gontijo Filho⁹ conducted a prospective observational study of non-tunneled CVC (116 patients) in 2003. Most patients were catheterized in the SCV (69%). The significant risk factors for contamination at the jugular vein were: >7 days catheterization and >3 invasive devices. This indicates that the patients with catheters at this site were more seriously affected, and therefore required more care by the health workers.

A significant association of the type of isolate at the insertion site and in the catheter tip also confirmed

the importance of the skin as a CRBSI reservoir. Although patients with catheters in the jugular vein were more severely ill and therefore had a greater bacterial contamination/infection risk when compared to those with CVC in the SCV, there were no quantitative differences in the skin contamination of the insertion site nor was there a greater contamination of the catheter tips in this vein.

Since the presence of infection was observed for a period of 7-day of CVC insertion, the low incidence of infection in the present study can be attributed to the incidence of infection being greater when CVC is *in situ* for more than 7 days.

Parameswaran *et al.*¹⁰ in their case-control study which was conducted over 19 months involving 232 patients at a tertiary care hospital with the objectives to determine the clinical and microbiological profiles of patients developing intravascular catheter-related local (localized catheter colonization and exit site) and systemic infections and their predisposing factors and to study the antibiotic sensitivity patterns of the organisms isolated found that the incidence of CRBSIs in their institute was 8.75 per 1000 catheter days. The most common organisms causing local infections were coagulase-negative *Staphylococci*, and those causing CRBSI were *S. aureus*.

Multidrug-resistant organisms accounted for 30.2% of the infections. Risk factors for the development of catheter-related infections included an immune compromised state, duration of the catheter *in situ*, femoral venous cannulation, and triple lumen catheters.

Choice of venous cannulation to minimize the risk of catheter-related infection in ascending order for risk of infection is the SCV, jugular vein, basilic vein and then the femoral vein. There was no role for empirical antibiotic therapy to prevent intravascular catheter-related local or systemic infections.

Similar results were found in the present study with *S. aureus* being the most common organism being isolated from the local site and incidence of infection being less with the subclavian route.

CONCLUSION

All the observations were statistically analyzed, and the following results were drawn:

The total incidence of infectious complications was 12% and the risk of infectious complications during 7 days of insertion was less. The internal jugular route was associated with higher incidence of infectious complications as compared to the subclavian route of CVC.

The study was conducted for a period of 7-day from the day of insertion, and the incidence of infection was found to be statistically insignificant and can be explained from various studies conducted which have found that infection rates were low if CVC's were placed for <7 days.

In conclusion, maximal sterility during insertion with suitable sterile-barrier precautions and scrupulous sterile aftercare of the wound and catheter hub can have a major impact reducing the level of CVC-related infection.

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Pulse Therapy - A Boon to Pemphigus: A Case Series from a Rural Tertiary Care Center

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Abstract

Background: Pemphigus is a group of autoimmune vesiculobullous disorders that carry high degree of mortality and morbidity. Dexamethasone-cyclophosphamide pulse (DCP) therapy has been proved to have promising outcome in the management of these diseases.

Aims: The objective of the study was to assess the outcome of DCP therapy in our pemphigus patients.

Methods: Pemphigus patients who were treated with DCP from 2005 to 2015 were prospectively and retrospectively analyzed.

Results: A total of 30 patients were enrolled. Male:female ratio was 1:1.3 with a mean age of 46.8 ± 15.8 with age range varying from 26 to 65 years. About 24 patients completed Phase I and were maintaining remission (80%). Out of 24, 5 were in Phase II, 6 were in Phase III, and 2 in Phase IV. Around 11 patients were declared cured. Only 3 patients relapsed (2 patients were in Phase II, 1 patient was in Phase III). Patients who relapsed were on irregular follow-up. No mortality was noted in our study. DCP therapy is not absolutely free from adverse effects. Most of the adverse effects were expected and tolerated and did not create any problem in continuing the pulse therapy. There was a slight increase in incidence of weight gain, cushingoid features, myalgia, pyogenic infections, oral candidiasis, headache, and hiccups. Laboratory parameters were within normal limits. Three patients showed an impaired glucose tolerance which reverted to normal with the continuation of pulse therapy.

Conclusion: DCP pulse therapy was effective in inducing, maintaining remission and offering cure for patients with pemphigus.

Key words: Cyclophosphamide, Dexamethasone, Pemphigus, Pulse therapy

INTRODUCTION

Pemphigus is a group of autoimmune disorders which present with blisters and erosions over skin, mucosa which is serious and life threatening. Dexamethasone-cyclophosphamide pulse (DCP) therapy designed by Pasricha *et al.* At All India Institute of Medical Sciences has revolutionized the management of pemphigus, since it was introduced, in 1982. If administered properly, DCP has the potential to offer cure for these diseases.¹⁻⁵

METHODS

Prospectively and retrospectively analyzed all pemphigus patients admitted in ward between 2005 and 2015. Diagnosis was based on clinical features, Tzanck smear, and skin biopsy. Immunofluorescence was not done due to non-availability. Baseline complete blood count, liver function test, HIV screening, renal function test, pus culture from erosions, serum electrolytes, electrocardiogram, chest X-ray, ultrasound abdomen was done for all patients before initiation of pulse therapy. Lab parameters were repeated on every subsequent pulse. Physician opinion was obtained before initiation of pulse therapy. Patients were maintained on daily dexamethasone to attain quick remission before initiation of pulse therapy. After evaluation, patients were started on dexamethasone 100 mg in 500 ml of 5% dextrose over 3 h for 3 consecutive days. Injection cyclophosphamide 500 mg was added to the same drip on the 2nd day. This

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constitutes one pulse. This was continued every 28 days until the patient achieved complete remission which was considered as Phase I. In between pulse patients were maintained on tablet cyclophosphamide 50 mg OD. Few patients who showed exacerbation of disease were maintained on oral steroids and few patients on interval pulse. After completion of Phase I, patient continued to receive the same dose of DCP for 9 more months which was considered as Phase II. In Phase III, patients were maintained only on tablet cyclophosphamide. In Phase IV, all drugs are stopped and patients are followed up for a period of 2-year. Patients that completed 2 years of disease free follow-up were declared cured. Data regarding age, sex, duration of disease, previous treatment details, comorbid diseases, phases of pulse, adverse effects were documented. Lab investigations such as urine analysis, complete hemogram, liver function tests, and renal function test were documented before each pulse. Pus culture was done from unhealthy erosions and pyogenic infections in needed patients.

RESULTS

Out of 30 patients followed up for DCP, 17 (56.6%) were females, 13 (43.3%) were males, male:female ratio was 1:1.3 with age range between 27 and 65 years. The highest incidence was noted in the age group of 41-50 (13 patients) followed by 8 patients in the age range of 31-40 years. The youngest range was in 4 patients (21-30 years) (Figure 1).

Disease Profile

Out of 30 patients, 28 was pemphigus vulgaris and 2 was pemphigus foliaceus. About 24 (80%) patients had severe skin and mucosal involvement (>30% body surface area), 6 (20%) patients had moderate skin and mucosal involvement (10-30% body surface area).

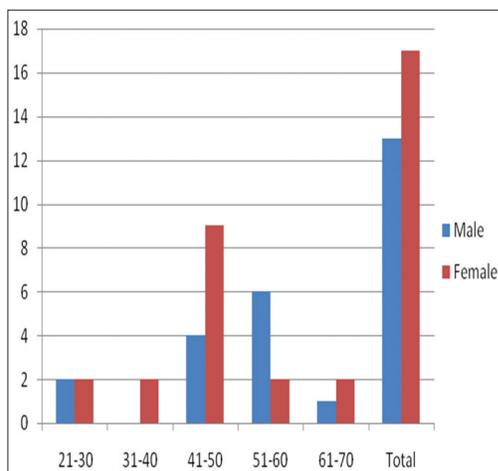


Figure 1: Age/sex distribution

Duration of Disease before Onset of DCP

Duration of disease before onset of DCP ranged from 5 days to 2 years. About 28 patients (95%) presented to us in the first episode.

Comorbidities

Out of 30 patients, 4 patients were diabetic, 2 patients had both diabetes and hypertension, one patient was a person living with HIV/AIDS on antiretroviral therapy, one was treated Hansen with recurrent Type I Lepra reaction.

Phases of DCP (Table 1)

Phase I

Among 30 patients 6 patients (20%) are in Phase I out of which 3 are on irregular follow-up with recurrent exacerbations. Around 24 patients (80%) attained remission out of which 5 patients were in Phase II, 6 patients in Phase III, and 2 patients in Phase IV, 11 patients (36%) were declared cured. Relapse was observed in 2 patients while on Phase II, one patient in Phase III due to irregular follow-up. Good compliance was seen in 80% of our patients. No mortality was observed in our study.

Remission was achieved in 10 patients within 1-5 pulses (Table 2). The majority of patients (12) attained remission with 6-10 pulses. However, 2 patients needed 11-15 pulses to attain remission.

Adverse Effects Noted during Pulse Therapy (Table 3)

Adverse effects noted were myalgia, hiccups, dyspepsia, muscle cramps and headache in the immediate week following pulse therapy. Long-term adverse effects noted were weight gain, cushingoid habitus, cataract. Pyogenic infections - furuncles, abscess at intravenous cannulation sites, perianal abscess were also noted and was more in patients with comorbidities like diabetes, HIV disease.

Table 1: Number of patients in phases of DCP

Phases	Male	Female
Phase I	3	3
Phase II	3	2
Phase III	2	4
Phase IV	0	2
Cured	5	6
Total (n=30)	13	17

DCP: Dexamethasone cyclophosphamide pulse

Table 2: Number pulses required attaining remission

Number of pulse	Male	Female
1-5	2	8
6-10	7	5
11-15	1	1
Total (n=24)	10	14

Table 3: Adverse effects

Adverse effects	Number of patients
Immediate	
Dyspepsia	8
Hiccoughs	3
Tiredness	10
Muscle cramps	4
Delayed	
Weight gain	6
Cushingoid features	6
Furuncles	5
Abscess at IV cannulation site	1
Perianal abscess	2
Cataract	1
Amenorrhea	3
Oligomenorrhea	4
Oral candidiasis	2

IV: Intravenous

Amenorrhea and oligomenorrhea were noted in 5 patients. Laboratory parameters were within normal limits except for 3 patients who showed impaired glucose tolerance while on pulse who were non-diabetic before onset of pulse but reverted to normal values once pulse therapy was stopped.

DISCUSSION

Pulse therapy has been proved to offer quick remission and complete cure in these patients which previously was considered to carry a high degree of mortality.^{1,5-7}

The results of our study show a positive outcome in terms of effectiveness. We were able to maintain remission in 80% (24 out of 30) patients.

Kandan and Thappa⁷ reported a remission rate of 87.5% and Sachidanand *et al.*³ reported remission rate of 82% which was comparable with our study. Patient compliance was good in 95% of our patients which was much higher than observations by Mahajan *et al.*⁶ with 58% drop out. Mortality was not seen in our study whereas Kandan and

Thappa⁷ reported mortality in 5 out of 65 patients treated and Pasricha *et al.*^{1,5} reported 19 deaths among 500 patients treated.

The adverse effects noted in our patients were tolerable, reversible, treatable and did not pose much problem in continuing the pulse therapy.

Even in patients with co-morbidities like diabetes and HIV disease adverse effects were comparable with the other patients except for slight increase in incidence of pyogenic infections. To our surprise, we noted that patient with recurrent Type 1 lepra reaction had no episode of lepra reaction while on treatment and follow-up.

CONCLUSION

The results of this study indicate a high degree of positive outcome in terms of effectiveness of pulse therapy in pemphigus. With this treatment modality, it is now possible to induce quick remission and offer cure in patients with these severe diseases.

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Profile of Rat Killer Poisoning Cases in a Tertiary Care Hospital at Mysore

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Abstract

Introduction: Rat killer poison consumption cases are among the second most common poisoning in developing countries. It is associated with significant mortality and morbidity. However, some of the cases get discharged without any effects. This is because of the variability in content. So, the chemical content of the rat killer poison decides the mortality and morbidity.

Purpose: The purpose of this study is to evaluate the clinical outcome of the rat killer poisoning cases with its relation to the chemical content of the poison.

Materials and Methods: It is a retrospective study conducted on patients admitted to K R Hospital, Mysore. As per inclusion criteria and exclusion criteria cases are included and excluded, and a prestructured proforma was used, and data were entered. The study is approved by the Institutional Ethical Committee.

Result: Most of the cases were young adults. Both the genders were equally affected. High mortality rate found in aluminum phosphide and zinc phosphide containing compounds consumption with cardiotoxicity and cardiogenic shock. Those cases with yellow phosphorus poisoning were stable on day 1 or 2, worsened on day 3 or 4 with multiple organ dysfunction syndromes.

Conclusion: So, the chemical content of poison is important for the prognosis and also intensive monitoring and early interventions.

Key words: Cardiotoxicity, Rodenticides, Toxic

INTRODUCTION

Rodenticides are a heterogeneous group of substances that exhibit markedly different toxicities to humans and rodents. They are among the most toxic substances regularly found in homes. The varieties of rodenticides used over the years.¹

CLASSIFICATION OF RODENTICIDES BASED ON TOXICITY

Highly Toxic Rodenticide

Highly toxic rodenticides are those substances with a single dose LD₅₀ of less than 50 mg/kg body weight.

Some of these compounds have largely been abandoned because of serious human toxicity. This group includes: (1) Aluminum phosphide, (2) Sodium monofluoroacetate, (3) Strychnine, (4) Zinc phosphide, (5) Yellow phosphorus, (6) Arsenic, and (7) Thallium.²

Metal phosphides have been used as a means of killing rodents and are considered single-dose fast acting rodenticides (death occurs commonly within 1-3 days after single bait ingestion). The acid in the digestive system reacts with the phosphide to generate the toxic phosphine gas. Zinc phosphide is typically added to rodent baits in a concentration of 0.75-2.0%. The baits have strong, pungent garlic-like odor characteristic for phosphine liberated by hydrolysis. The odor attracts (or, at least, does not repel) rodents, but has a repulsive effect on other mammals. The tablets or pellets (usually aluminum, calcium, or magnesium phosphide for fumigation/gassing) may also contain other chemicals which evolve ammonia, which helps to reduce the potential for spontaneous ignition or explosion of the phosphine gas.³

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Elemental Phosphorus

They exist in two forms—red and yellow. Red phosphorus is nonvolatile, insoluble, and unabsorbable, and therefore nontoxic when ingested. Yellow phosphorus (also referred to as white phosphorus), on the other hand, is a severe local and systemic toxin causing damage to gastrointestinal, hepatic, cardiovascular, and renal systems. White phosphorus is used as rodenticides and in fireworks. The most readily available source of yellow phosphorus today is rodenticides. Rodenticides are available as powders or pastes containing 2-5% of yellow phosphorus. Intoxication passes through three stages. The first stage occurs during the first 24 h in which patient is either asymptomatic or has signs and symptoms of local gastrointestinal irritation. The second stage occurs between 24 and 72 h after ingestion. It is an asymptomatic period, and the patient may be discharged prematurely. There may be the mild elevation of liver enzymes and bilirubin in this stage. The third stage (advanced) occurs after 72 h until the resolution of symptoms or death.⁴

Moderately Toxic Rodenticides

Among the moderately toxic rodenticides, those with LD₅₀ of more than 500 mg/kg body weight are: (1) Alpha-naphthyl-thiourea (ANTU) and (2) Dichlorodiphenyltrichloroethane (DDT).

Patients who ingest large quantities of ANTU may develop dyspnea, rales and cyanosis (secondary to pulmonary edema), and hypothermia. Poisoning from exposure to DDT can result in symptoms such as vomiting, tremors, and convulsions. How much exposure is required to cause severe illness or even death is, however, not certain.⁵

Low Toxicity Rodenticides

Low toxicity rodenticides are those with LD₅₀ between 500 and 5000 mg/kg body weight and include: (1) Red squill, (2) Norbormide, and (3) Anticoagulants warfarin-type rodenticides.

Red squill

Red squill contains several compounds with chemical and pharmacological properties similar to those of digitalis glycosides. Because of its emetic properties, poor gastrointestinal absorption, and decreased potency (compared to that of digitalis), red squill has seldom been associated with human toxicity.

Norbormide

Norbormide is an irreversible smooth muscle constrictor. It causes widespread ischemic necrosis and death in rats but does not appear to affect other animals or humans, presumably due to the presence of a specific smooth muscle norbormide receptor found only in rats.

Anticoagulants

Anticoagulants are defined as chronic (death occurs 1-2 weeks after ingestion of the lethal dose, rarely sooner), single-dose (second generation) or multiple-dose (first generation) rodenticides, acting by effective blocking of the Vitamin K cycle, resulting in inability to produce essential blood-clotting factors – mainly coagulation factors II (prothrombin) and VII (proconvertin).⁶

In addition to this specific metabolic disruption, massive toxic doses of 4-hydroxycoumarin or 4-hydroxythiacoumarin and indandione anticoagulants cause damage to tiny blood vessels (capillaries), increasing their permeability, causing diffuse internal bleedings (hemorrhagias). These effects are gradual, developing over several days.

Other

Other chemical poisons include:

- ANTU (ANTU; specific against Brown rat, *Rattus norvegicus*)
- Arsenic
- Barium (a toxic metal) compound
- Barium carbonate
- Bromethalin (which affects the nervous system, no antidote)
- Chloralose (narcotic acting condensation product of chloral and glucose)
- Crimidine (2-chloro-N,N,6-trimethylpyrimidin-4-amine; a synthetic convulsant poison, antivitamin B₆)
- 1,3-difluoro-2-propanol (“Gliftor” in the former USSR)
- Endrin (organochlorine cyclodiene insecticide, used in the past for extermination of voles in fields during winter by aircraft spraying)
- Fluoroacetamide (“1081”)
- Phosacetim (a delayed-action organophosphorus rodenticide)
- White phosphorus
- Pyrinuron (an urea derivative)
- Scilliroside
- Sodium fluoroacetate (“1080”)
- Strychnine
- Tetramethylenedisulfotetramine (tetramine)
- Thallium (a toxic heavy metal) compounds
- Urgan D2 (hydrogen cyanide absorbed in an inert carrier).⁷

MATERIALS AND METHODS

The present study was a retrospective study conducted during May 2014 to May 2015 in a tertiary care hospital in Mysuru. The study was conducted after obtaining the Institutional Ethical clearance. The study included 56 cases

of adults, with acute poisoning due to rat killer poisoning. Data regarding age, sex, marital status, occupation, type of poison, time and month of intake, route of exposure, and outcome of poisoning and associated co-morbid conditions were collected from the hospital records and documented in the prestructured proforma. Then, the data were analyzed by the descriptive statistical method.

RESULTS

In the present study, 56 cases of rat killer poisoning were reviewed retrospectively. In all the cases, the route of exposure was oral. Males (23 cases, 41.07%) and females (33 cases, 58.92%) and 28 cases (50%) were married (Table 1). The majority of the cases were in the age group of 11-30 years. It was also found that the instances of poisoning decreased with increasing age (Table 1). Occupation wise, poisoning was commonly found among homemakers (18 cases, 32.1%), male laborers (12 cases, 21.4%), and farmers (16 cases, 28.5 %) followed by and students (10 cases, 17.86%) (Table 2). In the present study, the most common poisoning agent was zinc phosphide (18 cases, 32.14%) followed by aluminum phosphide (12 cases, 21.4%) and yellow phosphorus (8 cases, 14.2%). An unknown compound which was not specified on the packet were found in 16 cases (28.57%). The mortality rate was high with aluminum phosphide (5 cases out of 12) and zinc phosphide (3 cases out of 18) (Table 3). LFT derangements seen with yellow phosphorus (3 cases, 37.5%) and aluminum phosphide (2 cases, 16.6%) followed by zinc phosphide (2 cases, 11.1%). ICU admissions were more for aluminum phosphide (10 out of 12 cases) followed by zinc phosphide (3 out of 18 cases) (Table 4).

DISCUSSION

In the present study, the most common poisoning agent was zinc phosphide. Females outnumbered males. Most of the cases were in the age group of 11-30 years. Acute poisoning was commonly seen among farmers, homemakers, and students in various national and international studies. In all the cases, the most common route of exposure was oral. The majority of cases were in the age group of 11-30 years (42 cases, 75%) which can be explained by the fact that the persons of this age group are suffering from stress of the modern lifestyles, failure in love, family problems, nuclear family concept, etc. Our study does not correlate with the study done by other study,⁸ in which incidence was high among males. Many cases were found among homemakers (18 cases, 32.1%), male laborers (12 cases, 21.4%), and farmers (16 cases, 28.5%) as these groups are more vulnerable groups and easily exposed to the poisoning agents. Poverty, inadequate income to run the family,

monsoon failure was responsible for higher incidence of poisoning among laborers and farmers.⁹ Factors, such as dowry, cruelty by the in-laws, family quarrels, maladjustment in married life, and dependence of women on husband, are responsible for the higher incidence of poisoning among homemakers. Failure in the exams or inability to cope up the high expectation from parents and teachers has increased the incidence of poisoning among students. High toxicity and non-availability of any specific antidote are responsible for higher mortality with rat killer poison.¹⁰ LFT derangements seen mostly with yellow phosphorus after 2-3 days of consumption in our study.

Aluminum phosphide and zinc phosphide cases admitted more in ICU for a cardiogenic shock with high mortality. Seasonal variation also alters poisoning statistics. More

Table 1: Age, marital status, and sex-wise distribution of victims

Age in years	Married	Unmarried	Male	Female
11-20	4	18	6	8
21-30	12	8	12	16
31-40	10	2	3	9
>40	2		2	0

Table 2: Occupation of the victim

Occupation	Number
Homemakers	18
Laborers	12
Students	10
Farmers	14
Drivers	2
Private job	0
Others	0

Table 3: Type of poisoning and outcome

Type of poison	Number of cases	Number of deaths	Mortality rate %
Aluminum phosphide	12	5	41.6
Zinc phosphide	18	3	16.6
Yellow phosphorus	8	0	0
Bromadiolone	2	0	0
Unknown compound	16	4	25

Table 4: Type of poison with LFT derangement and ICU admissions

Type of poison	LFT deranged cases	ICU admission
Aluminum phosphide	2	10
Zinc phosphide	2	3
Yellow phosphorus	3	0
Others	0	3

LFT derangements in the form of SGOT and SGPT elevation. SGOT: Serum glutamic oxaloacetic transaminase, SGPT: Serum glutamate pyruvate transaminase, LFT: Liver function tests, ICU: Intensive care unit

number of cases were reported during the summer season. It was observed, poisoning was common among productive age group (20-30 years) that produces a huge socioeconomic burden on the society. This study adds information to the existing data which help to develop prevention strategies.

CONCLUSION

The study concluded that most toxic rat killer poisons with high mortality are aluminum and zinc phosphide with high cardiotoxicity. Yellow phosphorus consumption associated with the late manifestation of liver cell injury and MODS so should be observed for one week without early discharge of the patient. As there are no antidotes for these compounds active symptomatic management with earliest stomach wash may be benefitted. Public population should get alerted with the high mortality rate of rat killer poison consumption and should prevent it.

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Evaluation of Cardiac Autonomic Dysfunction in Human Immunodeficiency Virus Infection and its Correlation with CD4 Levels

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Abstract

Introduction: The occurrence of autonomic dysfunction in human immunodeficiency virus (HIV) patients impacts their health care in several ways. Extra precaution is needed during invasive surgical procedures are to be done. Whether dys-autonomia is related to severity of HIV disease is still a matter of controversy.

Materials and Methods: This was a prospective, hospital-based study. 50 patients (25 HIV without AIDS and 25 HIV with AIDS) and 50 healthy age- and sex-matched controls were enrolled. Autonomic function was assessed by the following autonomic function tests. (1) Systolic blood pressure (BP) response to standing, (2) Diastolic BP response to the persistent handgrip, (3) Heart rate response to standing, (4) Heart rate response to Valsalva maneuver - Valsalva ratio, and (5) Heart rate variation to deep breathing. Grading was given for each autonomic function test. Results were classified into normal, borderline, and abnormal (scored 0.1 and 2, respectively).

Results: Mean age of patients in the study group was 35.08 ± 8.2 years and that of the control group was 35.12 ± 8.6 years. The majority of patients were in the age group of 26-35 years. Total number of males was 42 (84%) and females 8 (16%). 30% of HIV with AIDS had autonomic dysfunction and 12% of HIV without AIDS had an abnormal autonomic function. Abnormal Valsalva response was present in 60% of HIV with AIDS and in 40% of HIV without AIDS. Abnormal diastolic BP response to sustained handgrip was present in 36% of HIV with AIDS and in 20% of HIV without AIDS. Abnormal heart rate response to deep breathing was present in 48% of HIV with AIDS and in 36% of HIV without AIDS.

Conclusions: There was significant autonomic nervous system dysfunction in both HIV without AIDS and HIV with AIDS. Reduced heart rate variability was the most common manifestation of autonomic dysfunction noted in both HIV groups.

Key words: Autonomic dysfunction, Cardiac dysfunction, CD4 counts, Human immunodeficiency virus

INTRODUCTION

Human immunodeficiency virus (HIV) involves all organ systems including the nervous system. In addition to the central nervous system and peripheral nervous system, the autonomic nervous system can also be involved which has several implications in health care of HIV patients.¹ In the presence of autonomic neuropathy, additional precautions

have to be taken when invasive procedures are performed on HIV patients. Some of the antiretroviral drugs are also capable of causing autonomic neuropathy and hence presence or absence of preexisting neuropathy poses a problem in therapy also. Early detection of autonomic dysfunction helps in rehabilitation of HIV patients. Some of the changes appear to reverse on antiretroviral treatment (ART).²

Autonomic dysfunction occurs more frequently and with greater severity in patients with AIDS. However, it may be present in the early stages of HIV infection and appears to progress during the illness.³

In one of the earliest studies on this topic, Ronstadt *et al.* examined autonomic function in HIV patients at various

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stages of infection. They found evidence of substantial impairment with worsening as HIV progressed. Various studies have reported the prevalence of autonomic nervous system dysfunction from 4% to 76.5%.

There is scanty literature on autonomic effects of HIV infection in Indian patients; hence, this study was being taken up to address question of HIV and autonomic dysfunction in the Indian scenario.⁴

Aim of the Study

To evaluate the presence and extent of autonomic dysfunction in HIV/AIDS patients and to correlate autonomic neuropathy with levels of CD4.

MATERIALS AND METHODS

About 50 HIV-infected patients both outpatient and inpatient (25 without AIDS and 25 with AIDS) of both sexes aged between 15 years and 65 years were enrolled. 50 healthy age- and sex-matched healthy volunteers were recruited as controls. The study was carried out at JSS Medical College Hospital Mysuru, South India, between October 2007 and August 2009 (2 years). The Ethical Committee clearance was obtained from the JSS Institutional Ethical Committee. Informed written consent was obtained from all the all patients were evaluated according to a detailed proforma. Symptoms and signs of autonomic dysfunction were analyzed.

Inclusion Criteria

Patients with HIV infection patients of both sexes aged between 15 years and 65 years.

Exclusion Criteria

1. Patients with cardiovascular disease
2. Patients with uremia, diabetes mellitus, and severe anemia
3. Patients who were very ill
4. Patients with a history of current and chronic alcohol abuse.

Cardiac Autonomic Function was Tested by Various Maneuvers as Follows

Heart rate variation to Valsalva maneuver

The test was performed by asking the patient to blow through the tubing of the mercury manometer up to 40 mm Hg and to maintain mercury column at that level by blowing for 15 s. Continuous ECG was recorded during the procedure and fifteen seconds after the release of pressure.

The ratio of longest R-R interval after manoeuvre to the shortest interval during maneuver was measured and expressed as Valsalva ratio. A ratio of 1.21 or greater was taken as normal (no autonomic dysfunction). A ratio

of 1.11-1.20 as borderline and 1.10 or less as abnormal (autonomic dysfunction present).

Heart rate response to deep breathing

The subject was asked to breathe deeply and evenly at 6 breaths per minute, taking 5 s for inspiration and 5 s for expiration. ECG was continuously recorded. The longest and shortest R-R intervals during expiration and inspiration were measured and corresponding heart rates calculated. The difference between the maximum and minimum heart rates was calculated. A difference of more than 15 beats per minute was labeled as normal (no autonomic dysfunction) 11-15 beats per minute as borderline dysfunction. 10 beats per minute was considered as abnormal (autonomic dysfunction present).

Heart rate response on assuming standing posture from lying position

The ratio of the longest R-R interval to the shortest R-R interval after the patient moved quickly from supine to upright posture. The ratio of 1.04 or greater was taken as normal (no autonomic dysfunction). 1.01-1.03 as borderline and 1 or less as abnormal (autonomic dysfunction present).

Blood pressure (BP) response to standing up

BP response to standing up was performed by measuring the BP while the subject was lying quietly and then by making the patient to stand up and recording the BP after 3 min. A difference in systolic BP of <10 mm of Hg after patient standing up was taken as no autonomic dysfunction (normal). A fall of 11-29 mm of Hg as borderline dysfunction and a fall of more than 30 mm of Hg as abnormal (autonomic dysfunction present).

BP response to sustained handgrip

Two sphygmomanometers were used. The cuff of one was inflated to 10 mm of Hg then patient/subject was asked to compress the cuff with his hand was asked to maintain pressure for 3 min. BP was recorded with the other sphygmomanometer at the beginning and at the end. A rise of diastolic pressure at the end of procedure more than 16 mm of Hg was taken as no autonomic dysfunction (normal). A value of 11-15 mm as borderline and a reading of <10 mm of Hg as abnormal (autonomic dysfunction present).

For grading of cardiovascular autonomic function, results were classified as normal (no autonomic dysfunction), borderline, and abnormal (scored 0, 1, and 2, respectively). An overall score ≤ 3 considered to indicate normal autonomic function. Scores >3 and <8 were considered borderline and scores ≥ 8 were judged abnormal (autonomic dysfunction present).

CD4 count was done for all the patients and controls by flow cytometry.

Statistical Methods

The descriptive procedure was used to display univariate summary statistics for several variables in a single table and to calculate standardized values (z-scores).

The Independent-Samples “t” test was used to compare means for two groups of cases. All the statistical methods were carried out through the SPSS for Windows (version 16.0).

RESULTS

Mean age of patients in the study group was 35.08 ± 8.2 years and that of the control group was 35.12 ± 8.6 years. The majority of patients were in the age group of 26-35 years. Total number of males was 42% and females 8%. Male:female ratio was 8.4:1.6. The majority of the patients in the HIV without AIDS group had CD4 counts of above 500 cells/mm³ and the majority of the HIV with AIDS patients had CD4 counts in the range of 101-200 cells/mm³.

On analysis of heart rate response to standing between HIV with AIDS and HIV without AIDS group and control group, it was seen that there was a significant difference between HIV/AIDS patients group and control group (P = 0.002) (Table 1).

Analysis of Valsalva ratio in HIV without AIDS/HIV with AIDS and controls revealed that here was a significant difference between HIV/AIDS group and control group (P = 0.000) (Table 2).

Analysis of heart rate response to deep breathing between HIV without AIDS/HIV with AIDS and control group revealed that there was significant differences between HIV/AIDS patients group and control group (P = 0.000) (Table 3).

Analysis of systolic bp response to standing between HIV positive/AIDS and control group revealed that here was significant differences between HIV/AIDS patients group and control group (P < 0.00) (Table 4).

Analysis of diastolic bp response to sustained handgrip between HIV/AIDS and control group revealed significant differences between HIV/AIDS patients group and control group (P = 0.000) (Tables 5 and 6).

Autonomic function tests were abnormal in 8 (32%) HIV with AIDS patients but in only 3 (12%) HIV without

Table 1: Heart rate response to standing: HIV with AIDS and HIV without AIDS group and control group

Heart rate response to standing	HIV without AIDS (%)	HIV with AIDS (%)	Control (%)	Total (%)
Normal	13 (52.0)	15 (60.0)	44 (88.0)	72 (72.0)
Border line	9 (36.0)	5 (20.0)	6 (12.0)	20 (20.0)
AB normal	3 (12.0)	5 (20.0)	-	8 (8.0)
Total	25 (100.0)	25 (100.0)	50 (100.0)	100 (100.0)

P=0.002, HIV: Human immunodeficiency virus

Table 2: Valsalva ratio in HIV without AIDS/HIV with AIDS and controls

Valsalva ratio	HIV positive without AIDS (%)	Hiv positive +ve with AIDS (%)	Control (%)	Total (%)
Normal	6 (24.0)	5 (20.0)	40 (80.0)	51 (51.0)
Border line	9 (36.0)	5 (20.0)	10 (20.0)	24 (24.0)
AB normal	10 (40.0)	15 (60.0)	-	25 (25.0)
Total	25 (100.0)	25 (100.0)	50 (100.0)	100 (100.0)

P=0.000, HIV: Human immunodeficiency virus

Table 3: Analysis of heart rate response to deep breathing between HIV without AIDS/HIV with AIDS and control group

Heart rate response to deep breathing	HIV without AIDS (%)	HIV with AIDS (%)	Control (%)	Total (%)
Normal	10 (40.0)	8 (32.0)	40 (80.0)	58 (58.0)
Border line	6 (24.0)	5 (20.0)	4 (8.0)	15 (15.0)
Abnormal	9 (36.0)	12 (48.0)	6 (12.0)	27 (27.0)
Total	25 (100.0)	25 (100.0)	50 (100.0)	100 (100.0)

P=0.000, HIV: Human immunodeficiency virus

Table 4: Analysis of systolic BP response to standing between HIV positive/AIDS and control group

Systolic BP response to standing	HIV without AIDS (%)	HIV with AIDS (%)	Control (%)	Total (%)
Normal	21 (84.0)	8 (32.0)	46 (92.0)	75 (75.0)
Border Line	4 (16.0)	12 (48.0)	4 (8.0)	20 (20.0)
Abnormal	-	5 (20.0)	-	5 (5.0)
Total	25 (100.0)	25 (100.0)	50 (100.0)	100 (100.0)

P=0.000, BP: Blood pressure, HIV: Human immunodeficiency virus

Table 5: The analysis of diastolic BP response to sustained handgrip between HIV without AIDS, HIV with AIDS and control group

Diastolic BP response to sustained handgrip	HIV with AIDS (%)	HIV with AIDS (%)	Control (%)	Total (%)
Normal	9 (36.0)	3 (12.0)	43 (86.0)	55 (55.0)
Border line	11 (44.0)	13 (52.0)	7 (14.0)	31 (31.0)
Abnormal	5 (20.0)	9 (36.0)	-	14 (14.0)
Total	25 (100.0)	25 (100.0)	50 (100.0)	100 (100.0)

BP: Blood pressure, P=0.000, HIV: Human immunodeficiency virus

AIDS patients. None of the controls had abnormal function. Only 2 (8%) of 25 HIV with AIDS patients had a completely normal autonomic function. More than 55% of HIV-infected patients had borderline results. The results were statistically significant ($P = 0.000$) (Tables 7-9).

33.3% of those with CD4 counts between 201 and 400 had autonomic dysfunction.

Only 9.1% of those with CD4 counts between 401 and 600 had autonomic dysfunction.

35.3% of those with CD4 counts <200 had autonomic dysfunction. 20% of those with CD4 count between 201 and 400 CD4 had autonomic dysfunction. 50% of those with CD4 count between 401 and 600 CD4 level had autonomic dysfunction. The differences were not statistically significant $P = 0.866$ (Table 10).

In the HIV with AIDS on ART group, 57.1% had abnormal results, whereas only 22.2% of patients in the HIV with AIDS not on ART group had abnormal results. Antiretroviral therapy did not have a significant effect on autonomic function tests results ($P = 0.204$) (Table 11).

Analysis of autonomic function test results in HIV with AIDS and HIV with AIDS with opportunistic infections revealed that whereas 29.4% of patients in the former had abnormal results 37.5% of patients in the latter group had abnormal results. The presence of opportunistic

infection did not have significant effect on autonomic function ($P = 0.587$)

DISCUSSION

About 50 HIV/AIDS patients were studied to evaluate the presence and extent of autonomic dysfunction and to correlate autonomic neuropathy with levels of CD4.

The results and observation of the present study are compared and discussed with other studies as follows.

The occurrence of autonomic dysfunction in HIV with AIDS group and HIV without AIDS group was 32% and 12%, respectively. The results correlate with study done by Nzuobontane *et al.*⁵ and Rogdstadt *et al.*⁶

In the present study, age range of the study group was 19-60 years with mean age of 35.16 ± 9.17 years and age range of control group was 20-58 years with mean age of 35.0 ± 8.69 years. Rogdstadt *et al.*⁶ observed age range of 26-58 years with mean age of 38 years for study group and age range of 26-60 years with a median age of 38.12 years for the control group. The findings in our study group correlate with the above studies.

The present study showed higher preponderance in males which is consistent with results seen in previous studies.

In the present study, 34% of cases had CD4 count <200. 22% of cases had CD4 count 201-400 range, 26% of cases had CD4 range of 401-600 range, and 18% had >600 CD4, which is consistent with the study of Becker *et al.*, wherein maximum number of patients had CD4 count below 200.

Resting Heart Rate

In the present study, resting heart rate of more than 100 beats/min was found in 28% of HIV-positive group and 56% of AIDS group indicating resting tachycardia due to unopposed cardiac sympathetic activity. This is consistent with the study of Becker *et al.*,⁷ wherein resting heart rate was higher in HIV-infected group than in healthy subjects

Table 6: Frequency distribution of normal borderline, abnormal autonomic function between HIV without AIDS, HIV with aids and control group

Result	HIV without AIDS (%)	HIV with AIDS (%)	Control (%)	Total (%)
Normal	8 (32.0)	2 (8.0)	45 (90.0)	55 (55.0)
Border line	14 (56.0)	15 (60.0)	5 (10.0)	34 (34.0)
Abnormal	3 (12.0)	8 (32.0)	-	11 (11.0)
Total	25 (100.0)	25 (100.0)	50 (100.0)	100 (100.0)

$P=0.000$, HIV: Human immunodeficiency virus

Table 7: Comparative study of abnormal autonomic function between HIV without AIDS group and HIV with AIDS group

Autonomic function test	HIV with AIDS (%)			HIV without AIDS (%)			P value
	Normal	Borderline	Abnormal	Normal	Borderline	Abnormal	
Valsalva	5 (20)	5 (20)	15 (60)	6 (24)	9 (36)	10 (40)	NS
Heart rate response to standing	15 (60)	5 (20)	5 (20)	13 (52)	9 (36)	3 (12)	NS
Heart rate response to deep breathing	8 (32)	5 (20)	12 (48)	10 (40)	6 (24)	9 (36)	NS
Systolic fall in blood pressure on standing	8 (32)	12 (48)	5 (20)	21 (84)	4 (16)	0	<0.007
Diastolic blood pressure rise on sustained handgrip	3 (12)	13 (52)	9 (36)	9 (36)	11 (44)	5 (20)	NS

NS: Non significant, HIV: Human immunodeficiency virus

Table 8: The correlation of CD4 cell count with autonomic dysfunction in HIV without AIDS group

Result	CD4 cell count (%)			
	<200	201-400	401-600	600+
Normal	-	-	3 (27.3)	5 (62.5)
Border line	-	4 (66.7)	7 (63.6)	3 (37.5)
AB normal	-	2 (33.3)	1 (9.1)	-

The results were not statistically significant. $P=0.079$, HIV: Human immunodeficiency virus

Table 9: The correlation of CD4 cell count with autonomic dysfunction in HIV with AIDS group

Result	CD4 cell count (%)			
	<200	201-400	401-600	600+
Normal (no autonomic dysfunction)	2 (11.8)	-	-	-
Border line autonomic D	9 (52.9)	4 (80)	1 (50)	1 (100)
Abnormal	6 (35.3)	1 (20)	1 (50)	-

HIV: Human immunodeficiency virus

Table 10: Correlation of effect of antiretroviral therapy with autonomic dysfunction in HIV with AIDS patients

Result	AIDS (%)		Total (%)
	AIDS without ART (%)	AIDS with ART (%)	
Normal	2 (11.1)	-	2 (8.0)
Border line	12 (66.7)	3 (42.9)	15 (60.0)
Abnormal	4 (22.2)	4 (57.1)	8 (32.0)
Total	18 (100.0)	7 (100.0)	25 (100.0)

$P=0.204$, ART: Antiretroviral treatment, HIV: Human immunodeficiency virus

Table 11: Effect of opportunistic infections with autonomic dysfunction in aids patients

Result	AIDS (%)		Total (%)
	AIDS without opportunistic infections	AIDS with opportunistic infections	
Normal	2 (11.8)	-	2 (8.0)
Border line	10 (58.8)	5 (62.5)	15 (60.0)
Abnormal	5 (29.4)	3 (37.5)	8 (32.0)
Total	17 (100.0)	8 (100.0)	25 (100.0)

$P=0.587$

although it did not differ among pre-AIDS and AIDS patients.

Analysis of the results reveals that heart rate variability is reduced in HIV-seropositive individuals in early stages of infection without AIDS.

Similar observation was made in the study by Mittal *et al.*⁸ They showed that heart rate variability was decreased in patients with HIV infection without AIDS and that incipient autonomic dysfunction was present even early in the course of HIV

infection. This was in contrast to the earlier study by Becker *et al.*⁷ where it was reported that cardiac autonomic nervous system dysfunction was not significant in pre-AIDS patients.

HIV patients without AIDS did not have any HRV parameters significantly different from healthy controls ($P > 0.017$), whereas HIV with AIDS patients demonstrated reduced HRV in 14 parameters ($P = 0.0341$). The study by Becker demonstrated that HIV with AIDS patients exhibits a high degree of cardiac autonomic nervous dysfunction, whereas HIV-infected subjects have an intermediate position between HIV negative and AIDS.⁹

The results of our study are different from the study by Becker *et al.*,⁷ and the reasons for the same may be the faster progression of HIV infection and difference in subtype of HIV stain in an Indian setting.

Results of the present study suggest that autonomic dysfunction occurs in cases of AIDS and also in the early course of HIV infection. Similar observations were made in the study done by Nzuobontane *et al.*,⁵ Rogstad *et al.*,⁶ and Becker *et al.*⁷ The presence of abnormalities of various autonomic function test in present study is compared with studies of Nzuobontane *et al.*⁵ Most of the autonomic function tests were abnormal in present study, and the findings are similar to those reported by Nzuobontane *et al.*⁵

This study adopted a cross-sectional design and criteria for the diagnosis of autonomic dysfunction which was similar to the study by Nzubontane *et al.*⁵ However, this study did show significant differences in BP and heart rate tests, whereas they found only clear differences for BP tests. Probably, the divergence of results is related to differences in sample size, patient selection, fast progression of HIV infection, and difference in subtype of HIV strain in Indian setting.¹⁰

In the present study, 32% of patients of HIV with AIDS showed abnormal results which are comparable to the results of Nzuobontane *et al.*⁵ (27% AIDS) while it was less in the study of Rogstad *et al.*⁶ (20% AIDS). In the study, 12% of subjects of HIV without AIDS showed abnormal results which are comparable the study of Rogstad *et al.*⁶ (14% of HIV without AIDS) while it was less in the study of Nzubontane *et al.*⁵ (4.2% of HIV without AIDS). If borderline results are considered over 60-80% of HIV/AIDS patients did not have normal results.

In HIV-infected patients, simple tests such as BP responses to standing or handgrip can warn of cardiovascular autonomic dysfunction thus signaling the need for added precautions when invasive procedure are proposed.¹¹

The mean CD4 count range of the present study is higher than seen in the other studies. In our study, autonomic dysfunction occurred at a wide range of CD4 cell count. However, more number of abnormal results was found below 200 CD4 range and more number of normal results found in 600 CD4 counts 600 and above range. Although, results are statistically insignificant. *P* value - HIV without AIDS = 0.079 HIV with AIDS = 0.866.

In the present study as opposed to earlier other studies, we have included AIDS patients with opportunistic infections and those who were on ART to ascertain if the presence of opportunistic infection of ART had any effect on autonomic function.

37% of HIV with AIDS showed abnormal results, whereas HIV without AIDS patients showed 30% abnormal results. However, these results were statistically not significant (*P* = 0.587). Hence, it is concluded that the presence of opportunistic infection does not have any significant effects on autonomic function. Similarly, there was no statistically significant difference in prevalence of autonomic dysfunction between patients of HIV with AIDS who were on ART and HIV with AIDS without ART (*P* = 0.204).

CONCLUSION

It is concluded that there is significant autonomic nervous system dysfunction in both HIV without AIDS and HIV with AIDS. Reduced heart rate variability was found

to be the most common manifestation of autonomic dysfunction in both. There was no correlation between the CD4 level and the presence of autonomic nervous system dysfunction. Larger studies are needed to confirm the findings of this study.

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High-sensitivity C-reactive Protein? Is It Significant in Tuberculous Spondylitis

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Abstract

Introduction: Spinal tuberculosis (TB) is a common entity in Asian subcontinent, occurring in the first three decades of life. TB of spine most commonly affects the dorsolumbar spine region followed by cervical spine. Early diagnosis and treatment are necessary to avoid long-term disability. Elevated erythrocyte sedimentation rate (ESR) and positive mantoux test provide supportive evidence for the diagnosis of TB but are not specific. Imaging of spine is the most important preliminary tool to make the diagnosis of TB spondylitis. Acid-fast bacilli smear and culture are not positive in all the cases. In this study, we have assessed the role of high-sensitivity C-reactive protein (hs-CRP) in the diagnosis of TB spondylitis and in monitoring the clinical response to treatment.

Materials and Methods: This is a prospective study carried out in the Department of neurosurgery, Government General Hospital, Vijayawada, from July 2015 to February 2016. Patients with imageological features suggestive of TB of the spine were evaluated clinically, and blood samples were taken for measurement of hs-CRP. All these patients were evaluated clinically and radiologically and were correlated with inflammatory marker at the follow-up of for 3 months and 6 months.

Results: A total of 56 patients were included in the study and control group. hs-CRP was raised in 70.96% and 32% of patients in study group and control group with statistically significant $P = 0.004$. Patients with elevated hs-CRP had a worsen visual analogue scale score and neurological status (ASIA grade < C and NURICK grade > 2) as compared to patients with normal hs-CRP, but this correlation did not reach the level statistical significance.

Conclusion: Elevated hs-CRP is a useful marker to supplement the diagnosis of TB of spine and monitoring the patients for the response to treatment. Elevated hs-CRP strongly correlates with vertebral body collapse and presence of soft tissue component in TB of spine. Larger clinical studies are required to validate this results of ours in endemic regions.

Key words: High-sensitivity C-reactive protein, Tuberculosis, Spine

INTRODUCTION

TB spondylitis was first described in 1776 by Percival Pott.¹ It accounts for 2-3% of total cases of tuberculosis (TB).² It has become a major health hazard after HIV has emerged in the western world.³ TB Infection can vary from an acute presentation over several days to a more prolonged, chronic course over a period of weeks or months, with a latent period of 1-week to 3-year.⁴ It can be devastating because of its ability to cause bone destruction, deformity, and permanent neurological deficits.¹ Early diagnosis and

treatment are necessary to avoid long-term disability. Elevated erythrocyte sedimentation rate (ESR) and positive mantoux test provide supportive evidence for the diagnosis of TB but are not specific. Various imaging modalities such as X-ray, computed tomography (CT) scan, and magnetic resonance imaging (MRI) scan of spine help in diagnosis of TB and in defining the extent of TB. Acid-fast bacillus (AFB) smear and culture are gold standard methods for confirmation of diagnosis but it is not conclusive in all the cases.⁵ In this study, we have tried to assess and define the role of high-sensitivity C-reactive protein (hs-CRP), in the diagnosis of TB spondylitis and in monitoring the clinical response to treatment.

MATERIALS AND METHODS

Study Population

This is a prospective study carried out in the Department of neurosurgery, Government General Hospital, Vijayawada,

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from July 2015 to March 2016. Patients presenting with a backache with or without neurological deficits were evaluated with MRI spine (plain and contrast images). Patients with imageological features suggestive of TB of spine were included in the study group. Patients with proven neoplastic disorders or degenerative conditions of spine were included in the control group. Patients on anti-TB therapy for more than 1 month, spinal infection in HIV positive patients, patients with focal or systemic infections other than spine for past 1 month and patients with autoimmune disease were excluded in this study.

A total of 31 patients were included in the study group, and 25 patients were included in the control group respectively. All the patients were evaluated clinically and imageologically and measurement of inflammatory markers *viz.* ESR, hs-CRP before starting treatment was performed. Patients requiring decompression or stabilization of spine were operated upon and biopsy was taken intraoperatively. Postoperatively they were started upon anti-TB chemotherapy as per WHO protocol.⁵ The rest of patients not requiring surgery were started on anti-TB treatment. All these patients were evaluated clinically and hs-CRP levels were repeated at 3 months and 6 months follow-up. Pre-treatment imageological and clinical findings were correlated with serum hs-CRP. Post-treatment clinical response to anti-TB chemotherapy was correlated with post-treatment levels of serum hs-CRP. Serum inflammatory levels were assessed in the control group once before starting treatment and correlated with clinical findings.

Clinical Evaluation

At presentation all the patients in study and control group were examined clinically and severity of pain was assessed by visual analogue score (VAS), with a score of 0 for patients with no pain and 10 for patients who are bed ridden due to severe pain. Neurological deficits were graded using American Spinal Injury Association Impairment Scale (ASIA) and NURICK grading system. VAS, ASIA, and NURICK grading systems are described in Appendices A-C, respectively.

Imageological Evaluation

All the patients in the study and control group were evaluated with plain radiographs CT spine and MRI spine with contrast. Patients with classical imageological evidence of end plate changes, paradiscal vertebral involvement, intensity changes in the vertebral body (VB) with or without epidural or prevertebral or paraspinal soft tissue component were suspected to be having TB and were included in the study group. Patients without the evidence of above changes and with imageology showing evidence of degenerative changes or neoplasms were included in the control group. A number of vertebral bodies involved, presence or absence of soft tissue shadow, the collapse

of VB, presence or absence of spinal deformity were correlated with the level of inflammatory markers in serum and serum results were analyzed.

Inflammatory Marker - hs-CRP

Inflammation is a stereotyped biological response of tissues to harmful stimuli, such as pathogens, damaged cells, or irritants. In this study we are assessing the level of inflammatory marker (hs-CRP) is evaluated in the blood.

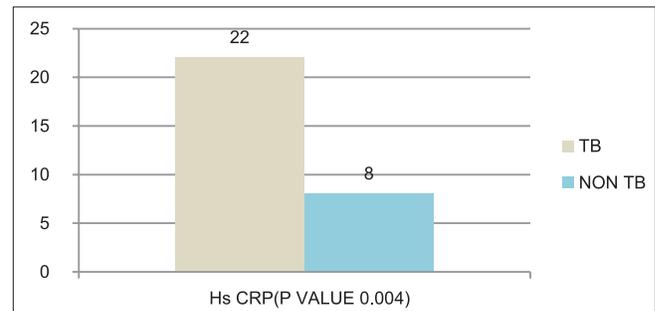
Statistical Analysis

MINITAB version 16 was used for analysis of the data and Microsoft word and Excel have been used to generate Graphs 1-3 and Tables 1-3, etc. Continuous variables are presented as mean and categorical variables are presented in number (%). Statistical significance has been arrived using Chi-square test. A $P < 0.005$ has been considered statistically significant.

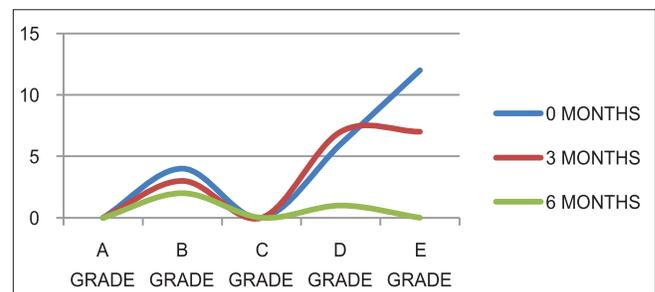
RESULTS

Patient Characteristics

A total of 31 patients were included in the study group, and 25 patients were included in the control group. The study group had patients ranging from 10 years to 70 years with a mean of 34 years. About 17 patients were males and 14 were females. In the control group, the patients had age ranging from 18 years to 80 years with a mean age of 50 years. Around 14 patients were males and 11 were females.



Graph 1: Correlation of high-sensitivity C-reactive protein in tuberculosis (TB) and non-TB spine patients



Graph 2: Correlation of elevated high-sensitivity C-reactive protein patients with neurological status (American Spinal Injury Association grade)

Clinical Characteristics

All patients presented with back pain or neck pain. The VAS score ranged from 2 to 8 with a mean score of 4.51 and mean duration of 4.5 months. About 19 patients had ASIA Grade E, 7 had Grade D, 5 had Grade B. Exactly 16 patients had NURICK Grade 0, 6 had Grade I, 6 had Grade II, 1 had Grade III and two had Grade IV myelopathy.

Imageological Characteristics

The spinal deformity was seen in 6 (19.35%) patients. One VB was involved in 8 (25.80%), two vertebral bodies in 18 (58.06%), three vertebral bodies in 3 (9.67%), four or more vertebral bodies were involved in 2 (6.45%) patients. Soft tissue involvement was seen in 21 (67.74%) of patients. VB collapse was seen in 11 (35.48 %) of patients (Figures 1-3).

Table 1: Correlation of elevated hs-CRP with clinic imageological findings (statistical significant)

Clinical and image Findings	hs-CRP		P value
	Raised	Not raised	
NURICK grade			0.170
<2	19	9	
≥2	3	0	
ASIA grade			0.329
≤C	4	1	
>C	18	8	
No of VB			0.170
≤2	17	9	
>2	5	0	
Deformity of Spine			0.398
Present	5	1	
Absent	17	8	
Collapse of VB			0.002
Present	11	0	
Absent	11	9	
Soft tissue			0.004
Present	18	3	
Absent	4	6	

hs-CRP: High-sensitivity C-reactive protein, VB: Vertebral body, ASIA: American Spinal Injury Association

Table 2: Correlation of severity of pain with level hs-CRP

Months	VAS	hs-CRP (mg/l)
0 months (n=31)	4.51	20.84
3 months (n=30)	2.13	8.38
6 months (n=25)	0.8	3.64

VAS: Visual analogue scale

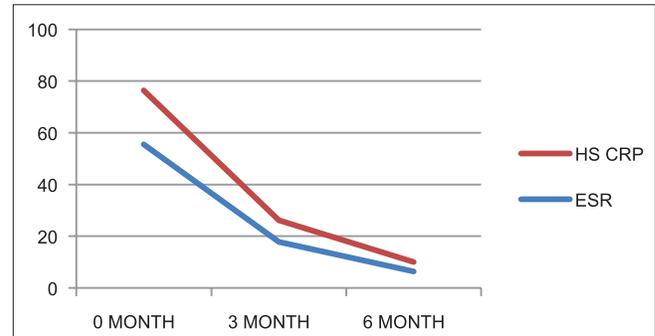
Table 3: Correlation of NURICK grade (myelopathy/ radiculopathy) with level of hs-CRP

Months	NURICK grade	hs-CRP
0 months (n=31)	0.64	20.84
3 months (n=30)	0.48	8.38
6 months (n=25)	0.32	3.64

hs-CRP: High-sensitivity C-reactive protein

hs-CRP in TB and Non TB Patients

hs-CRP was raised in 70.96% of patients in study group and 32% of patients in control group. The difference was statistically significant with a P = 0.004. Serum ferritin was raised in 14.81% of patients in study group and 8.69% of



Graph 3: Regression of erythrocyte sedimentation rate and high-sensitivity C-reactive protein levels during the course of antithrombotic trialists



Figure 1: Tuberculosis spine (T2W sagittal image) shows end plate destruction and epidural soft tissue



Figure 2: Tuberculosis spine (T2W sagittal image) shows collapsed vertebral body and pre vertebral soft tissue

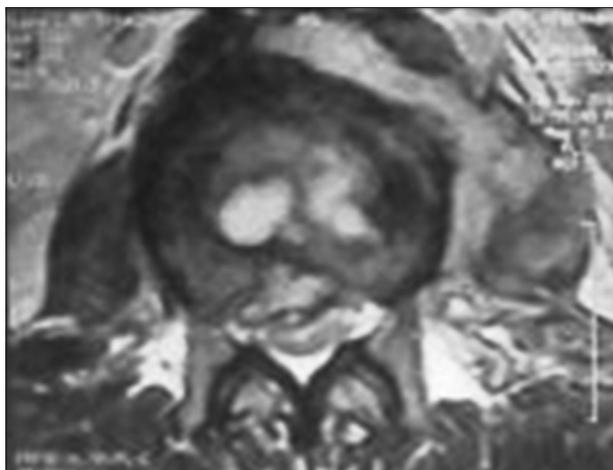


Figure 3: Tuberculosis spine (T2W axial image) shows epidural and paraspinal soft tissue

patients in control group. The difference was statistically insignificant with a $P = 0.555$. ESR was raised in 80.64% of patients in study group and 8% of patients in control group. The difference was statistically significant with a $P = 0.003$. Thus raised hs-CRP and ESR provided supportive evidence for the diagnosis of TB.

All the patients in study group with elevated hs-CRP except one had VAS score > 4 . All the patients in study group with elevated serum ferritin had VAS score > 4 . The level of hs-CRP correlate with the severity of pain. In follow-up as VAS score improved with treatment, the levels of hs-CRP is decreased and at 6 months, hs-CRP reached the baseline level of 5 mg/dl in all except three. In the remaining three, hs-CRP showed a decreasing trend. Similarly, as shown in Table 1, patients with elevated hs-CRP had a worse neurological status (ASIA Grade $< C$ and NURICK Grade > 2) compared to patients with normal hs-CRP. But this correlation didn't reach the level statistical significance.

DISCUSSION

Spinal TB is common in the first three decades of life,² affecting mostly young adults in poor socio economic status. TB of spine most commonly affects the dorso-lumbar spine region followed by cervical spine. Spinal TB is a slowly progressive disease and diagnostic delay is of major concern. A number of neoplastic, degenerative and bony tumors like metastasis, osteoblastoma, aneurysmal bone cyst mimic TB spine. TB responds well to anti TB therapy and biopsy with a demonstration of AFB smear or growth of TB bacilli colonies on culture media is gold standard. A biopsy is not always possible in early stages of disease. As imaging is not specific and biopsy is not always possible,⁶ other methods for diagnosis of spinal TB are always required especially in

endemic regions. In this study, we have assessed the role of hs-CRP in diagnosis of TB spine.

When biopsy confirmation of TB is not available, elevated levels of serum inflammatory markers may provide collaborative evidence for diagnosis of TB spine. C-reactive protein was the first acute-phase protein to be described and is an extremely sensitive systemic marker of inflammation and tissue damage.⁷ Weng *et al.*⁸ suggested spinal TB to be included in the differential diagnosis of chronic back pain in elderly patients with elevated ESR. Similarly, Spinal TB should also be included in the differential diagnosis of chronic back pain in patients with elevated hs-CRP.⁹

In our study, hs-CRP was raised in 70.96% of patients with study group and 32% of patients in the control group. The difference was statistically significant ($P = 0.004$). Thus elevated hs-CRP provided a good collaborative evidence for diagnosis of TB spine in our patient. According to Shanly *et al.*,¹⁰ described less common variant of TB of spine, which is limited to a single VB may lead to VB collapse and development of vertebra plana. According to our study, patients with collapse of VB and raised hs-CRP have a high probability of harboring a TB of spine.

Sturmer *et al.* found the concentration of hs-CRP to be directly proportional to the severity of inflammation and pain. In our study group, most of the patients with raised hs-CRP had deformity of spine, extensive soft tissue component, VB collapse and extensive VB involvement ($> two VB's$). They also had a poorer VAS score (VAS score > 4), poorer neurological status (NURICK Grade > 2 , ASIA Grade $< C$) at presentation. Severity of pain (VAS score), neurological status (ASIA grade, NURICK grade), spinal deformity and number of vertebral bodies involved had a correlation with raised hs-CRP, but correlation was not statistically significant. Soft tissue involvement and the presence of VB collapse correlated with hs-CRP levels, and the correlation was statistically significant (Table 1).

hs-CRP is a nonspecific biochemical marker of inflammation and its concentration in blood is useful for monitoring the response of inflammation to treatment.¹¹ According to Mahadev *et al.*, most of patients who responded to treatment demonstrated a decrease in their CRP value by at least 50%.¹² In our study group, at 3 and 6 months follow-up, improved clinical status (VAS score and neurological status) was associated with fall in hs-CRP levels. At the end of 3 months follow-up, all patients showed reduction in hs-CRP values, which continued to do so till the end of 6 months. In all patients except three in the study group, the hs CRP levels reached baseline value

of 5 mg/l by 6 months and the remaining three patients also showed a diminishing trend. The average reduction in hs CRP was approximately by 50% at the end of 3 months and another 50% by next for 6 months. There was a proportionate reduction in the CRP levels with treatment.

In our study hs-CRP levels, the values declined with decreasing VAS score. However, Stürmer *et al.*, found higher levels of hs-CRP in patients with higher pain levels.¹³ In their observation neither in acute back ache nor chronic back ache, there was correlation of hs-CRP levels in clinical course of disease in the 6-month period. This is contrary to our findings. Wang *et al.*,¹⁴ achieved excellent results with ultra-short course of anti-TB chemotherapy course (4.5 months) in conjunction with partial excision of pathologic vertebrae and clinical improvement was associated with decreased ESR, CRP levels. Similarly, in our study, hs-CRP levels decreased in response to chemotherapy (Table 2). At 3 and 6 months of chemotherapy with or without surgical intervention and correlated well with improvement of neurological status (ASIA and NURICK grade - Graph 2 and Table 3). Hence, hs-CRP levels were found useful to monitor the response to treatment. According to Pawar *et al.*,¹⁵ resistance to 1st line TB drug should be considered in the absence of clinical and imageological improvement. Similarly, resistance to TB drug should be considered in the absence of declining trend in hs-CRP levels.

ESR is widely used for monitoring clinical progress in patients with TB.¹² It is cheap, easy to perform and does not require expensive equipment. Ring *et al.* have found 94% of patients with TB spine in their series was elevated ESR at presentation.⁷ ESR rarely exceeded 55 mm/h in TB of spine.⁵ hs-CRP is less sensitive and specific (70.96% and 68%) compared to ESR (80% and 76%) for diagnosis of TB spine. However, hs-CRP responds more rapidly to treatment compared to ESR as shown in Graph 3. Based on study of Syed Ather Enam *et al.*, when compared with CRP, ESR may provide clinicians more useful information in evaluating the treatment response of spinal TB.⁷ Our study also strongly proposed that the serial monitoring of hs-CRP could be considered as valuable index, to assess the progression or regression of the disease to the treatment (Graph 3).

CONCLUSION

We can conclude from above findings that the hs-CRP is a useful marker to supplement the diagnosis of the TB of

spine. The hs-CRP is significantly elevated in those patients with the presence soft tissue component and collapse of VB. The serial measurements of serum values of hs-CRP were useful in assessing the treatment response of the patient.

Limitation of Study

The study population was small and the role of this hs-CRP in the diagnosis of TB of spine in the presence of simultaneous infection elsewhere in the body is not studied. The TB was suspected on the basis of imageology. Only 50% patients had biopsy confirmation of TB.

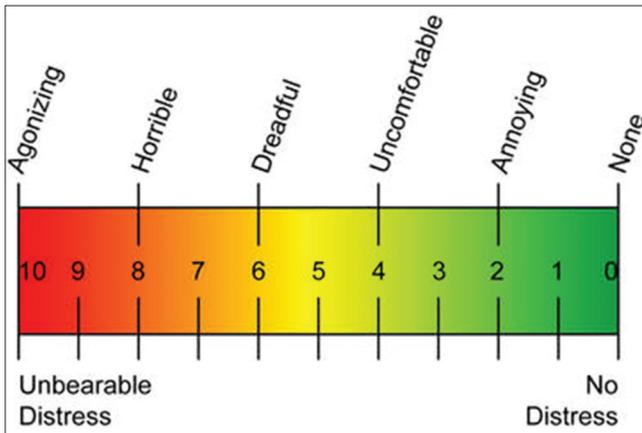
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APPENDICES



Appendix A: Visual analogue scale

Appendix B: ASIA impairment scale

Grade A	Complete lack of motor and sensory function below the level of injury (including the anal area)
Grade B	Some sensation below the level of the injury (including anal sensation)
Grade C	Some muscle movement is spared below the level of injury, but 50% of the muscles below the level of injury cannot move against gravity
Grade D	Most (more than 50%) of the muscles that are spared below the level of injury are strong enough to move against gravity
Grade E	Normal neurological status (no sensory or motor or autonomic disturbances)

Appendix C: NURICK scale

Grade 0	Signs or symptoms of root involvement but without evidence of spinal cord disease
Grade 1	Signs of spinal cord disease but no difficulty in walking
Grade 2	Slight difficulty in walking which does not prevent full-time employment
Grade 3	Difficulty in walking which prevented full time employment or the ability to do all housework, but which was not so severe as to require someone else's help to walk
Grade 4	Able to walk only with someone else's help or with the aid of a frame
Grade 5	Chairbound or bedridden

Complement Levels in Chronic Obstructive Pulmonary Disease: Correlation with Pulmonary Function and Radiological Emphysema Score

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Abstract

Background: There are currently lacunae in our understanding the role of complements in chronic obstructive pulmonary disease (COPD). It has been postulated that there might be a quantitative relationship between complement consumption and elastic tissue destruction.

Materials and Methods: This was a prospective study with 35 patients of COPD as cases and 35 controls. Cases were divided into two groups based on the degree of airway obstruction and on radiological emphysema score. Complement C₃ and C₄ levels were measured and the results were analyzed.

Results: Comparison of mean complement C₃ revealed no correlation among cases with mild (Cases 120.33 mg/dl, Controls 120 mg/dl $P = 0.97$) and moderate obstruction (cases 110 mg/dl controls 119.7 mg/dl $P = 0.662$). Significantly lower C₃ levels were observed with severe obstruction (cases 86.4 mg/dl controls 117 mg/dl $P = 0.017$). C₄ levels revealed no correlation among cases with mild obstruction (cases 22.5 mg/dl controls 23.92 mg/d $P = 0.616$) significantly lower C₄ levels were observed with moderate obstruction (cases 17.9 mg/dl controls 24 mg/dl $P = 0.004$) and in severe obstruction (cases 16 mg/dl controls 24.8 mg/dl $P = 0.005$). C₃ levels compared with controls showed no statistical significance with an emphysema score 0-6 (cases 121.8 mg/dl controls 122.1 mg/dl $P = 0.988$) and with emphysema score 7-10 (cases 104.4 mg/dl controls 116.1 mg/dl $P = 0.412$). Significantly lower C₃ levels were observed with emphysema score >10 (cases 82.5 mg/dl, controls 118.9 mg/dl $P = 0.017$). Complement C₄ levels compared with controls revealed no significant correlation in emphysema score between 0 and 6 (cases 22.7 mg/dl, controls 23.5 mg/dl $P = 0.725$). Significant lower C₄ levels were observed with emphysema score 7-10 (cases 18.3 mg/dl, controls 23.3 mg/dl $P = 0.003$) and with emphysema score >10 (cases 15.9 mg/dl, controls 22.9 mg/dl $P = 0.023$).

Conclusion: This study showed a direct correlation between the severity of COPD and complement levels. Serum complements may serve as marker for COPD severity.

Key words: Airway disease, Chronic bronchitis, Complement activation, Elastases

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is defined as a disease state characterized by airflow limitation that is not fully reversible.¹ COPD includes emphysema, an

anatomically defined condition characterized by destruction and enlargement of the lung alveoli; chronic bronchitis, a clinically defined condition with a chronic cough and phlegm; and small airways disease, a condition in which small bronchioles are narrowed. COPD is also a disease of increasing public health importance around the world. Estimates suggest that COPD will rise from the sixth to the third most common cause of death worldwide by 2020.² Although a great deal is known about etiopathogenesis of COPD, there are still significant lacunae in understanding of the role of immunity in the part played by recurrent infections in COPD. There are several conflicting results in studies which looked at the association between serum

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complement levels and various radiological and functional indices reflecting the severity of emphysema in patients with COPD. Patients with COPD have been shown to exhibit lower serum levels of complement components C₃ and C₄ than healthy subjects, and this may indicate sustained complement activation as a result of recurrent respiratory tract infections.

Activation of complement leads to influx of inflammatory cells into the lung parenchyma with subsequent release of elastases and oxidants that cause damage to elastic lung tissue. It has been postulated that there might be a quantitative relationship between complement consumption and degree of elastic tissue destruction. There have been studies which demonstrate that COPD patients with lower levels of C₄ are those who experience respiratory infections and tend to have more radiological signs of Emphysema and have a predominant small airway resistance.³ However, a small study from Turkey and a few other studies elsewhere found no correlation between the level of complement and severity of COPD indicating lack of clear cut knowledge about the complement role in COPD.⁴ The dichotomy in the results of various studies indicates the present gap in the knowledge about the role of complement in COPD. Given very few studies carried out in our population regarding this matter hence we took up this study.

MATERIALS AND METHODS

This was a hospital based, prospective, observational, comparative, analytical study carried out during the period October 2011 to September 2013. This study was done at JSS Medical College teaching hospital, a tertiary care referral hospital at Mysuru City, Karnataka State, South India. About 35 patients of COPD of both genders and age between 40 and 70 years were enrolled. Excluded were (a) patients with immunological disorders that might interfere with complement activation (systemic lupus erythematosus, rheumatoid arthritis, and neoplasms), (b) Patients unable to perform pulmonary function tests (PFT), (c) pregnancy (d), Those with associated bronchial asthma. About 35 age and sex matched health volunteers were taken as controls.

Ethical clearance was obtained from the JSS Medical College Institutional Ethical Committee (JSS/MC/IEC/3086/2009-2010). Informed written consent was obtained from all patients or their legal entourage.

Cases were divided into three groups based on PFT as follows: Mild obstruction (A1): Forced expiratory

volume in 1 s/forced vital capacity (FEV₁/FVC)<0.70 (FEV₁ ≥ 80% normal), moderate obstruction (A2): FEV₁/FVC<0.70 (FEV₁ 50-79% normal), severe and very severe obstruction (A3): FEV₁/FVC<0.70 (FEV₁ 30-49% normal). Cases were also divided into three more groups based on the radiological emphysema score as follows: Mild lung destruction (E1) Emphysema score 0-6, moderate lung destruction (E2) Emphysema score 7-10, and severe lung destruction (E3) Emphysema score >10.

PFT was performed using Spiroback-G machine. Chest radiographs (Posteroanterior [PA] and lateral views) were obtained with the patients upright and holding their breath at full inspiration.⁵ Blood samples were collected in ethylenediaminetetraacetic acid impregnated vacutainer and stored at -20°C till they could be transported and analyzed for C₃ and C₄ complement levels. Serum C₃ and C₄ levels were determined by immunoturbidity method in a lab accredited with NABL. This method enhances sensitivity and specificity using analyte-specific antibodies for detection and quantitation with higher precision and longer stability.

Data were analyzed using SPSS version 16.0 for Windows (SPSS Inc., Chicago, IL). Analysis included descriptive statistics, contingency coefficient analysis with independent samples *t*-test.

RESULTS

Out of the total 70 subjects, 35 were patients with COPD taken as cases (50%) and 35 were healthy controls (50%) of the 35 patients with COPD, 20 (57%) were males and 15 (43%) were females (Table 1). More cases were in age group 61-65 (28%) and 66-70 (22%) years. Table 2 depicts correlation between C3 and C4 in both cases and controls.

Comparison of mean complement C₃ revealed no correlation among cases with mild obstruction (cases 120.33 mg/dl controls 120 mg/dl *P* = 0.97) and with moderate obstruction (cases 110 mg/dl controls 119.7 mg/dl *P* = 0.662). However, statistically significant lower serum C₃ levels were observed among patients with severe obstruction (cases 86.4 mg/dl controls 117 mg/dl *P* = 0.017) (Graph 1).

Table 1: Baseline characteristics

Characteristics	Cases	Controls
Total number of subjects	35	35
Gender		
Males	20	18
Females	15	17
Mean age	60 years	60 years

Comparison of mean complement C₄ levels revealed no correlation among cases with mild obstruction (cases 22.5 mg/dl controls 23.92 mg/d P = 0.616). However statistically significant lower serum C₄ levels were observed among patients with moderate obstruction (cases 17.9 mg/dl controls 24 mg/dl P = 0.004) and in those with severe obstruction (cases 16 mg/dl controls 24.8 mg/dl P = 0.005) (Graph 2).

Complement C₃ levels compared with controls showed no statistical significance among cases with an emphysema score (0-6) cases (121.8 mg/dl controls 122.1 mg/dl P = 0.988) and with emphysema score 7-10 cases (104.4 mg/dl controls 116.1 mg/dl P = 0.412). However statistically significant lower serum C₃ levels were observed among patients with emphysema score >10 (cases 82.5 mg/dl controls 118.9 mg/dl P = 0.017) (Graph 3).

Complement C₄ levels when compared with controls revealed no statistical significance observed among cases with an emphysema score between (0 and 6) (cases 22.7 mg/dl controls 23.5 mg/dl P = 0.725). However statistically significant lower serum C₄ levels were observed with emphysema score 7-10 (cases 18.3 mg/dl controls 23.3 mg/dl P = 0.003) with emphysema score >10 (cases 15.9 mg/dl controls 22.9 mg/dl P = 0.023) (Graph 4).

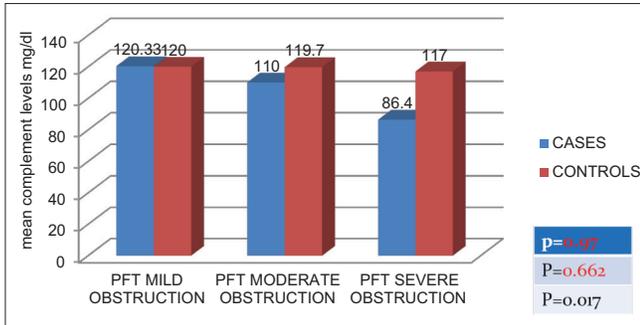
DISCUSSION

Complement proteins are a part of humoral defense, and they have the characteristic of interacting with certain antibody molecules once these have combined with antigen. Quantitatively, C₃ and C₄ comprise approximately two-thirds of the complement system. The classic complement pathway is activated by either antibody-coated targets such as microorganisms or antigen-antibody complexes, while the alternative complement pathway is activated directly by bacterial polysaccharides.

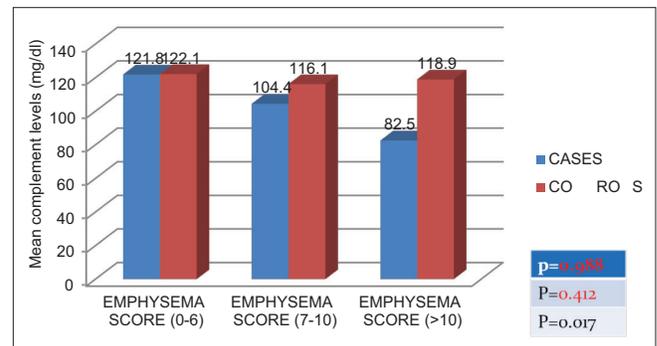
In this study, out of 35 cases 57% (n = 20) were males and 43% (n = 15) were females. The male to female sex

Table 2: Correlation of complements in both cases and controls

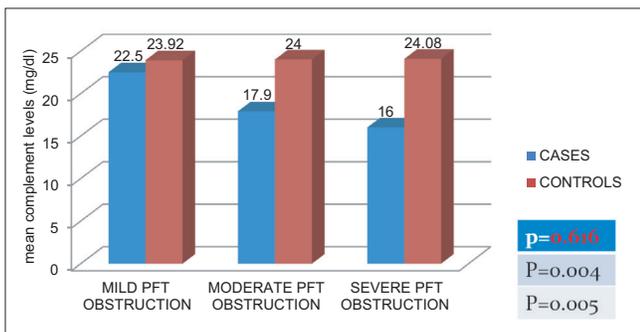
Type of Complement	n	Mean (mg/dl)	Standard deviation	t value	P value
C ₃					
Total cases	35	104	37.4	1.95	0.054
Total controls	35	120.2	34.2		
C ₄					
Total cases	35	19.17	5.5	3.12	0.002
Total controls	35	23.43	5.9		



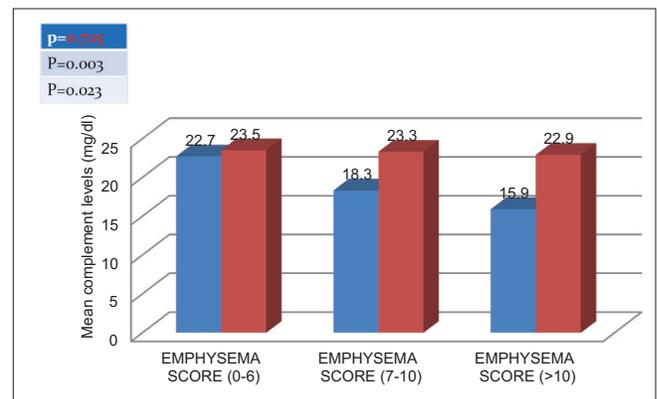
Graph 1: C₃ complement levels among three pulmonary function tests severity groups compared to age and sex matched controls



Graph 3: C₃ complement levels among three emphysema severity groups compared to age and sex matched controls



Graph 2: C₄ complement levels among three pulmonary function tests severity groups compared to age and sex matched controls



Graph 4: C₄ complement levels among three emphysema severity groups compared to age and sex matched controls

ratio was 1.3:1. This was in accordance with study done by Jindal *et al.*⁶

In this study, the maximum number of cases of COPD and exacerbations (60%) ($n = 21$) were admitted during rainy and winter seasons (July-December). A similar trend was seen in a study done by Jenkins *et al.*⁷ Factors potentially contributing to this include increased exposure to viral infections, increased host susceptibility; greater time spent indoors, reduced physical activity and temperature-related reduction in lung function.

Patients with severe PFT obstruction were compared with age and sex matched controls. C_3 and C_4 complement levels were calculated for both cases and controls. We observed a significant difference in mean values of complements C_3 and C_4 for both cases and controls and we also observed statistical significance for both C_3 ($P = 0.017$) and C_4 ($P = 0.005$). Similar observations were made by Chauhan *et al.*⁸ where they observed both serum C_3 (IU) and C_4 (IU) were lower in COPD patients ($C_3 = 95.9 \pm 33.11$, $C_4 = 113.6 \pm 62.4$) than in control ($C_3 = 167.3 \pm 25.42$, $C_4 = 205 \pm 76.5$; $P < 0.05$).

In the studies by Marc *et al.*⁹ and Fisun *et al.*,¹⁰ there was no significant difference observed in C_3 and C_4 levels between patients with COPD and healthy control subjects. The results are contrary to that seen in our study.

When total COPD patients with different degree of obstruction were compared with controls though there was no statistically significant difference in serum C_3 levels ($P = 0.054$), there was statistically significant difference in mean C_3 values were observed, and there was statistically significant difference observed for serum C_4 levels ($P = 0.002$). Similar observations were noticed by Kosmas *et al.*³ and Serpil *et al.*⁴

In this study, COPD patients with Emphysema score 0-6 (E1) were compared with age and sex-matched controls for complement levels C_3 and C_4 . When COPD patients with emphysema score (0-6) were compared with healthy sex and age matched controls, there was no significant difference between serum C_3 , C_4 levels observed.

When COPD patients with emphysema score (7-10) were compared with controls, although significant difference observed in mean C_3 values, these values were statistically not significant ($P = 0.412$). However, statistically significant difference ($P = 0.003$) observed in C_4 values.

When COPD patients with emphysema score (>10) were compared with controls, statistical significance observed in both C_3 ($P = 0.017$), C_4 ($P = 0.023$) levels, similar

observations were made by Burki and Krumpelman¹¹ and Chugh *et al.*,¹² in their studies.

Findings arising from this study showed that for patients with COPD, particularly moderate to severe degree COPD (moderate to severe obstruction, high emphysema score) had significantly low serum complement C_3 , C_4 levels compared to healthy controls.

The probable reason for lower serum levels of complement components C_3 and C_4 in COPD patients compared to healthy controls could be because of sustained complement activation secondary to repeated respiratory infections¹³ leading to influx of inflammatory cells into the lung parenchyma with subsequent release of elastases and oxidants that cause damage to elastic lung tissue. This leads to the logical inference that there might be a quantitative relationship between complement consumption and degree of elastic tissue destruction.

This study has several strengths: More numbers of subjects were included in our study when compared to other similar studies. A better method (immunoturbidometry) which has a higher sensitivity and specificity was used to estimate C_3 and C_4 levels compared to other studies.

There are certain limitations in our study. Although more number of patients were enrolled in this study compared to other similar studies, this is still a small study and a larger number of cases might have given more meaningful results. We could have used CT scan to measure the emphysema score although chest X-ray is also a standardized modality to assess the severity of lung destruction.

CONCLUSION

This study showed a direct correlation between the severity of COPD and serum complement levels. Lower levels of complements were seen in more severe COPD. Serum complements levels may well serve as marker for COPD severity. Further large-scale studies needed in this regard.

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Microscopic Study of Left Middle Cerebral Artery in Different Age Groups

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Abstract

Background: It has been described earlier by many authors that there is an age linked increase in thickness of layers of cerebral vessels.

Objective: A microscopic study of left middle cerebral artery in different age groups to observe the sequence of changes in the vessel wall, with advancing age.

Materials and Methods: Left middle cerebral artery from 30 specimens of different age groups were taken, sections made and stained. The changes in the layers were observed and measured.

Results: The left middle cerebral artery showed progressive thickening of layers with age. Intima showed intimal cushions IEL become prominent and showed splitting.

Conclusion: The left middle cerebral artery showed progressive thickening of layers with age. Intima showed intimal cushions IEL become prominent and showed splitting. The presence of intimal cushion and widening of the artery due to large media defect can lead to atherosclerosis.

Application: Thickening of the layers of the left middle cerebral artery can lead to progressive deterioration in nutrition. This knowledge is imperative for the neurosurgeons in pre-operative planning.

Key words: Atherosclerosis, Tunica intima, Tunica media

INTRODUCTION

A thorough knowledge of arterial circulation in the brain is essential due to the present days increasing frequency and danger of intracranial vascular lesions which form the third most common cause of death. The histological changes associated with the middle cerebral artery in different ages and sexes show the presence of intimal cushions (IC). The widening of arteries due to large media is a cause of cerebral insufficiency.

MATERIALS AND METHODS

The left middle cerebral artery from 30 brain specimens belonging to different age groups and both sexes were taken. Bits of 1 cm were taken, fixed in 10% formalin, separately processed, cleared and blocked in paraffin wax. Sections of 6 μ thickness were cut and stained using the following stains.

1. Hematoxylin and eosin
2. Verhoeff's elastic stain counter stained with Van Gieson's stain
3. Masson's trichrome stain.

The changes in the thickness of tunica intima, media, and adventitia were observed under low and high powers of the light microscope. The relative thickness of intima, media, and adventitia was tabulated. It was observed that intima was thin and composed of a single layer of endothelial cells with internal elastic lamina (IEL) and a well-developed media in the fetus.

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Tunica media became thicker in the first and second decades.

The IEL also became more prominent. The intimal thickening was uniform in the fourth decade. In the fifth decade, The intimal thickening became localized at places. In the seventh decade, the ICs were seen projecting into the lumen. The IEL showed splitting and atheromatous plaques.

DISCUSSION

Cerebral arteries like the muscular arteries, such as the muscular arteries, were composed of tunica intima, media, and adventitia with a thin media and a prominent IEL and ill-defined external elastic lamina.

The tunica intima was observed to proliferate with age from the second decade till the seventh in accordance with Das Alternals *et al.*,¹ who also described an age linked increase in the thickness of the layer leading to progressive deterioration in nutrition. Baker² described the IEL was the first to show aging changes as early as the third decade and the lamina becomes fragmented, reduplicated, and later loses its uniformity. This was also seen here. The IEL showed changes such as splitting.

Physiological ICs in the young individuals has been described by Hassler.³ It was observed here that these thickening became more prominent in the seventh decade.

Windows in IEL of cerebral arteries were also noticed by Hassler⁴ which were reduced in number and size with increasing age leading to atherosclerosis. This has also been noticed here.

Media increases in thickness with age as in accordance with Baker,⁵ who described this thickening is due to increase in collagenous tissue and muscular elements.

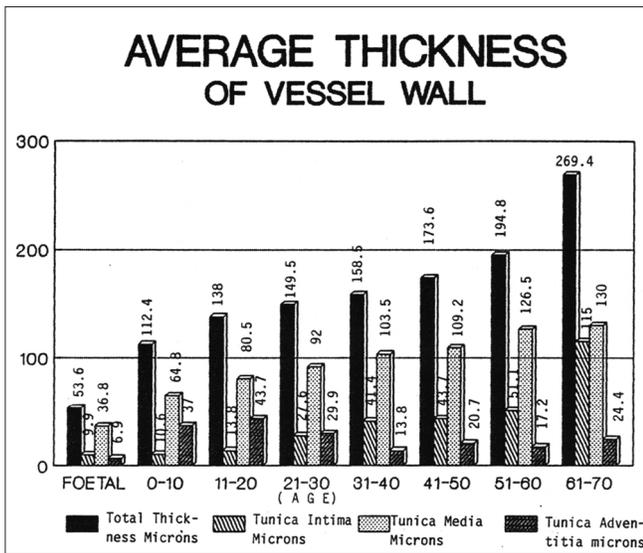


Figure 1: Bar diagram showing the thickness of vessel wall layers in different age groups

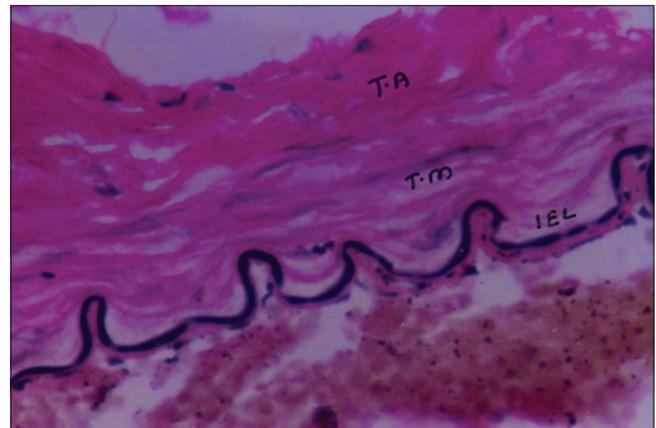


Figure 3: Transverse section of left middle cerebral artery of a 25-year-old male Verhoeff's staining x200

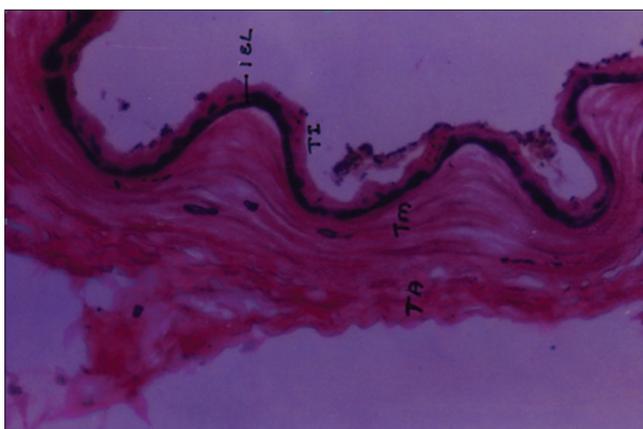


Figure 2: Transverse section of left middle cerebral artery of a 15-year-old male Verhoeff's staining x200

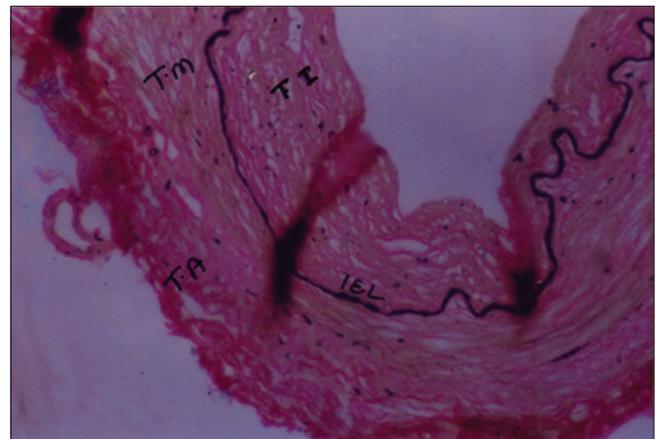


Figure 4: Transverse section of left middle cerebral artery of a 65-year-old male showing intimal cushions Verhoeff's staining x100



Figure 5: Transverse section of the left middle cerebral artery of a 65-year-old male showing splitting of the internal elastic lamina. Verhoeff's staining x200

The adventitia does not show much change here which is in contrast to the study of Das Alternals² *et al.*

RESULTS

The histological study of left middle cerebral artery conducted in 30 human brain showed progressive thickening with age in the tunica intima and media. IEL became prominent with age and showed splitting.

Intima became localized at places in form of intimal cushions. (Figures 1-5).

CONCLUSION

A histological study of left middle cerebral arteries was conducted in 30 human brains. The post mortem specimens and the full term stillborn fetuses have been used to understand the natural changes occurring with age.

The intima and media showed progressive thickening with age. The presence of ICs and widening of the arteries due to large media defects with advancing age can lead to pathological changes such as atherosclerosis causing cerebral insufficiency. This knowledge is imperative for the neurosurgeons in pre-operative planning.

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Randomized Controlled Study to Compare the Efficacy of Intravenous Palonosetron and Intravenous Ondansetron in Preventing Post-operative Nausea and Vomiting in Laparoscopic Surgeries

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Abstract

Introduction: Post-operative nausea and vomiting (PONV) are two of the most common and unpleasant side effects following anesthesia and surgery resulting in complications such as dehydration, gastric aspiration, and wound dehiscence. Laparoscopic surgery is minimally invasive with faster recovery, shorter hospital stay but PONV remains a major cause for morbidity.

Purpose: The purpose of the study was to compare the efficacy of intravenous (IV) palonosetron and IV ondansetron in preventing PONV in laparoscopic surgeries.

Materials and Methods: This randomized, double-blinded, controlled study was conducted in the Department of Anaesthesiology, SMVMCH, Puducherry, India. 100 adult patients were divided into two groups of 50 each, randomized to receive 0.075 mg of palonosetron and 4 mg of ondansetron before induction. The occurrence of nausea, vomiting and severity of nausea according to a visual analog scale (VAS: 0 - No nausea; 10 - Worst nausea) were observed immediately after the end of surgery at 0-2 h, 2-6 h, 6-12 h, and 12-24 h post-surgery. Injection metoclopramide (10 mg IV) was used as a rescue antiemetic when one episode of PONV occurred or at VAS >5 and the patient requested for treatment. Details of any adverse events and their overall satisfaction were recorded.

Results: The two groups were comparable regarding age, gender, weight, and category of surgery. The incidence of post-operative nausea and overall PONV were lower in Group P than Group O, which was statistically significant ($P < 0.05$). The requirement of rescue medication was lower in Group P but statistically not significant. Adverse events in both groups were statistically non-significant. Patient satisfaction was better with Group P though statistically not significant.

Conclusion: Palonosetron 0.075 mg IV produced a lower incidence of PONV compared with ondansetron 4 mg IV in patients undergoing laparoscopic surgeries in the first 24 h with better patient satisfaction.

Key words: Adverse events, Nausea, Ondansetron, Palonosetron, Patient satisfaction, Rescue medication, Vomiting

INTRODUCTION

Post-operative nausea and vomiting (PONV) are two of the most common and unpleasant side effects following

anesthesia and surgery.¹ Patients not only rank the absence of PONV as being important² but also rank it more important than an earlier discharge from an ambulatory surgical unit.³ PONV can be very distressing to the patient, sometimes more than the surgery itself, and it can result in several complications such as dehydration, gastric aspiration, and wound dehiscence.⁴⁻⁶

The overall incidence of PONV after general anesthesia in outpatients has been reported to be 37% although several factors including age, sex, history of PONV, and opiate administration influence the risk.⁷ Even patients with zero

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known risk factors carry a 10% risk of PONV. This risk increases dramatically to 61% and 79%, respectively, when 3 or 4 risk factors exist (female gender, non-smoker, history of motion sickness, post-operative opioid use, and history of PONV).⁸

Laparoscopic surgery provides tremendous benefits to patients including faster recovery, shorter hospital stay, and prompt return to normal activities. Despite the minimally invasive nature of laparoscopy, high incidence of PONV remains a major cause for morbidity.⁹

Post-operative nausea and/or vomiting can be defined as nausea and/or vomiting within 24 h of surgery.^{10,11} Nausea and vomiting are associated with decreased quality of life and patient satisfaction.^{12,13}

Factors that reportedly affect the incidence of PONV include female sex, non-smoker, history of PONV, motion sickness, lengthy surgical duration, inhalational anesthetics, nitrous oxide, intra-operative and post-operative use of opioids. In addition, severe anxiety before surgery, the type of surgery, intra-operative fluid therapy, and increased duration of anesthesia also affect the incidence of PONV.¹⁴ Female gender, motion sickness, history of PONV, non-smoker, and post-operative use of opioids are known to be the most predictive factors among all the factors.¹⁵

The 5-hydroxytryptamine-3 (5-HT₃) receptor antagonists are popular drugs for PONV prophylaxis because of their similar efficacy to droperidol or dexamethasone and their favorable side-effect profile.¹⁶ Ondansetron was the first commercially available 5-HT₃ receptor antagonist. Thereafter, granisetron, dolasetron, tropisetron, ramosetron, and palonosetron were introduced. Many studies have confirmed that this class of antiemetics exhibited better prophylactic efficacies compared with the older traditional drugs including droperidol, perphenazine, or metoclopramide.¹⁷⁻¹⁹

Palonosetron is a new, potent, selective 5-HT₃ receptor antagonist with a strong receptor binding affinity and a long elimination half-life and, therefore, a long duration of efficacy.^{20,21} Palonosetron is a pharmacologically distinct 5-HT₃ RA with a greater binding affinity and longer half-life than older agents in this class.²² Binding isotherms, equilibrium diagnostic tests, and kinetic diagnostic tests show that palonosetron is an allosteric antagonist with positive cooperativity, unlike ondansetron and granisetron. Differential effects on [³H]-ligand binding indicate that palonosetron interacts at different or additional sites on the 5-HT₃ receptor compared with the binding profiles of granisetron or ondansetron. Unlike these agents, palonosetron also elicits 5-HT₃ receptor internalization and

promotes extended inhibition of receptor activity.²³ The aim of the study is to compare the efficacy of intravenous (IV) palonosetron and IV ondansetron in preventing PONV in patients undergoing laparoscopic surgeries.

MATERIALS AND METHODS

This is a randomized controlled clinical study comparing the efficacy of a single pre-induction dose of palonosetron (0.075 mg) in Group P and ondansetron (4 mg) in Group O as per Good Clinical Practice Guidelines by WHO and Ethics. The sample size was calculated on the basis of the primary outcome measure. It was estimated that 49 subjects would be required per group to detect 2/3rd reduction in the frequency of PONV from the control treatment (from 40% to 15%) with 80% power and 10% probability of type one error. Hence, in the present study, 50 patients per group were selected. Totally, 100 adults belonging to the age group of 18-60 years of both sexes scheduled for elective laparoscopic surgeries were divided into two groups, Group P (palonosetron) and Group O (ondansetron) of 50 people each. Patients included were American Society of Anesthesiologists I-II with patients aged 18-60 years, non-smoker, no history of motion sickness or previous PONV, and elective laparoscopic surgery. Patients excluded were pregnancy and lactation, administration of an antiemetic medication, antipsychotic medications or steroids within 24 h before surgery, the presence of a cardiovascular or respiratory disease, obesity (body mass index >35 kg/m²), renal or hepatic dysfunction, history of allergy to either of the drugs. Double-blinded randomization was followed with 1:1 ratio on the basis of computer-generated random numbered list, and allocation was concealed by serially numbered sealed envelopes. 100 adult patients were randomly allocated into two groups: Group P (palonosetron) and Group O (ondansetron) of 50 each. In the pre-anesthetic room, IV access was secured, and baseline parameters were observed and recorded such as heart rate, mean arterial pressure, and oxygen saturation. All patients in Group P received 0.075 mg of palonosetron and Group O received 4 mg of ondansetron before induction. Drugs were given by another anesthesiologist not involved in this study. After premedication with injection glycopyrrolate 0.004 mg kg⁻¹, injection midazolam 0.05 mg kg⁻¹, injection fentanyl 2 µg kg⁻¹, and after adequate pre-oxygenation, anesthesia was induced by injection propofol 2 mg kg⁻¹ followed by injection atracurium 0.5 mg kg⁻¹ to facilitate laryngoscopy and intubation. Anesthesia was maintained with 70% nitrous oxide in oxygen and 0.5-2% sevoflurane. At the completion of surgery, patients received injection neostigmine 0.05 mg kg⁻¹ and glycopyrrolate 0.004 mg kg⁻¹, for reversal of neuromuscular blockade and extubated.

Then, patients were observed for the baseline parameters in the recovery room for 1 h. The occurrence of nausea and vomiting and the severity of nausea according to a visual analog scale (VAS; 0, no nausea; 10, worst nausea) were observed immediately after the end of surgery at 0-2 h, 2-6 h, 6-12 h, and 12-24 h post-surgery. Nausea is defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit, whereas an episode of vomiting is defined as vomiting (forceful expulsion of gastric contents from the mouth) or retching (labored spasmodic, rhythmic contractions of the respiratory muscles without expulsion of gastric contents). Injection Metoclopramide (10 mg IV) was used as a rescue antiemetic when one episode of PONV occurred or at VAS >5 and the patient requested for treatment. If metoclopramide treatment was ineffective, ondansetron 4 mg IV was administered. A complete response was defined as the absence of PONV and no use of rescue antiemetic. Details of any adverse effects including a headache, dizziness, and constipation were recorded. Patients were also asked to rate their overall satisfaction on a three-point scale (satisfied, neutral, and unsatisfied) 24 h after surgery completion. The data were entered and analyzed using statistical software using Epi Info 3.4.3 version and SPSS version 20. Z-test for the difference between the means was used to analyze age and weight of study participants. Chi-square test was applied to study gender wise distribution, category of surgery, to compare the frequency of PONV, overall nausea and vomiting, requirement of rescue medication, adverse events (headache and dizziness), and patient satisfaction. Fisher's exact test was used to compare the incidence of constipation in the study participants. The level of significance was fixed at 0.05.

RESULTS

A total of 100 patients were included in this study. The two groups were similar regarding age, weight, and gender as in Table 1. In our study (Table 2), mean age in ondansetron group is 31.50 ± 9.945 years; and in palonosetron group, it is 34.32 ± 10.750 years and suggesting that both the groups have similar age characteristics and are statistically not significant ($P = 0.176$). In our study (Table 3), mean weight in ondansetron group is 57.68 ± 7.435 , and in palonosetron group, it is 56.68 ± 5.648 and suggesting that both the groups have comparable demographic characteristics and are statistically not significant ($P = 0.451$). In this study, (Table 4) 34% were males and 66% were females in group ondansetron and 30% were males and 70% were females in group palonosetron, suggesting that both the groups have comparable demographic characteristics. When we compared the following surgeries in both the groups, namely, abdominal, abdominal/gynecological, diagnostic,

diagnostic/gynecological, and gynecological (Table 5), we found that they were not statistically significant ($P = 0.692$). In our study (Table 6-10), the incidence of post-operative nausea was lower in palonosetron group compared to ondansetron group. This was found to be statistically significant in first 2 h ($P = 0.046$) (Table 6) and overall 24 h ($P = 0.001$) (Tables 11-15). In our study, the incidence of post-operative vomiting was lower in palonosetron group compared to ondansetron group, but they were not statistically significant. In our study (Table 16), the

Table 1: Participants demographic data in both groups

Characteristics	Mean \pm SD (n=50)		P value
	Group O	Group P	
Age	31.5 \pm 9.945	34.32 \pm 10.750	0.176
Weight	57.68 \pm 7.435	56.68 \pm 5.648	0.451
Gender			
Female	33	35	0.668
Male	17	15	

SD: Standard deviation, Group P: Palonosetron, Group O: Ondansetron

Table 2: Age distribution of study participants in both groups

Age (years)	Mean \pm SD	P value
Group O (n=50)	31.50 \pm 9.945	0.176
Group P (n=50)	34.32 \pm 10.750	

SD: Standard deviation, Group P: Palonosetron, Group O: Ondansetron

Table 3: Mean weight of study participants in both groups

Weight (kg)	Mean \pm SD	P value
Group O (n=50)	57.68 \pm 7.435	0.451
Group P (n=50)	56.68 \pm 5.648	

SD: Standard deviation, Group P: Palonosetron, Group O: Ondansetron

Table 4: Gender wise distribution of study participants in both groups

Sex	Group O	Group P	Total
Female	33	35	68
Male	17	15	32
Total	50	50	100

Group P: Palonosetron, Group O: Ondansetron

Table 5: Category of surgery in both groups

Surgery	Group O	Group P	Total	P value
Abdominal	32	34	66	
Abdominal/gynecological	0	1	1	
Diagnostic	9	5	14	0.692
Diagnostic/gynecological	0	1	1	
Gynecological	9	9	18	
Total	50	50	100	

Table 6: Comparison of frequency of post-operative nausea episodes in patients administered with palonosetron and ondansetron at 0-2 h

Time and Occurrence	Group O	Group P	Total	P value
0-2 h				
No	36	44	80	0.046
Yes	14	6	20	
Total	50	50	100	

Group P: Palonosetron, Group O: Ondansetron

Table 7: Comparison of frequency of post-operative nausea episodes in patients administered with palonosetron and ondansetron at 2-6 h

Time and Occurrence	Group O	Group P	Total	P value
2-6 h				
No	39	45	84	0.102
Yes	11	5	16	
Total	50	50	100	

Group P: Palonosetron, Group O: Ondansetron

Table 8: Comparison of frequency of post-operative nausea episodes in patients administered with palonosetron and ondansetron at 6-12 h

Time and Occurrence	Group O	Group P	Total	P value
6-12 h				
No	33	40	73	0.115
Yes	17	10	27	
Total	50	50	100	

Group P: Palonosetron, Group O: Ondansetron

Table 9: Comparison of frequency of post-operative nausea episodes in patients administered with palonosetron and ondansetron at 12-24 h

Time and Occurrence	Group O	Group P	Total	P value
12-24 h				
No	34	42	76	0.061
Yes	16	8	24	
Total	50	50	100	

Group P: Palonosetron, Group O: Ondansetron

incidence of PONV was lower in palonosetron group compared to ondansetron group. This was found to be statistically significant in first 2 h ($P = 0.046$) and overall 24 h ($P = 0.003$). In our study, (Tables 17, 18) 9 patients from ondansetron group and 6 patients from palonosetron group required rescue medication. This was statistically not significant. In this study, (Tables 19,20) we have compared 3 adverse events between the two groups, namely, headache, dizziness, and constipation. The headache was found in 12% of ondansetron group and 8% of palonosetron

Table 10: Comparison of frequency of post-operative nausea episodes in patients administered with palonosetron and ondansetron at 0-24 h

Time and Occurrence	Group O	Group P	Total	P value*
0-24 h				
No	15	32	47	0.001
Yes	35	18	53	
Total	50	50	100	

* $P < 0.05$ (significant), Group P: Palonosetron, Group O: Ondansetron

Table 11: Comparison of frequency of post-operative vomiting episodes in patients administered with palonosetron and ondansetron 0-2 h

Time and Occurrence	Group O	Group P	Total	P value
0-2 h				
No	45	48	93	0.436
Yes	5	2	7	
Total	50	50	100	

Group P: Palonosetron, Group O: Ondansetron

Table 12: Comparison of frequency of post-operative vomiting episodes in patients administered with palonosetron and ondansetron 2-6 h

Time and Occurrence	Group O	Group P	Total	P value
2-6 h				
No	45	47	92	0.715
Yes	5	3	8	
Total	50	50	100	

Group P: Palonosetron, Group O: Ondansetron

Table 13: Comparison of frequency of post-operative vomiting episodes in patients administered with palonosetron and ondansetron 6-12 h

Time and Occurrence	Group O	Group P	Total	P value
6-12 h				
No	42	44	86	0.564
Yes	8	6	14	
Total	50	50	100	

Group P: Palonosetron, Group O: Ondansetron

group. Dizziness was found in 12% of ondansetron group and 12% of palonosetron group. Constipation was found in 6% of ondansetron group and 8% of palonosetron group. They were not statistically significant. In this study, (Table 21) 50% patients from ondansetron group and 68% patients from palonosetron group were satisfied with the prophylactic drug administered. 38% from ondansetron group and 22% from palonosetron group had a neutral response. 12% from ondansetron group and 10% from palonosetron group were unsatisfied. Despite the above result, patient satisfaction was statistically not significant.

Table 14: Comparison of frequency of post-operative vomiting episodes in patients administered with palonosetron and ondansetron 12-24 h

Time and Occurrence	Group O	Group P	Total	P value
12-24 h				
No	43	45	88	0.538
Yes	7	5	12	
Total	50	50	100	

Group P: Palonosetron, Group O: Ondansetron

Table 15: Comparison of frequency of post-operative vomiting episodes in patients administered with palonosetron and ondansetron 0-24 h

Time and Occurrence	Group O	Group P	Total	P value
0-24 h				
No	32	36	68	0.391
Yes	18	14	32	
Total	50	50	100	

Group P: Palonosetron, Group O: Ondansetron

Table 16: Comparison of frequency of overall PONV episodes in patients administered with palonosetron and ondansetron

Time and Occurrence	Group O	Group P	Total	P value*
0-24 h				
No	15	30	45	0.003
Yes	35	20	55	
Total	50	50	100	

*P<0.05 (significant), PONV: Post-operative nausea and vomiting, Group P: Palonosetron, Group O: Ondansetron

Table 17: Requirement of rescue medication in both groups

Rescue medication	Frequency	Percentage
Group O		
No	41	82.0
Yes	9	18.0
Total	50	100.0
Group P		
No	44	88.0
Yes	6	12.0
Total	50	100.0

Group P: Palonosetron, Group O: Ondansetron

DISCUSSION

PONV is a complication that causes discomfort and dissatisfaction in patients who undergo surgery.²⁴ Post-operative period is associated with the variable incidence of nausea and vomiting depending on the duration of surgery, the type of anesthetic agents used (dose, inhalational drugs, and opioids), smoking habit etc.²⁵ 5-HT₃ receptor

Table 18: Comparison of rescue medication in both groups

Rescue medication	Group O	Group P	Total	P value
Rescue medication				
Yes	9	6	15	0.401
No	41	44	85	
Total	50	50	100	

Group P: Palonosetron, Group O: Ondansetron

Table 19: Adverse events in both groups

Adverse events	n (%)	
	Group O	Group P
Headache	6 (12.0)	4 (8.0)
Dizziness	6 (12.0)	6 (12.0)
Constipation	3 (6.0)	4 (8.0)

Group P: Palonosetron, Group O: Ondansetron

Table 20: Comparison of adverse events in patients administered with palonosetron and ondansetron

Adverse events	Group O	Group P	Total	P value
Headache				
Yes	6	4	10	0.505
No	44	46	90	
Total	50	50	100	
Dizziness				
Yes	6	6	12	0.100
No	44	44	88	
Total	50	50	100	
Constipation				
Yes	3	4	7	0.100
No	47	46	93	
Total	50	50	100	

Group P: Palonosetron, Group O: Ondansetron

Table 21: Comparison of patient satisfaction in patients undergoing surgery who received palonosetron and ondansetron before anesthesia

Patient satisfaction	n=50 (%)		Total n=100	P value
	Group O	Group P		
Satisfied	25 (50)	34 (68)	59	0.165
Neutral	19 (38)	11 (22)	30	
Unsatisfied	6 (12)	5 (10)	11	

Group P: Palonosetron, Group O: Ondansetron

stimulation is the primary event in the initiation of vomiting reflex.²⁶ These receptors are situated on the nerve terminal of the vagus nerve in the periphery and centrally on the chemoreceptor trigger zone (CTZ) of the area postrema.²⁴ Anesthetic agents initiate the vomiting reflex by stimulating the central 5-HT₃ receptors on the CTZ and also by releasing serotonin from the enterochromaffin cells of the small intestine and subsequent stimulation of 5-HT₃ receptors on vagus nerve afferent fibers.²⁴ The use of prophylactic antiemetics is intended to prevent episodes

of vomiting, eliminate or lessen the severity of nausea, and minimize or remove the need for PONV rescue medications.²⁷ 5-HT₃ RAs are generally safe at the usual doses used to prevent or treat PONV, with no dose-related sedation or extrapyramidal reactions and no significant effects on vital signs.²⁸ Ondansetron is a selective 5-HT₃ (serotonin) receptor antagonist used for prevention of PONV. It is given in 4 mg and 8 mg doses, but it has been shown in various studies that 4 mg is the optimal dose as increasing the dose to 8 mg does not confer any additional beneficial effect.²⁹⁻³¹ Palonosetron is a second generation serotonin 5-HT₃ receptor antagonist. Unlike other antagonists, it has unique structural, pharmacological, clinical characteristics. Other antagonists directly compete with serotonin, but palonosetron has an indirect effect by its allosteric binding with 5-HT₃ receptors.²² Furthermore, it suppresses the response induced by substance P has negative cooperativity with neurokinin-1 receptors by cross-talk and creates an antiemetic effect.²³ These explain strong receptor-affinity of palonosetron and its long plasma half-life. Kovac *et al.*³² demonstrated that palonosetron 75 µg is the more effective dose for the prevention of PONV after major gynecological and laparoscopic surgery than 25 µg and 50 µg.³² We did not include a control group receiving placebo in our study. Aspinall and Goodman³³ have suggested that if active drugs are available, placebo-controlled trials may be unethical because PONV are very much distressing after laparoscopic surgery.³³ Bhattacharjee *et al.*³⁴ have reported that prophylactic therapy with palonosetron is more effective than granisetron in the prevention of PONV after laparoscopic cholecystectomy in the 24-48 h post-operative period, though not in the first 24 h. Kim *et al.*³⁵ concluded in his study that ramosetron 0.3 mg IV and ondansetron 8 mg IV were equally effective in decreasing the incidence of PONV and severity of nausea in high-risk female patients during the first 24 h after surgery. Although there were no significant differences between ramosetron and ondansetron in decreasing the incidence of PONV, severity of nausea, need for additional rescue antiemetics, or patient satisfaction rate, ramosetron appears to be a more effective antiemetic agent because it requires less additional rescue antiemetics after surgery. Candiotti *et al.*³⁶ reported that palonosetron and ondansetron did not show differences in the primary efficacy endpoint of complete control during the 72 h after study drug administration. There was a trend toward less emesis in the 0-72 h period favoring palonosetron. In our study, we compared the efficacy of palonosetron and ondansetron in the prevention of PONV in laparoscopic surgeries over a period of 24-h. In the study by Gupta *et al.*,³⁷ the incidence of PONV was maximal during the first 4 h and was more in the patients of ondansetron group as compared to patients of palonosetron and granisetron group. In our study, the incidence of post-operative nausea

was compared over 0-2 h, 2-6 h, 6-12 h, 12-24 h, and 0-24 h. The incidence was 14 in ondansetron group and 6 in palonosetron group in 0-2 h which was statistically significant ($P = 0.046$). Similarly, the incidence was 35 in ondansetron group and 18 in palonosetron group in 0-24 h which was statistically significant ($P = 0.001$). In our study, post-operative vomiting was compared over 0-2 h, 2-6 h, 6-12 h, 12-24 h, and 0-24 h. The incidence was 18 in ondansetron group and 14 in palonosetron group over 0-24 h. Though the incidence was lower in palonosetron group than ondansetron group, they were not statistically significant ($P = 0.391$). In our study, overall PONV was compared between the two groups in 0-2 h, 2-6 h, 6-12 h, 12-24 h, and 0-24 h. The incidence of overall PONV was 14 in ondansetron group and 6 in palonosetron group in 0-2 h. Similarly, the incidence of overall PONV was 35 in ondansetron group and 20 in palonosetron group. This was statistically significant in first 2 h ($P = 0.046$) and 0-24 h ($P = 0.003$). Adverse effects with single IV dose of the study drugs were not serious, and there were no significant differences in the incidence of the headache, dizziness, and constipation between the groups. Concerns have raised over the QTc interval prolonging the effect of ondansetron and the risk of ventricular tachycardia. However, there was no QTc interval prolongation or other electrocardiography abnormalities in this study. Thus, both palonosetron and ondansetron are devoid of clinically important adverse effects when used in this manner. In our study, 3 adverse events were compared, namely, headache, dizziness, and constipation. Of these, the incidence of the headache was more in ondansetron group; dizziness was similar between the two groups, and constipation was more in palonosetron group. This was statistically not significant. In our study, rescue medication was required in 12% of palonosetron group and 18% of ondansetron group. This holds for the first 24-h period following surgery. It remains to be explored if the same is true for the next 24-h.

CONCLUSION

Palonosetron 0.075 mg IV produced a lower incidence of PONV compared with ondansetron 4 mg IV in patients undergoing laparoscopic surgeries in the first 24 h with better patient satisfaction.

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Fetal Biometry in Late 3rd Trimester for Gestational Age Indian Standards

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Abstract

Introduction: Ultrasound (USG) study in antenatal patients is a very valuable tool especially when it comes to estimation of gestational age. Fetal biometry in late 3rd trimester differs very much in Indians compared to their western peers.

Objective: To frame out a fetal biometry chart in late 3rd trimester as per Indian standards and thereby eliminate the chance of being deceived by western charts in the case of term pregnancies.

Materials and Methods: A prospective study was conducted with study sample of 340 cases during a 12-month period. SPSS 16.0 Mann-Whitney *U*-test, the χ^2 for qualitative and students *t*-test for quantitative variables. A *P* = 0.05 was considered significant.

Results: (1) There was definite discrepancy in Indian standard values of fetal biometry, being less than their western counterparts in late 3rd trimester, (2) average fetal weight of Indian babies at term was found 2.9 kg compared to 3.6 kg in western group.

Conclusion: There should be a fetal biometry chart by Indian standards incorporated in USG machines instead of relying on western charts.

Key words: Fetal biometry, Indian standards, Late 3rd trimester, Ultrasound study

INTRODUCTION

Most of the ultrasound (USG) machines incorporate a chart of fetal biometry and gestational age by Western standards, e.g., Hadlock *et al.*,¹ Sabbagha *et al.*,² Jeanty *et al.*,^{3,4} and Campbells *et al.*⁵ Even though fetal age estimation by USG in late pregnancy is not a reliable method, we intend to frame a chart for the 3rd trimester fetal biometry by Indian standards. There is definite deviation of values to the lower side in comparison to western charts.

Aim of Study

1. To establish a variation in fetal biometry in 3rd trimester in Indian population comparing with the western population

2. To develop a nomogram for the Indian population in relation to fetal biometry for gestational age in late 3rd trimester.

Inclusions Criteria

- Only cases with early documented gestational age were included
- Biparietal diameter (BPD) and femoral length (FL) were the two main parameters considered. Abdominal circumference (AC) and head circumference (HC) also noted
- Estimated fetal weight calculation was noted from the default chart in USG machines.

Exclusion Criteria

- Macrosomic babies outside 10th and 90th percentile expected for Indian standards were excluded
- Grossly obese mothers excluded due to less clarity in imaging
- Cases of oligohydramnios
- Cases of growth retardation/fetal anomalies
- Other parameters such as humeral length, binocular

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distance, and cerebellar measurements were not considered.

MATERIALS AND METHODS

We had a study of fetal biometry and fetal age correlation of babies beyond 32 weeks of pregnancies in Kannur Medical College OBG Department during a 12-month period from July 1, 2013, to June 30, 2014, and data from 340 cases during the period were collected and analyzed.

The cases selected was from booked antenatal cases attending our clinic and also from those in our study group for elective induction at 38 weeks + gestation.

Most of these cases had 1st and 2nd trimester (around 20 weeks) USG reports with reliable documentation of gestational age. The cases included primigravida as well as multigravida. The USG was done by the first author with 19 years expertise in obstetric USG scanning.

The machine used for the purpose was Wipro Logic Alpha 200 and a curvilinear abdominal probe with 3.5 MHz frequency was used.

RESULTS

Its observed that average baby in India weighs 2.8-3 kg by 38-40 weeks, whereas by western standards average baby weight at term is 3.6 kg.

It is observed that up to 32 weeks the biometry - BPD, FL, AC, HC parameters do not differ much between western and Indian standards. From 32 weeks onward, there are lesser values for the above parameters in Indian babies compared to corresponding periods of Western babies. This disparity is seen widened as age advances.

The above disparity is explained perhaps by racial and ethnic reasons of Indian babies being less in weight to their western peers. The following chart of Indian versus Western standards of fetal biometry is self-illustrative.

Table 1 showing Western versus Indian standards of fetal biometry from 32 to 40 weeks.

Fetal biometry and estimated fetal weight Western versus Indian standards at 37 and 38 weeks (Figure 1).

Fetal biometry and estimated fetal weight Western versus Indian standards at 39 and 40 weeks (Figure 2).

By the study, we have developed a chart of fetal biometry and estimated fetal weight for gestational age 32-40 weeks

Table 1: Western Vs Indian chart for Fetal biometry-32 to 40 weeks

Weeks	BPD (cm)		FL		HC		AC		EFW (kg)	
	West	India	West	India	West	India	West	India	West	India
32	7.9	7.9	6.3	6	29.7	28.5	28	26.8	1.81	1.72
33	8.2	8	6.5	6.1	30.4	28.8	29	28.2	2.01	1.9
34	8.4	8.1	6.6	6.3	31.2	29.2	30	28.7	2.22	1.99
35	8.6	8.3	6.8	6.6	31.8	30	30.9	29.6	2.43	2.15
36	8.8	8.5	7	6.7	32.5	30.9	31.8	30.1	2.65	2.3
37	9	8.6	7.2	6.9	33.6	31.3	32.7	31.3	2.89	2.45
38	9.1	8.7	7.3	7	33.6	31.5	33.6	32.5	3.15	2.62
39	9.3	8.8	7.5	7.1	34.1	32.1	34.5	32.7	3.36	2.78
40	9.5	9	7.6	7.2	34.5	32.9	35.4	33.4	3.52	2.96

EFW: Estimated fetal weight, BPD: Biparietal diameter, FL: Femural length, HC: Head circumference, AC: Abdominal circumference

in Indian population. Our study correlates well with the study of Rajan *et al.*,⁶⁻⁸ 1993 both in fetal biometry and estimated fetal weight.

Variation of estimated fetal weight from 32 to 40 weeks in Western versus Indian standards (Figure 3).

DISCUSSION

The duration of pregnancy is classically described in menstrual age by adding 40 weeks to the last menstrual period (Nagle's rule). The clinical application of USG in obstetrics was introduced and popularized by Ian Donald in Glasgow in 1958. Nowadays the real-time imaging with high-resolution probes has revolutionized antenatal USG study. The most effective way to date pregnancy is by USG even though late 3rd trimester scan for gestational age is not that reliable.

The variation in gestational age calculation by USG, 1st trimester \pm 7 days, 2nd trimester \pm 10-14 days, 3rd trimester \pm 14-21 days.

The formula for estimated fetal weight shows an error up to \pm 10% of the predicted value.

In our study, we have compared our findings taking Hadlock *et al.*,⁹ as the main western representative as this is the default chart provided in most of the USG machines.

All the Western standard charts show a BPD at 40 weeks ranging from 95 to 98 mm (baby weight - 3.5-4 kg) whereas Rajan *et al.*, and our study (Indian standards) show average BPD 90 mm with estimated fetal weight (EFW) around 2.9-3 kg. Hence, unless the reporting sonologist take this into consideration, a 40 weeks Indian baby maybe reported as 36-37 weeks by Western standards. This discrepancy is there in FL, HC, and AC as well.

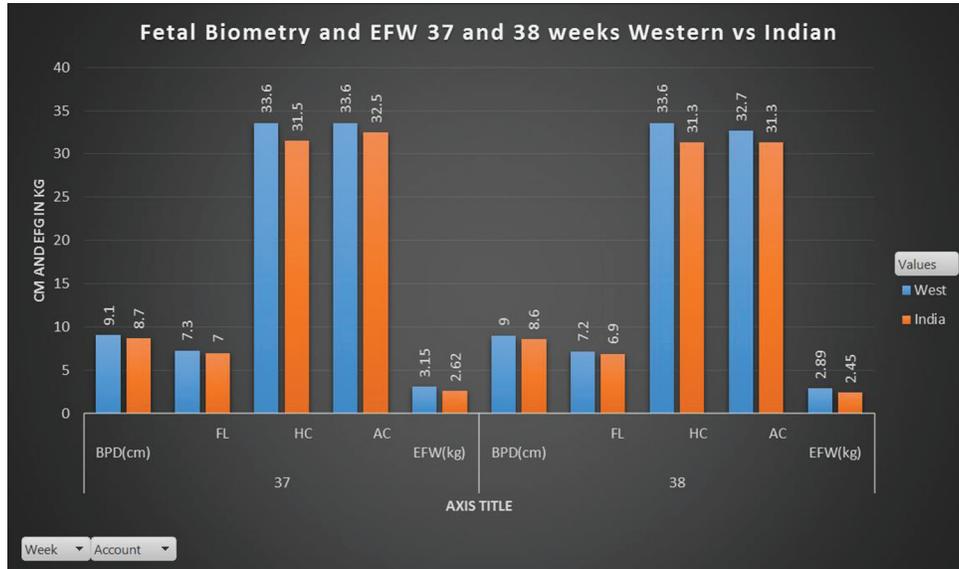


Figure 1: Fetal biometry and estimated fetal weight 37 and 38 weeks Western versus Indian

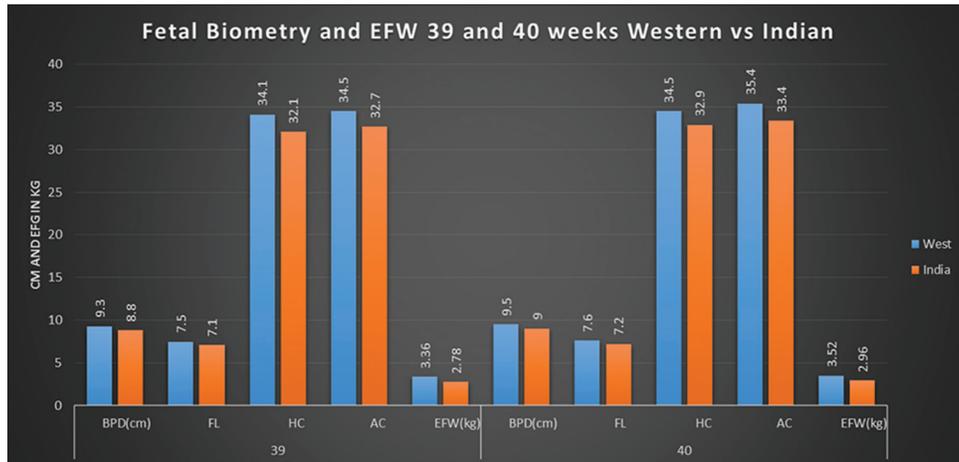


Figure 2: Fetal biometry and estimated fetal weight 39 and 40 weeks Western versus Indian

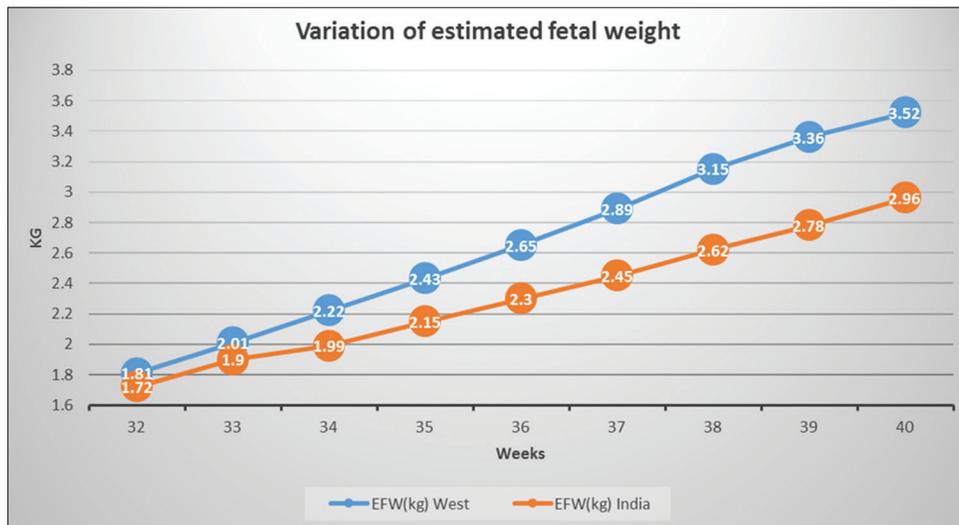


Figure 3: Variation of estimated fetal weight

The status of placental grading AFI and BPP has to be considered in this context. A biophysical profile and a Doppler study in high-risk pregnancies were considered near term.

There are many tables and normograms that describe the normal growth of various fetal parameters. Thenormograms developed for a particular population need not be true for another population especially in late 3rd trimester and we are highlighting the above point in our study.

CONCLUSION

Newborn in India weighs <3 kg, whereas Western newborns weigh 3.6 kg in an average. Hence toward term, there is a discrepancy in all fetal biometric parameters between Indian babies and their Western counterparts. However, the EFW shows a real value as it depends on the actual biometry recorded. BPD and FL are the best parameters for fetal age in late pregnancy, but the fetal weight is mainly reflected by the AC. An experienced sonologist and a machine with good resolution are a must for a true evaluation. In our study, an average gain in weight of 160 g per week is observed from 36 to 40 weeks. Always a reliable 1st trimester scan will help a lot when there is confusion.

Hence, at least, some of the obstetricians who are unaware of the above situation may be deceived by sonology report done outside. Hence, even though a late trimester scan is not that reliable for gestational age, the obstetrician should be always vigilant about the above scenario.

We make a conclusion that all the machines should have software for fetal biometry and estimated fetal weight with Indian standards as framed out in our study.

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Coronary Artery Involvement in Diabetic and Non-diabetic Patients with Acute Coronary Syndrome

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Abstract

Introduction: Coronary artery disease (CAD) accounts for the major chunk of mortality in diabetes. Coronary angiography or arteriography remains the “gold-standard” technique for diagnosing and evaluating CAD.

Materials and Methods: 1000 patients with acute coronary syndrome (ACS), 500 patients who are diabetic, and 500 who are non-diabetic admitted in SSIMS hospital, selected randomly during a period of 1-year. Random blood sugar, fasting blood sugar, and glycosylated hemoglobin (HbA1c) were done in all patients with ACS and were taken up for coronary angiography.

Results: Peak incidence of ACS in diabetes was in third and fourth decades as compared to the fifth and sixth decades in non-diabetics. 240 (48%) out of 500 diabetics with ACS and Type 2 diabetes mellitus for 5-10 years. 223 (44%) out of 500 diabetic patients had triple or multivessel disease (MVD) compared to 82 (16%) out of 500 non-diabetics. Out of 1000 patients of both diabetics and non-diabetics with ACS, a total number of vessels involved were 1994, out of which 61.3% are involved in diabetics and 38.6% in non-diabetics. About 233 (46%) out of 500 diabetic patients required coronary artery bypass grafting (CABG) as treatment outcome. Higher the HbA1c levels of >8.5%, 69.2% had triple/MVD and 191 (73.1%) out of 235 patients who had to undergo CABG had HbA1c levels >8.5%.

Conclusion: ACS in diabetic patients presented earlier in life, the severity and extent of CAD and incidence of MVD was significantly high in diabetics when compared to non-diabetics with ACS. Diabetics with poor control having high levels of HbA1c, more number of coronary vessel involvement, the mode of treatment required in them was CABG.

Key words: Acute coronary syndrome, Coronary angiogram, Diabetes mellitus

INTRODUCTION

Coronary artery disease (CAD) accounts for the major chunk of mortality in diabetes. CAD alone accounts for 40% of deaths in diabetics during the fourth decade of life, and this amounts to 50-70% of deaths above the age of 65 years.¹ Valuable parameters such as patients history, thorough physical examination, non-invasive

techniques such as resting electrocardiograph (ECG), Holter monitoring, stress echocardiography, stress thallium imaging, and stress test are few important in establishing the diagnosis of myocardial ischemia in diabetes but to get the definitive diagnosis of CAD (coronary artery disease) requires invasive diagnostic modality like coronary angiography.

Coronary angiography is considered and remains the “gold-standard” technique for diagnosing and evaluating CAD.²

Hence, the present study was undertaken in an attempt to find, how acute coronary syndrome (ACS) in diabetics differs from that of non-diabetics, with special emphasis is given on patient’s angiographic profile.

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Objective

The objectives were to study angiographic extents, type of vessels, number of vessels, severity, composition of lesion, and any complicated lesion involving coronary artery and its branches in patients with ACS and to compare the same in diabetic and non-diabetic patients with ACS.

MATERIALS AND METHODS

The present study is a cross-sectional study. This study was conducted on 1000 patients with ACS among which 50 patients who are diabetics and other 50 patients who are non-diabetics admitted in S.S. Institute of Medical Sciences, Davangere, Karnataka, India. Patients who matched the inclusion and exclusion criteria were selected randomly during approximately 1½ years formed the study group. Patients were divided into two groups. Group 1 (diabetic) were previously known diabetic or first time detected diabetic by American Diabetes Association (ADA) criteria presenting with ACS and Group 2 (non-diabetic) consisted of cases presenting with ACS who is non-diabetic or not fulfilling ADA criteria. Patients having impaired fasting plasma glucose (FPG ≤ 126 mg/dl but ≥ 110 mg/dl, PPPG 140-200 mg/dl) presenting with ACS were excluded from the study.

Investigations such as complete hemogram, fasting blood glucose levels by collection method, random blood glucose levels, blood urea, serum creatinine, lipid profile, cardiac enzymes; creatine phosphokinase-M, ECG, 2D ECHO, Treadmill test, coronary angiogram, and glycosylated hemoglobin (HbA1c) in diabetic and newly detected diabetes mellitus (DM) was done.

Those patients who complaints about acute chest pain or breathlessness were diagnosed to check ACS based on ECG and cardiac enzymes. Random blood sugar and along with that fasting blood sugar were done for all the patients. Patients with ACS having diabetics and non-diabetics were treated. Once patients were stabilized was taken up for coronary angiography which was performed by the standard Judkins technique after adequate preparation.

Indication for performing coronary angiography was unstable angina, non-ST-segment elevation myocardial infarction (STEMI) and STEMI, and post-infarct angina.

Severity of lesions was graded as follows:

Grade 0: No disease

Grade 1: Intimal disease $< 50\%$ stenosis

Grade 2: 50-69% stenosis

Grade 3: 70-95% stenosis

Grade 4: 96-99% stenosis

Grade 5: Total occlusion.

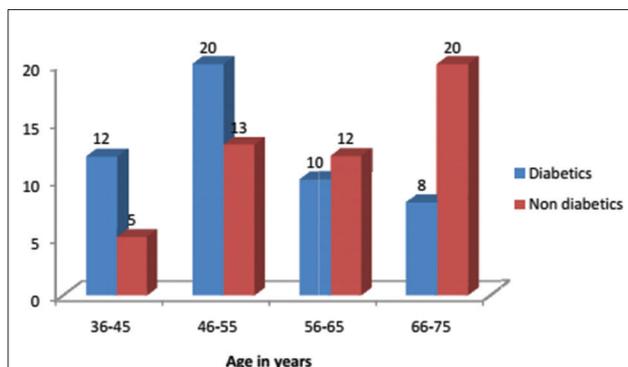
Coronary artery whose narrowing was graded more than or equal to 70% was considered as significant stenosis. HbA1c was done in all the diabetics' patients and in newly detected Type 2 DM patients. Classification of the diabetic patients was done with their HbA1c control scores as < 7 is good control, 7-8.5 is fair control, and > 8.5 poor control. Depending on these findings, a further treatment plan was planned that whether the patient requires medical line of management, percutaneous transluminal coronary angioplasty (PTCA), or coronary artery bypass grafting (CABG).

Statistical Analysis

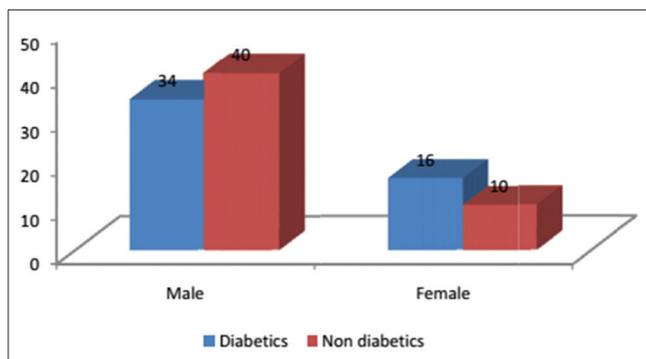
Data collected was represented as number and percentages in tabular form. Chi-square test was used to determine any significant difference between two groups. $P < 0.05$ was considered for statistical significance.

RESULTS

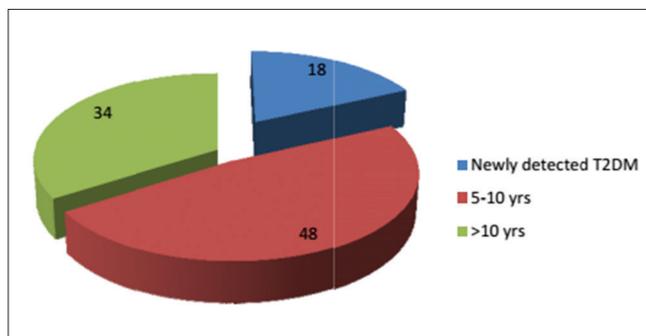
The peak incidence of ACS in diabetics was in the fourth and fifth decades as compared to the fifth and sixth decades in non-diabetics. In our study, we found that the risk of developing of ACS in females was more in diabetics compared to non-diabetics. 18% of the patients were newly detected and diagnosed as diabetic and 34% had a longer duration of diabetes of > 10 years. Left ventricular dysfunction was relatively more common (46%) in diabetics than in non-diabetics (10%). The incidence of triple vessel disease in diabetics was much higher (44%) compared to non-diabetics (16%). The incidence of double vessel disease was slightly higher (26%) compared to non-diabetics (20%). Out of 1000 patients of both diabetics and non-diabetics with ACS, total number of vessels involved are 1990, out of which 61.3% are involved in diabetics were as 38.6% in non-diabetics which is significant suggesting patients with diabetics have more number of the vessel involved. A statistically significant difference in the involvement of left main coronary artery (LMCA) in diabetics (7.5%) compared to non-diabetics (1%). Furthermore, total occlusion was significantly high in diabetics (20%) as compared to 6% in non-diabetics. The incidence of triple vessel disease was significantly higher in patients with duration of diabetes more than 10 years (94%). 46% of diabetic patients required CABG as treatment option compared to 16% of non-diabetics. In patients with HbA1c of < 7 (good control), 85.7% had single vessel involvement and no triple vessel disease. Whereas patients with HbA1c > 8.5 (poor control) had 69.2% of triple/multivessel disease (MVD) and 7.7% of single vessel involvement. In our study, patients with poor control of HbA1c > 8.5 , 73.1% of them had to undergo CABG whereas with good control of HbA1c < 7 , 85.7% of them underwent PTCA (Graphs 1-7).



Graph 1: Age distribution



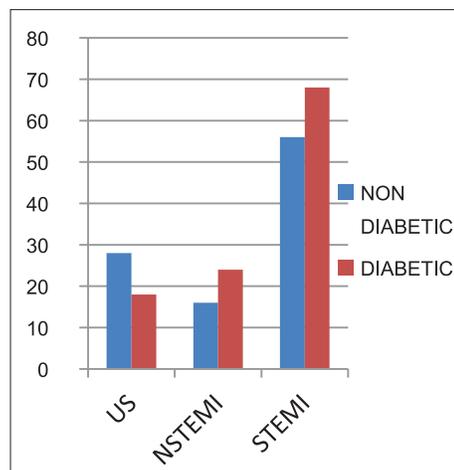
Graph 2: Sex incidence



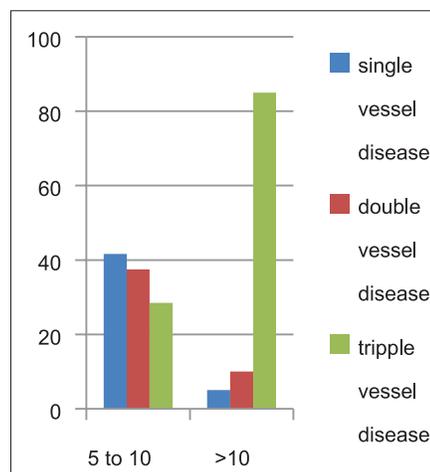
Graph 3: Duration of diabetes

DISCUSSION

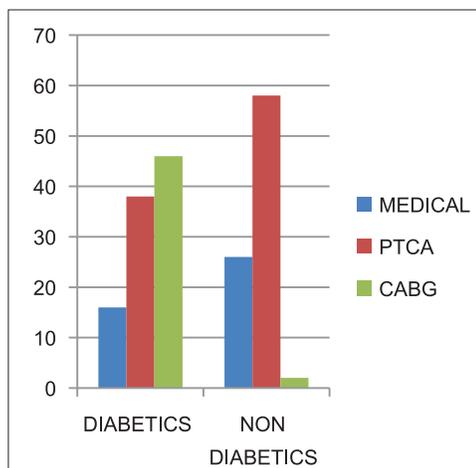
The incidence of triple/MVD was significantly higher with the duration of diabetes >10 years (94.1%). These findings correlate with the other study by Fox *et al.*,³ showing the risk of coronary heart disease was 1.38 times higher for each 10 years increase in the duration of diabetes (95% confidence interval, 0.99-1.92). In our study, diabetic patients with higher HbA1c levels, 73.1% of them had CABG as treatment outcome. Suggesting prevalence of elevated HbA1c levels in patients undergoing coronary artery bypass surgery. These findings correlate with other study conducted by Engoren *et al.*⁴ In our study, coronary angiography revealed that the incidence of MVD in



Graph 4: Type of acute coronary syndrome

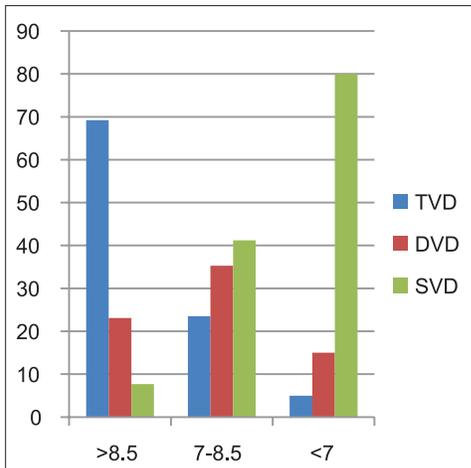


Graph 5: Number of vessels involved



Graph 6: Treatment option

diabetics was much higher (50%) compared to non-diabetics which were only 16%. This finding correlates with the other study by Calton *et al.*,⁵ showed a higher incidence of MVD in diabetics (57.3%) compared to 41.3%



Graph 7: Significance of glycosylated hemoglobin control with vessels involved

in non-diabetics. In another study conducted at CMC Vellore (1996) also showed that MVD was more common in diabetics (87.5% vs. 79.6%) in 2 separate groups of 516 diabetic and non-diabetic patients. In a study by Henry *et al.*,⁶ and Sousa *et al.*,⁷ there was increased the incidence of triple vessel disease, and more diffuse lesions were noted. In our study, the number of patients having total occlusion was 20% in diabetics and 6% in non-diabetics. This finding is statistically significant ($P < 0.01$). Hence, the extent and severity of CAD were significantly high in diabetic patients with ACS when compared to non-diabetic with ACS. This finding was similar in other studies such as Mossavi *et al.*,⁸ Uddin *et al.*,⁹ Nicholls *et al.*,¹⁰ and Rana *et al.*,¹¹ where they found the angiographic extent and severity of CAD was high in diabetic patients with ACS.

CONCLUSION

ACS in diabetic patients presented much earlier in life than non-diabetic patients. The severity and extent of CAD in diabetics was more compared to non-diabetics.

Involvement of LMCA was significantly high in diabetics. The severity of stenosis and total occlusion of vessels were more commonly seen in diabetic patients. The incidence of the triple vessel or MVD was significantly higher with the duration of diabetes more than 10 years. The majority of the diabetic patients with ACS require CABG as the main mode of treatment. In diabetic patients, the incidence of triple or MVD and requiring CABG as the mode of treatment was with poor glycemic control.

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Awareness of Anemia among Pregnant Women and Impact of Demographic Factors on their Hemoglobin Status

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Abstract

Background: The objective of this study is to find out the awareness of anemia in a different demographic group of pregnant women and its influence on their hemoglobin (Hb) level.

Materials and Methods: This is a cross-sectional study conducted in Obstetrics and Gynecology Department at Government Theni Medical College and Hospital, Theni, Tamil Nadu, India. It is carried out on 600 pregnant women who were randomly selected in the antenatal clinic over a period of 6-month from June 2015 to December 2015. Women attending antenatal clinic were obtained a verbal consent and requested to fill up the questionnaire, and 1 ml of blood was collected to assess their Hb level.

Results: Majority of the subjects were multigravida 76% and primi accounts to 24%. In our study, the literacy rate was 68%, and illiteracy rate was 32%. The majority of the women (72%) were in the mean age of 20-29 years, teenage pregnancies (<20 years) were 18%, and elderly (>30 years) were 10%. The majority of the patients registered were in the 1st trimester. Hb level less than 11 g is taken as anemia. Out of 600 women, 459 (76.5%) are aware of anemia and 47% knows anemia is more common in pregnant women. 53.5% of the women know about its complications and role of iron therapy (75.5%) sociodemographic factors, such as literacy rate, socioeconomic status, and iron consumption, are highly significant factors, which affect the Hb status of the study group.

Conclusion: Creating awareness among pregnant women regarding diet rich in iron, importance of regular intake of iron tablets, and complications of anemia will prevent the incidence of anemia and thereby the maternal mortality. Routine iron and folic acid supplementation significantly improve the Hb status among the pregnant women.

Key words: Anemia, Antenatal women, Hemoglobin, Iron tablet

INTRODUCTION

Maternal mortality is the prime health indicator in any society. Anemia accounts for the majority of maternal death. Health service in a country should lower the incidence of anemia to improve the health status. As per NFHS 3, the incidence of anemia in India between age group 15-49 years in 55.3% and a survey in pregnant women revealed 87% of women were anemic. In India, anemia is directly or indirectly responsible for 40% of maternal deaths. There is 8-10 fold increase in maternal

mortality ratio when the hemoglobin (Hb) falls below 5 g/dl. Maternal anemia is associated with poor intrauterine growth and risk of preterm and low birth weight babies. The only way to prevent maternal death arising from anemia is by early detection and effective management in addition to creating awareness and health education.

This study focuses on the prevalence of awareness of anemia among antenatal women and association of knowledge and practice of taking iron rich food and iron supplementation with the Hb level. This study also assesses the relationship between selected demographic variables and Hb level.

MATERIALS AND METHODS

This is a cross-sectional study conducted at the Department of Obstetrics and Gynecology at Government Theni

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Medical College and Hospital, Theni, Tamil Nadu, India during the period of 6-month from June 2015 to December 2016 with sample size 600 to study the awareness of anemia among pregnant women, to analyze the impact of demographic variables on anemia and to know the role of routine Fe and folic acid supplements in reducing the incidence of anemia. The Institutional Ethical Committee Approval was obtained. Patients were randomly selected and were asked to fill a questionnaire in the local language to test their knowledge, attitude, and practice regarding anemia. 1 ml of blood was collected, and Hb level was assessed by calorimeter in a central lab. The Hb level of 11 g% is taken as cut off. Patient with Hb <11 g% were considered as anemia.

RESULTS

About 600 antenatal women belonging to different gestational age were interviewed about their awareness regarding anemia, out of it 76.5% are aware of anemia. Only 47% of our study population knows anemia is more common in pregnant women. The majority of the women knows about its complication (53.5%) and the role of iron therapy (75.5%) (Table 1). In our study group (Figure 1), 51% had a regular intake of iron tablets, 32% had irregular intake, and 17% had not taken iron supplementation. Figure 2 depicts the distribution of study population based on literacy.

Among 600 patients, 72% belongs to 20-29 years age group. On studying the possible determinants using Chi-square test, it was found that age ($P = 0.5087$) and parity ($P = 0.1320$) does not decide the degree of anemia. The significant determinants are literacy ($P < 0.0000001$), socioeconomic status ($P < 0.0000001$), and gestational age ($P < 0.0000001$) (Table 2).

On statistical analysis, we have come to a conclusion that literacy rate, socioeconomic status, and iron consumption are highly significant factors which are directly affecting the severity of anemia as compared to parity and age.

Table 1: Awareness of anemia and knowledge regarding anemia and its complications and iron therapy (n=600)

Knowledge	Correct responders (%)	Wrong responders (%)	Ignorant (%)
Anemia	459 (76.5)	96 (16)	45 (7.5)
Anemia in pregnancy	282 (47)	225 (37.5)	93 (15.5)
Complications of anemia	321 (53.5)	234 (39)	45 (7.5)
Iron therapy	453 (75.5)	45 (7.5)	102 (17)

DISCUSSION

The present study reveals overall 76.5% of the participants had good knowledge regarding anemia which is comparable to a study conducted in Karnataka by Yadav and Banjade¹ and study conducted by Maj Sivapriya and Parida, Pune.²

A study by Gautam *et al.*,³ shows even though 66% of pregnant women were aware of anemia, 21% their participants attributed iron supplementation is essential in pregnancy. In our study population, 75.5% were aware of iron therapy which is comparable to study conducted by Dorairajan *et al.*⁴ An association between regular intake and Hb level which is statistically significant in NFHS 3 survey⁵ reports shows only 23.1% of pregnant women consumed iron and folic acid for 90 days, whereas in our study 51% had regular intake of iron and folic tablets.

In a similar study conducted in Pondicherry private institution by Neveditha and Shanthini⁶ various demographic factors are compared to the degree of anemia which showed none

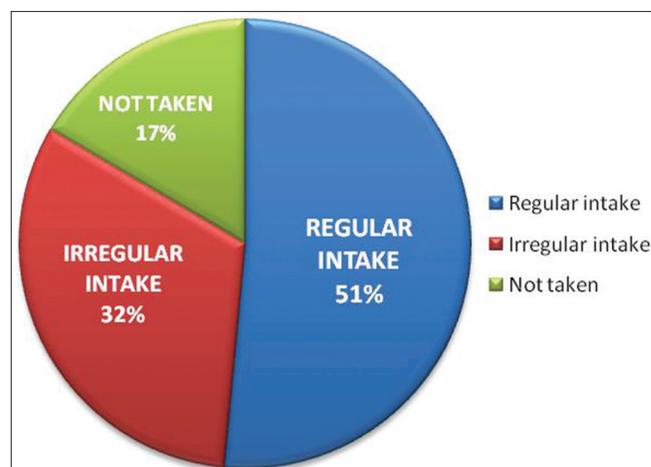


Figure 1: Distribution of study population based on iron intake

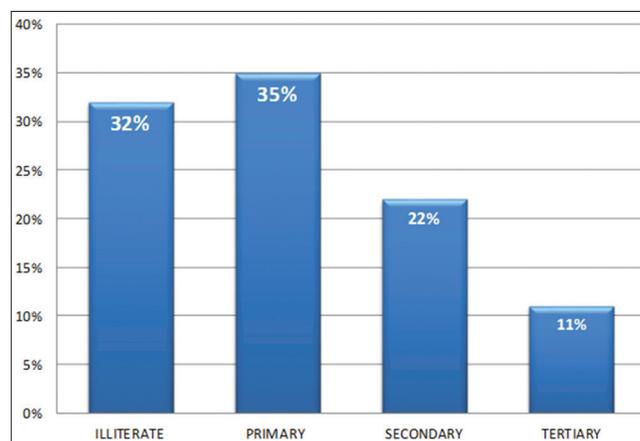


Figure 2: Literacy rate among study population and association with anemia

Table 2: Impact of demographic variables on anemic status

Variables	Numbers (%)	Anemic (%)	Non-anemic (%)	Chi-square, degree of freedom, P value
Age				
Teenage (<20)	108 (18)	72 (67)	36 (33)	0.44, df=1
Middle (20-29)	432 (72)	254 (59)	178 (41)	P=0.5087
Elderly (>30)	60 (10)	25 (42)	35 (58)	Not significant
Parity				
Primigravida	144 (24)	89 (62)	55 (38)	1.253, df=1,
Multigravida	456 (76)	305 (67)	151 (33)	P≤0.1320 Not significant
Education status				
Illiterate	192 (32)	169 (88)	23 (22)	70.71, df=1
Primary	210 (35)	147 (70)	63 (30)	P≤0.0000001
Secondary	132 (22)	53 (40)	79 (60)	Highly significant
Tertiary	66 (11)	15 (22)	51 (88)	
Socioeconomic status				
Grade 2	12	3 (25)	9 (75)	153.8, df=2
Grade 3	360	234 (65)	126 (35)	P≤0.0000001
Grade 4	228	167(73)	61(27)	
Gestational age				
1 st trimester	438 (73)	136 (31)	302 (69)	8.17, df=1
2 nd trimester	114 (19)	66 (58)	48 (42)	P≤0.0000001
3 rd trimester	48 (8)	31 (64)	17 (36)	Highly significant

of the demographic factors influenced the Hb level. In contrast to this, our present study reveals the statistically significant association of literacy, socioeconomic status, intake of iron with Hb level by assessing *P* value and Chi-square test, degree of freedom by open Epi Software Version 3.03 a method. Similar results were obtained in studies conducted by Maskey *et al.*,⁷ Mohammad *et al.*,⁸ and Kelsey.⁹ Two factors are not significant, namely, age and parity in our study population which were proved statistically by Chi-square test.

CONCLUSION

Our present study shows the lack of knowledge among antenatal mothers regarding anemia and its complications. Sociodemographic factors such as literacy, socioeconomic status influence Hb level directly which is statistically proven in this study. Regular intake of iron and folate improves Hb level. Hence, creating awareness about iron supplementation and health education can grossly reduce the incidence of anemia in antenatal population and thereby prevents anemia related mortality and morbidity.

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Custom-made Pressure Earring for Sustained Compression on Auricular Keloid: A Case Report

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Abstract

Keloids occur from overgrowth of scar tissue and may arise following an insult to the deep dermis. Keloids of ear lobe are common complications of ear piercing, although its exact etiology remains unknown. They are often itchy, painful, and uncomfortable to the patient. Pressure therapy is widely used in the management of hypertrophic and keloid scars. An 11-year-old female patient having a keloid on the right ear lobe was referred from the Department of Plastic Surgery for the fabrication of a pressure clip. The following is a case report of a custom designed pressure clip for the management of an auricular keloid.

Key words: Earlobe keloid, Keloid, Pressure clip

INTRODUCTION

Keloid of the ear is a difficult condition to treat. Although there are many theories about keloid formation, their etiology is still unknown. It is difficult to surgically excise keloid completely and cause primary skin closure on external ear compared to other body sites. Pressure therapy is widely used in the management of auricular keloid, usually in combination with corticosteroid injection or surgery.¹ Various pressure devices for the treatment of auricular keloids are U-loop pressure clip,² spring loaded pressure devices, Snyder's compression suture,³ Bent spring pressure earring, etc.

To be effective, a compression device must provide uniform sustained compression. Furthermore, the appliance should be cosmetically acceptable, inexpensive, and easy to fabricate.⁴

In this case report, the fabrication of a pressure earring using a binder clip for sustained compression on the auricular keloid is discussed.

CASE REPORT

An 11-year-old female patient having a keloid on the right ear lobe was referred from the Department of Plastic Surgery for the fabrication of a pressure clip. The patient complained of swelling on the back of right earlobe since 1 year. The swelling was causing emotional stress to the young patient due to esthetic impairment. There was a history of ear piercing at the age of 10 years. A small swelling appeared on the back of right earlobe after 2 months of piercing, which gradually increased in size and continued to grow until it reached the present size. On examination, a small, oval, sessile, tender, smooth-surfaced swelling was present on the back of the right ear lobe, measuring 7 mm superoinferiorly and 6 mm anteroposteriorly (Figure 1). The patient was on regular intralesional injection of corticosteroid. Custom-made methyl methacrylate pressure appliance was planned to be used for compression of the keloid.

Preparation of the Patient

The skin over the patient's ear and keloid was lubricated with petroleum jelly. A lubricated cotton pellet was placed in the external auditory meatus.

Impression Procedure

A cylindrical container of approximately 6 inches diameter with openings at both ends was used as a tray for the impression procedure. Thin mix of irreversible

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hydrocolloid impression material (Zelgan; Dentsply, India) was poured into the container. Gauze pieces were placed over it and a thin mix of plaster of Paris was poured over the irreversible hydrocolloid impression material for support (Figure 2). Completed impression was retrieved and then poured in Type III dental stone (Figures 3 and 4).

Steps in Fabrication

1. A small binder clip was selected for delivering sustained pressure on the keloid
2. The pressing lever (handle) of the binder clip was shortened for esthetics (Figure 5)
3. To make the binder clip active after its fabrication, a small amount of putty material was allowed to set inside the clip in a slightly opened position (Figure 6)
4. The binder clip was positioned over the cast and stabilized in place using a small amount of putty impression material (Figure 7)
5. Pressure plates were fabricated using tooth colored polymethylmethacrylate resin (Figure 8). The undercuts in the binder clip provided retention for the acrylic resin

6. Putty was removed from the inside of the clip and characterization was done to make the appliance more esthetically acceptable to the young patient (Figure 9)
7. Pressure of the clip was made comfortable to the wearer by putting a vertical slit at the elastic web (closed end) of the binder clip
8. A 2 mm layer of the intaglio surface of the appliance was uniformly removed and lined with silicone soft denture liner to provide a cushioning effect. The patient was taught how to wear the appliance (Figure 10)
9. The patient was instructed to use the pressure appliance for 12 h a day for 4-6 months⁵
10. Periodic recall at 2 weeks intervals was also scheduled. The patient was instructed to keep the keloid area and the appliance meticulously clean.

DISCUSSION

The auricular keloid is a recognized complication of ear piercing, and it has cosmetic implications.⁶ An earlobe



Figure 1: Keloid on the posterior surface of right earlobe



Figure 3: Hydrocolloid impression of right ear



Figure 2: Impression procedure



Figure 4: Stone cast obtained from impression



Figure 5: Pressing lever arms shortened for esthetics



Figure 8: Acrylic pressure plates fabricated over binder clip



Figure 6: Putty allowed to set inside the clip in slightly opened position



Figure 9: Pressure earring appliance

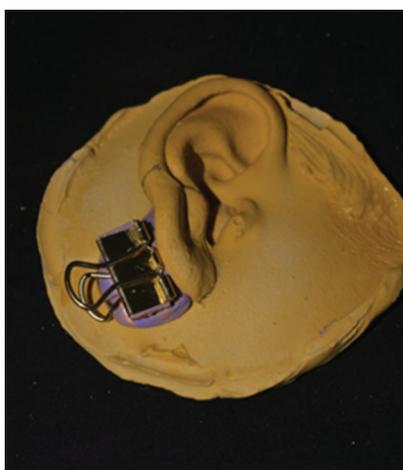


Figure 7: Binder clip positioned and stabilized over the cast



Figure 10: Patient with the pressure appliance

keloid presents a technically challenging task to the clinician. Treatment of ear keloid is complicated and is characterized by discomfort and high recurrence rates.⁷

The treatment of ear keloids relies heavily on the use of either steroids or radiotherapy and with either methods, some adjuvant surgery may be needed. Unfortunately, it is not always successful and may involve repeated surgeries

and steroid administration, which is painful. Radiotherapy is unpredictable in its effect and may produce various undesirable results.⁴

Compression therapy is effective for the keloid treatment by creating a hypoxic microenvironment resulting in tissue degradation and thereby reducing the size of the lesion.⁸ Through compression therapy, tissue metabolism and fibroblast proliferation are reduced. Compression has also been shown to increase collagenase activity and induce mast cell stabilization which ultimately lead to attenuation of hypertrophy and pruritic symptoms.⁹ Prefabricated devices are not indicated because they may lead to insufficient or excessive pressure, bleeding or ulceration of the site and is often uncomfortable to the wearer.

Custom-made pressure appliances provide uniform pressure by confining the soft tissue to the internal dimensions of the appliance. Furthermore, they are inexpensive and easily applied and removed by the patient and can be used for the treatment of both a helix and earlobe keloid.¹⁰ The patient compliance is essential when using post-operative pressure therapy for the treatment of keloids, as it may recur as soon as the external pressure is relieved. The patient training and cooperation may further decrease the recurrence rate of ear keloids.¹¹

CONCLUSION

A custom-made pressure appliance made from a binder clip for sustained compression of an auricular keloid is described. During the healing period, the appliance can

be adjusted by soft denture liners. By enlarging the slit in the closed end of the clip, the compression pressure can be reduced and it may be used as a passive appliance for the prophylaxis of recurrence in surgically removed ear keloid. For a successful outcome, the patient must use the appliance according to the instructions and undergo a regular follow-up.

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Management of Homicidal Cut Throat Open Airway Injury: A Case Report

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Abstract

Cut throat injuries though rare, but pose a challenge to an anesthesiologist in securing the airway to provide oxygenation and to prevent aspiration. Distortion of the anatomy of the airway, bleeding at the site, and risk of aspiration complicate the process of securing the airway. The crucial time of intervention is usually lost; as the patient is brought to the hospital after sufficient time has elapsed. Placing an endotracheal tube through laryngoscopy or directly through the airway defect is of prime concern. Further management includes repair of the wound and rehabilitation. Here, we report a case of homicidal cut throat injury to airway exposing the true vocal cords.

Key words: Aspiration, Bleeding, Hypoxia, Larynx, Tracheostomy

INTRODUCTION

Cut throat injuries may be rare but can be life-threatening due to complications such as aspiration of blood and risk of hypoxia. These can be suicidal or homicidal.

They result in the transection of the hypopharynx, larynx, and trachea and are sometimes associated with injuries to the carotid artery, internal jugular vein, and esophagus.¹ The most common site of the tracheal transection is the junction of cricoid with trachea due to weak connective tissue in this area.²

Management of cut throat injuries requires a multi-disciplinary approach.³ The role of an anesthesiologist in instituting an airway using an endotracheal intubation or tracheostomy before wound exploration and repair of transected tissues, is challenging, as such injuries are most of the time associated with distortion of the normal anatomy of the airway.

Here, we present a case of homicidal cut throat injury to the airway leading to aspiration and hypoxia.

CASE REPORT

A 27-year-old male patient came to the emergency room with the homicidal cut throat. The injury had occurred an hour ago he came to the emergency room. The patient was aggressive, pale and had difficulty in breathing. The wound was horizontal just above the level of vocal cords over the infrahyoid region exposing the vocal cords outside. There was oozing of blood from the wound. There were no other injuries on the body. Blood pressure was 90/60 mm Hg, pulse rate 120/min, oxygen saturation was 82%, and respiratory rate 36/min. On auscultation, chest had bilateral crepitations. Immediately, the airway was secured with 7.5 internal diameters endotracheal tube passed through the exposed vocal cords, cuff inflated and auscultated for bilateral air entry. The endotracheal tube was suctioned and aspirated for blood. Then, the oxygenation was maintained through Ambu ventilation with 4 L of oxygen. Ryle's tube 18 passed through nasogastric route and aspirated for blood.

Two 18 Gauge cannulae secured on both upper limbs. Fluid resuscitation started. Urinary catheterization also done. Blood samples sent for investigations and arrangement of

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blood. Investigations revealed hemoglobin 9.2 g/dl, total WBC count 16,000 cells/Cumm, bleeding time 2.4 min, urea 32, and creatinine 1.1. Arterial blood gas (ABG) analysis done.

The patient immediately taken to the operating room without waiting for the investigations. After checking the anesthesia machine and suction apparatus, he was connected to blood pressure, electrocardiogram, and pulse oximetry monitors. Oxygenation maintained by connecting ET tube to anesthesia machine via Bains circuit. Injections glycopyrrolate 0.2 mg, midazolam 1 mg, fentanyl 125 µg, and ketamine 80 mg in titrated doses given. Then, injection vecuronium 6 mg given for muscle relaxation. Ventilation maintained by connecting to anesthesia machine ventilator with oxygen, nitrous and isoflurane inhalational anesthesia. The tracheotomy tube of 8 mm internal diameter placed after retracting strap muscles and the thyroid isthmus. The endotracheal tube was withdrawn gradually until the vocal cords and after confirming the position of the tracheostomy tube in the trachea, the endotracheal tube was taken out.

ENT surgeon gave a thorough wash to the wound and explored the same. Bleeding vessels were coagulated and hemostasis achieved. Patient's vitals stabilized. Blood pressure 110/70 mm of Hg, pulse rate 92/min, and oxygen saturation of 100%. Thyroid cartilage was damaged and hence repaired. The laryngeal mucosa also repaired. Appropriate antibiotics given. 1.5 L of crystalloids and 1 unit of blood transfused intraoperatively.

The patient was shifted to intensive care unit (ICU) after the surgery with the tracheotomy tube in place. He is ventilated for the next 12 h under appropriate sedation. Vitals were stable. Nutrition maintained through Ryle's tube. After 12 h, the patient was weaned off from the ventilator and monitored. X-ray chest was done immediately after the surgery to look for any radiological signs of aspiration that was negative. The patient weaned off from the ventilator. Then, an uncuffed tracheostomy tube number 7 inserted and was encouraged to speak from the fourth day of surgery. On the sixth day of surgery, tracheostomy tube removed. The patient was discharged home on the ninth day.

DISCUSSION

The most important initial management of cut throat injuries is securing the airway with the placement of tracheal or tracheostomy tube because complications due to aspiration of blood, major vessel injury, and hypoxia often complicate the scenario.⁴ Our patient though would have

maintained oxygenation through the airway defect, but the aspiration of blood complicated the situation.

Airway injuries are associated with injuries to the hypopharynx, larynx, airway, and major vessels in the neck leading to aspiration, hypoxia, and bleeding.⁵ In our patient, fortunately, there was no injury to the carotid artery or internal jugular vein. There was an injury to the airway above the level of true vocal cords leading to respiratory distress, aspiration, and hypoxia. Radiological investigations not done due to the emergency of the situation and airway had to be secured.

ABG analysis done after securing the airway as the patient had respiratory distress and was hypoxic. ABG was done to look for metabolic acidosis and base deficit as the injury was few hours old, and there was bleeding from the injury site.

The preferred technique is awake intubation under topical or regional block.⁶ However, we never had the time to perform this as our patient required tracheal intubation due to hypoxia.

Intraoperatively, 1.5 L of crystalloids and 1 unit of blood was transfused, and patient maintained stable hemodynamics throughout.

Isoflurane given for the maintenance of balanced anesthesia along with midazolam, fentanyl, vecuronium, and ketamine. Hemodynamic disturbance prevented using lower minimum alveolar concentration of volatile anesthetics. Ryle's tube used to aspirate the stomach and prevent further aspiration. The patient was electively ventilated for next 12 h (synchronized intermittent mandatory ventilation mode with FiO₂-40%, positive end expiratory pressure-6, respiratory rate - 12, tidal volume - 450 ml), and gradually weaned off.

Cut throat injuries either suicidal or homicidal, require prompt attention and intervention to protect the airway, prevent aspiration, and hypoxia. Further management includes repair of the airway, vessel or digestive tract injuries. This requires a team work with involvement of anesthesiologist, psychiatrist, intensivist, speech therapist and otolaryngologist working together.³

CONCLUSION

Securing the airway, either by intubation through laryngoscopy or airway defect, or by tracheostomy, is of the prime concern in traumatic airway injuries. Complications such as aspiration of blood, hypoxia, and bleeding have to be prevented. Surgical wound closure follows next.

After surgery, proper ICU care, respiratory therapies, hemodynamic monitoring, speech therapy, counseling altogether help in the recovery of the patient.

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Carcinosarcoma of Breast: A Rare Case Report with Review of Literature

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Abstract

Breast cancer is a heterogeneous type of cancer, and many different histology types exist. Carcinosarcoma of the breast is a rare entity and consists of two distinct cell lines comprising epithelial and mesenchymal components. It is usually larger in size than epithelial breast cancers and is characterized by a rapid increase in size. The majority are with high grade and triple negative receptor status causing aggressive behavior nature of the disease. The treatment of carcinosarcoma should follow the guidelines for treatment of invasive breast cancer. The prognosis of the tumor is less favorable compared to more common types of breast cancers such as infiltrating ductal or lobular carcinomas. We reported a case of carcinosarcoma of the right side breast in a 47-year-old woman.

Key words: Breast, Carcinosarcoma, Management, Prognosis

INTRODUCTION

Breast malignancies affect 12.3% of women during their lifetime, and an estimated incidence of 232,340 new cases diagnosed in 2013.¹ Carcinosarcoma of the breast consists of malignant sarcomatoid metaplasia of epithelial carcinoma. It is also known as metaplastic carcinoma and is a rare entity. It consists of 0.08-0.2% of all breast cancers.² Controversy exists regarding its origin. The biphasic differentiation of cells such as epithelial and mesenchymal characteristics showing the possibility of myoepithelial origin or differentiation.³ Carcinosarcoma has aggressive clinical behavior⁴ with larger size during the presentation and rapid in an increase in size than epithelial breast carcinomas.⁵ Prognosis is less favorable in comparison to invasive ductal or lobular carcinoma.⁵ We report a case of carcinosarcoma of the right side breast in a 47 years female.

CASE REPORT

A 47-year-old perimenopausal woman presented with a lump in the right breast upper outer quadrant with rapid growth in one and half months. Physical examination revealed a mass of size 5 cm × 6 cm in the upper outer quadrant of right breast. There were no skin or chest wall involvement, and the nipple-areolar complex was found to be normal. Ultrasonography showed a solid hypochoic mass of size 5 cm × 5.5 cm in the right breast upper outer quadrant with irregular boundaries. Mammography finding revealed a radiopaque lesion of size 4.7 cm × 4.8 cm in upper outer quadrant of the right breast with irregular margins (Figure 1). Core biopsy from the breast lump showed features of carcinosarcoma. Estrogen receptor, progesterone receptor, and HER-2/neu receptor status were found to be negative. On immunohistochemical examination, epithelial component showed keratin positivity and mesenchymal component showed vimentin positivity. Modified radical mastectomy was performed. Gross examination of the specimen showed a 5 cm × 4 cm × 3.5 cm grayish-brown-colored tumor. Microscopic examination showed the presence of diffuse sheets of tumor tissue separated by fibrocollagenous stroma (Figure 2). Highly pleomorphic tumor cells found with eosinophilic cytoplasm and hyperchromatic nuclei and prominent nucleoli (Figure 3). High mitotic activity found

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in the background. The patient received six cycles of adjuvant chemotherapy with ifosfamide and adriamycin-based regimen followed by adjuvant external beam radiotherapy of 50 Gy in 25 fractions to the right chest wall. The patient is under regular follow-up since last 22 months without any disease.

DISCUSSION

Breast cancer is a heterogeneous disease with regard to histopathological types. The most common histopathology is infiltrating ductal carcinoma, which accounts for about 80% of all breast cancers.⁶ Carcinosarcoma is an aggressive and rare neoplasm of the breast. Its incidence is 0.1% of all breast malignancies.⁷

It is comprised malignant epithelial tissue (carcinoma) mixed with malignant mesenchymal cells (sarcoma). The cell of origin of these tumors is still controversy. Myoepithelial cells originate from a single stem cell-like spindle cells and also may develop from existing cystosarcoma phyllodes, fibroadenoma, and cystic backgrounds.⁸⁻¹¹ Carcinosarcoma shows the myoepithelial origin and histopathologically, consists of both carcinomatous and sarcomatous components. The epithelial component may cause undifferentiated carcinoma, adenocarcinoma, in situ carcinoma, infiltrative ductal carcinoma or squamous carcinoma, whereas the mesenchymal component consists of fibroblastic, chondroblastic, or osteoblastic areas.^{5,12-14} The majority are seen in poorly differentiated, high-grade forms.² Estrogen receptor, progesterone receptors, and HER-2/neu oncogene are not commonly expressed in this tumor.⁶ This “triple negative” phenotype in this tumor is more aggressive and are unlikely responds to targeted therapy or hormonal therapy.²

Immunohistochemistry is the gold standard investigation in the diagnosis of carcinosarcomas. Immunohistochemical examination shows positivity for keratin (55%), vimentin (98%), actin (77%), and S-100 protein (55%).¹⁵

Its high-grade nature and negativity for estrogen and progesterone receptors show the aggressiveness of the tumor. Majority tumors show overexpression of the epidermal growth factor receptor (HER-1/EGFR) protein and may serve as a potential therapeutic target for EGFR inhibitors.

Most of the cases present in women more than 50 years of age. Clinical features are similar to those seen in patients with invasive ductal carcinoma.⁵ Usually, carcinosarcoma of breast presents as unilateral, well defined, painless lump, larger in size, often painful and without any preference for

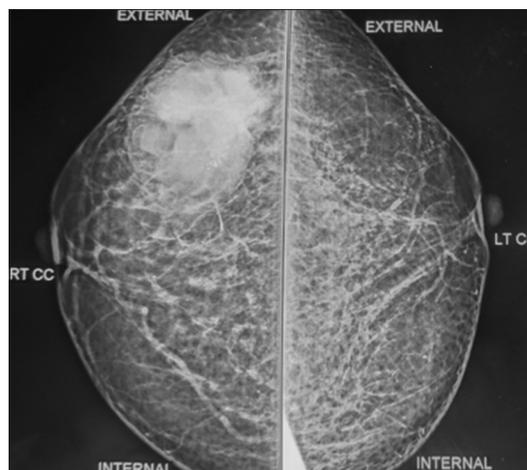


Figure 1: Mammogram of the breast showing a radio-opaque lesion in upper outer quadrant of the right breast

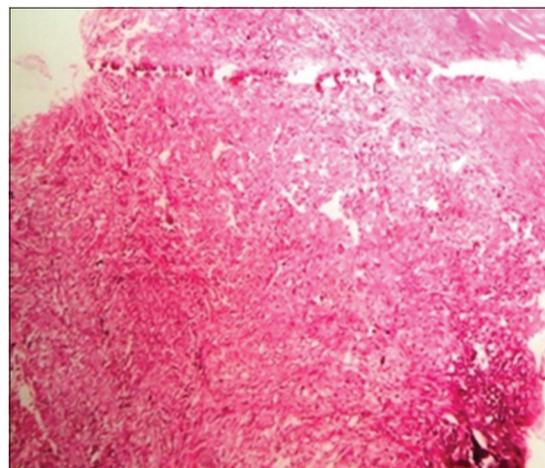


Figure 2: Microsection shows presence of tumor tissue in diffuse sheets separated by fibrocollagenous stroma (H and E, x100)

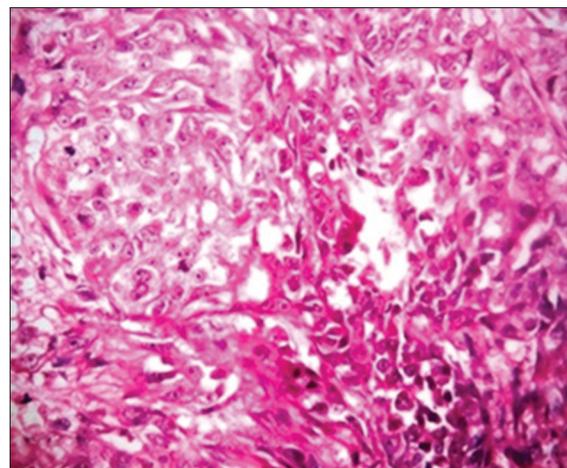


Figure 3: Microsection shows highly pleomorphic cells with moderate amount of eosinophilic cytoplasm, pleomorphic hyperchromatic nuclei, prominent nucleoli at many places. High mitotic count (H and E, x400)

any particular age group.¹⁶ Rarely, nipple discharge, nipple retraction, or skin ulceration may also be present.⁵

Distant metastasis occurs via the blood and lymphatic circulation. It has a lower incidence of lymph nodal metastasis than that of infiltrating duct carcinoma.¹⁷ The lower chance of the lymph node positivity is due to rare lymphatic spread in carcinosarcoma of the breast. However, the hematogenous metastatic potential is high particularly to extranodal sites such as lung and bone.⁶ Lung is the most common distant metastatic site.¹⁸

Sonographic finding of carcinosarcoma of breast shows heterogeneous or hypoechoic solid mass and may also be described as a round, oval, or lobular shape complex echogenicity with solid and cystic components which may be related to necrosis and cystic degeneration and most frequently demonstrate posterior acoustic enhancement (compared with posterior shadowing).¹⁹ Mammographically, imaging features are benign with round or oval shapes, circumscribed margins and the lesions are non-calcified with a high rate of architectural distortion.⁶ The magnetic resonance imaging exam includes T2 hyperintensity and lesions containing ring-like, homogenous, heterogeneous, or non-enhancing internal components.⁶ These non-enhancing T2 high-signal-intensity internal components correlate with necrosis, cyst, and chondroid matrix on pathology findings.¹⁹

There are some difficulties in diagnosis and treatment of carcinosarcoma. A multidisciplinary treatment approach should be required during management process. There are no standard management guidelines for carcinosarcoma due to the rarity of the disease-causing limited research data. In general, the treatment of carcinosarcoma should follow the guidelines for treatment of invasive breast cancer. Mastectomy with or without axillary lymph node dissection followed by post-operative chemotherapy and radiation therapy are the treatment options.²⁰ Axillary lymph node dissection should be omitted from standard mastectomy procedure because of uncommon lymphatic spread in this type of malignancy.²¹ Neoplastic cells disposed to local recurrence due to their prevalence in the perivascular tissue.¹⁰ Prevention of local recurrence is very important in the management course, and radiotherapy should be considered in preventing recurrence. Anthracycline/taxane-based chemotherapy is recommended for chemotherapy schedule in carcinosarcoma of breast.²² Patients treated with neoadjuvant or adjuvant anthracycline-based chemotherapy showed a better clinical outcome compared to those treated with cyclophosphamide, methotrexate, 5-fluorouracil.²³ Neoadjuvant chemotherapy for carcinosarcoma breast was less effective than for conventional adenocarcinoma.

Despite the aggressive type of tumor, no significant difference was found when it was compared to high-grade receptor-negative infiltrative carcinomas.³ Overall, carcinosarcoma is an aggressive type of breast cancer with a worse prognosis than classical breast carcinomas. Tumor size, differentiation rate, high histologic grade, atypia, and active pleomorphic spindle cells play a role in prognosis.² Poor prognostic factors include age younger than 39 years at presentation, skin invasion, and size >5 cm.⁸ 5 years overall survival is 49-68% in carcinosarcoma of breast.^{5,24} The 5 years survival rates for tumor, nodes, metastasis (TNM) clinical Stages I, II, and III are 100%, 63%, and 35%, respectively.¹⁵ Our case is recurrence- and metastasis-free in the 8th month under follow-up.

CONCLUSION

Pretreatment accurate diagnosis of carcinosarcoma breast with its TNM staging is essential to optimize the treatment process in both surgery and adjuvant therapy toward this aggressive breast cancer subtype. It may help to avoid unnecessary axillary lymph node dissection during surgery. Therefore, further research needs to be performed to evaluate the potential and outcome of such therapy in patients with carcinosarcoma of the breast.

Carcinosarcoma of the breast is a rare entity, and a few numbers of cases have been published in the literature. To know the similar and different characterizing aspects of breast cancer, diagnosed cases should be reported with a literature review.

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Rehabilitation of an Acquired Skull Defect Using Custom Made Titanium Cranial Prosthesis: A Case Report

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Abstract

Cranial defects may occur from congenital malformations, trauma, or a disease. Such defects will influence both the physical and mental state of the patient. Management of the skull defect is necessary to reduce the patient anxiety and protect the brain tissue underneath. Obtaining good esthetic result during cranioplasty is often challenging. Several materials are being used for the cranioplasty procedure. Of the several materials used to perform cranioplasty, methyl methacrylate, and titanium have remained as the most viable alternatives. Cranioplasty can be performed using different materials and techniques. This article illustrates a case report of rehabilitation of a patient with a skull defect using a titanium cranial prosthesis.

Key words: Cranial implant, Cranioplasty, Skull defects, Titanium cranial implant

INTRODUCTION

Cranial defects can occur from congenital malformations, infection, trauma, and pathological tumors. The surgical management and prosthetic rehabilitation of an acquired skull defect are a challenge to the practitioner. Rehabilitation of cranial defect is essential to minimize patient apprehension, protect the underlying brain, provide pain relief at the site, and improve esthetics.^{1,2} This article presents the rehabilitation of a patient with an acquired skull defect using a custom made titanium implant.

CASE REPORT

A 27-year-old male patient reported to the Department of Prosthodontics, Government Dental College, Trivandrum, with an acquired skull defect following a road traffic accident. The patient was referred from the Department of

Neurosurgery, Government Medical College, Trivandrum following a decompressive craniectomy. On examination, a skull defect of 7 cm × 5 cm was present in the frontal area of the skull (Figure 1). It was decided to fabricate a titanium cranial prosthesis for rehabilitating the skull defect.

Impression Procedure

The construction of cranial prosthesis includes various stages such as moulage impression and working cast fabrication, sculpture and making of the wax pattern, mold fabrication, and processing of the prosthesis.²

A marking was made 3-4 mm beyond the outermost borders of the cranial defect using an indelible pen. The wax was adapted to the defect area to act as a tray for the impression material. A lightly mixed alginate impression material was then poured onto the defect area carefully without trapping air. After placing cotton tufts onto the setting impression material, a second pour of lightly mixed Plaster of Paris was placed over it to provide a rigid support to the impression material (Figures 2 and 3). The impression obtained was evaluated for any voids or inaccuracies (Figure 4). Type-III dental stone was mixed and poured into the alginate impression to obtain the cast. The border lines marked were transferred to the cast.

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Figure 1: Cranial defect in the frontal part of skull



Figure 3: Thin mixture of Plaster of Paris placed over the impression



Figure 2: Cotton tufts placed over the hydrocolloid impression while it sets

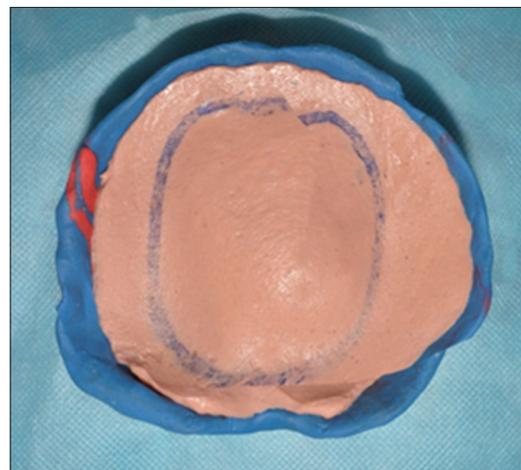


Figure 4: Impression of the cranial defect

Cranial Prosthesis Fabrication

The design of the prosthesis was discussed with the neurosurgeon, and the wax pattern was fabricated following the contours of the skull. The patient was recalled for a try-in procedure to evaluate the accurate fit of the wax pattern along the margins (Figure 5). A titanium cranial prosthesis was fabricated from the wax pattern (Jayon Implants Pvt Ltd. Lab, Palakkad, Kerala) (Figure 6). Holes of 2 mm dimensions were drilled onto the surface of the titanium prosthesis to prevent the development of epidural hematoma, and allow for ingrowth of fibrous connective tissue to assist in stabilization. Furthermore, the holes help to secure the prosthesis to the bony defect.³

Surgical Placement of Cranial Implant

Reflection of the surgical area was done to expose the margins of the defect. The cranial prosthesis was adjusted with a trimmer so as to correctly adapt over the edges of the defect (Figure 7). Titanium screws were used to secure the prosthesis into the exact position. The suction drain placed soon after the surgical procedure was removed on the 2nd day.

Post-operative care instructions were given, and follow-up visits were scheduled. During the follow-up visit, the esthetic results were observed to be satisfactory (Figure 8).

DISCUSSION

Obtaining good esthetic result during cranioplasty is often challenging. Several materials are being used for the cranioplasty procedure. Of the several materials used to perform cranioplasty, methyl methacrylate and titanium have remained as the most viable alternatives.⁴ Compared to methyl methacrylate, titanium is expensive and difficult to pre-fabricate. However, methyl methacrylate can cause exothermic reactions, which may damage the surrounding tissues and lead to subgaleal exudative fluid and infection.^{5,6} Titanium has low modulus of elasticity, low density, and a very low rate of corrosion. It is non-toxic, elicits no inflammatory reaction and has an infection rate of under 2%.⁷⁻⁹ Although computer-aided design-computer-aided manufacturing generated titanium cranial prostheses have been introduced,^{10,11} patients may not give consent due to economic reasons.



Figure 5: Try-in of the wax pattern

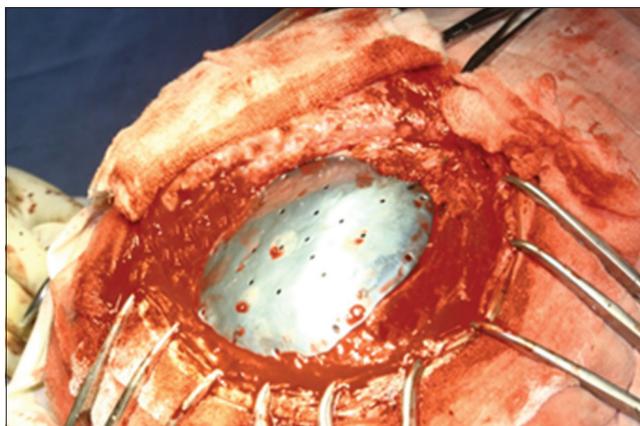


Figure 7: Surgical placement of cranial prosthesis



Figure 6: Titanium cranial prosthesis



Figure 8: Post-operative result after 3 weeks

CONCLUSION

Prefabricated cranial prostheses simplify the cranioplasty procedure by decreasing the time required for adjustment of the prosthesis during the surgery. Although prefabricated poly-methyl methacrylate prostheses are inexpensive, titanium is generally opted due to its non-corrosive nature, low density and decreased risk of infection. This case report describes the rehabilitation of a person with an acquired skull defect using a custom made titanium cranial prosthesis.

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Gaze Palsy with Diplopia in Hyper Homocysteinemia: A Rare Neuro-ophthalmic Presentation

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Abstract

Diagnosis of gaze palsy is indeed a challenging task. This is a masquerade of a serious neurological disorder, probable yet to have full-blown manifestation. It is imperative that only a high index of suspicion can lead to prompt referral and mitigate life-threatening complications. It requires quick ophthalmic evaluation and prompt neurological referral. From the perspective of an ophthalmologist, a high index of suspicion and a thorough knowledge of neuro-ophthalmology are basic prerequisites. The extraocular muscle involvement, if localized based on other associated features, can aid rapid diagnosis. Here, we present a case of 34-year-old male patient presented to ophthalmology Outpatient Department in February 1st week, with complaints of diplopia since 1 day.

Key words: Cerebrovascular accident, Diplopia, Gaze palsy, Homocysteinemia, Pontine infarct

INTRODUCTION

Diplopia may be the harbinger of serious neurological pathology. A patient presenting to ophthalmology outpatient with acute diplopia may be on the verge of a life-threatening cerebrovascular accident (CVA). They may be otherwise healthy adults, presenting to ophthalmology outpatient as they are seriously disturbed by the double vision.

CASE REPORT

A 34-year-old male patient presented to Ophthalmology Outpatient Department in February 1st week, with complaints of diplopia since 1 day. No other ocular complaints were reported. Attendant complained of cross-eyed look while staring, on and off in the last couple of days. The patient was not a smoker or alcoholic.

On Examination

Visual acuity was 6/6 N6 both eyes, with normal color vision. Adnexal and anterior segment examination were normal bilaterally. Hirschberg corneal reflex revealed normal ocular posture. The pupillary reaction was normal - To direct and consensual reflexes, accommodation reflex was present, both eyes. Extraocular movements were full and normal unilaterally, with physiological nystagmus at extremes of gaze, in both eyes. However, the versions were abnormal. Both dextro and levo versions showed variable and inconsistent movements; sometimes, there was a limitation of movement in the abducting eye and sometimes in the adducting eye. Convergence could not be elicited due to diplopia in the primary position. Uncover test revealed esophoria in both eyes, but the disturbing diplopia in primary gaze caused inconsistent findings on repetition. 3rd, 4th, and 6th cranial nerve examinations were essentially normal. Slit lamp examination was essentially normal, with intraocular pressure of 14 mm of Hg in both eyes.

Diplopia charting was done. The result is as follows:

Diplopia charting could not localize the extraocular muscle; it was present even in primary gaze.

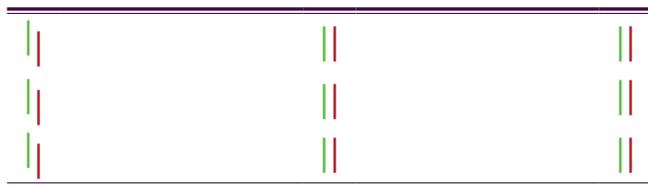
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Fundus examination revealed sectorial disc edema; superonasally, in both eyes. Induced venous pulsations were present (Figures 1 and 2).

General physical examination; the patient was lanky with marfanoid features - Arm span greater than height (Figure 3). No arachnodactyly was present. Systemic examination was otherwise normal.

On further questioning, the patient complained of mild dysarthria and ataxia described by the patient as a sensation of “trembling.” The presence of normal

duction with abnormal horizontal and vertical vergences, a clinical diagnosis of GAZE PALSY was made: Multiple sclerosis was the chief suspicion, as the probable cause of the anomaly. The patient was referred to physician and neurologist immediately with a warning of a possible CVA.

Physician and neurologist referral opined a possible cerebrovascular event and opined that a space occupying lesion is to be ruled out. ENT opinion was sought, found normal.

Management

Investigations

Routine blood and urine investigations were normal. Serum homocysteine was found to be $>65 \mu\text{mol/L}$ (accepted adult levels $>30 \mu\text{mol/L}$). Magnetic resonance imaging (MRI) brain revealed infarct in the dorsal pons and midbrain involving the peri-aqueductal region. Hyperintense spot in the right maxillary sinus was opined as “antral cyst” by the ENT specialist (Figures 4 and 5).

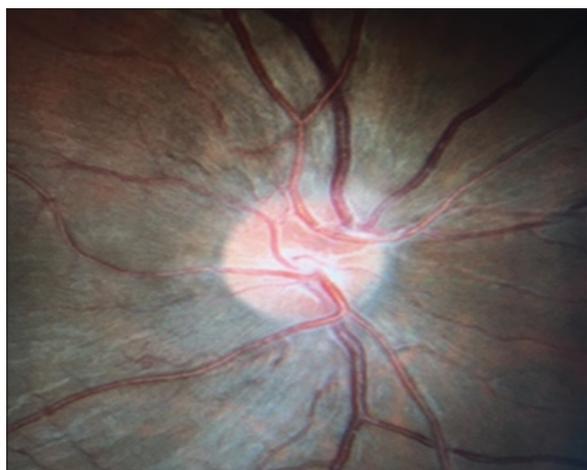


Figure 1: Fundus picture of right eye showing sectorial disc edema, superonasally

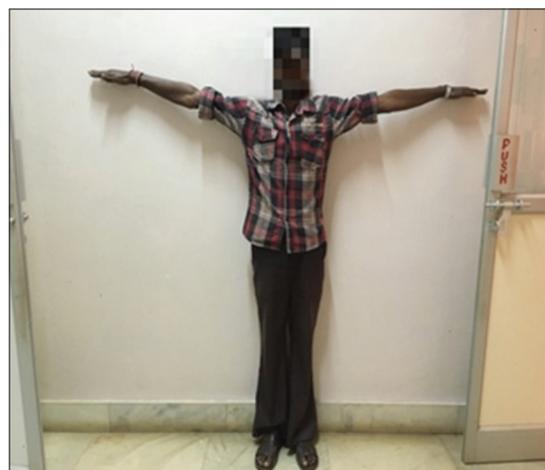


Figure 3: Patient showing increased arms span



Figure 2: Fundus picture of left eye showing sectorial disc edema, superonasally

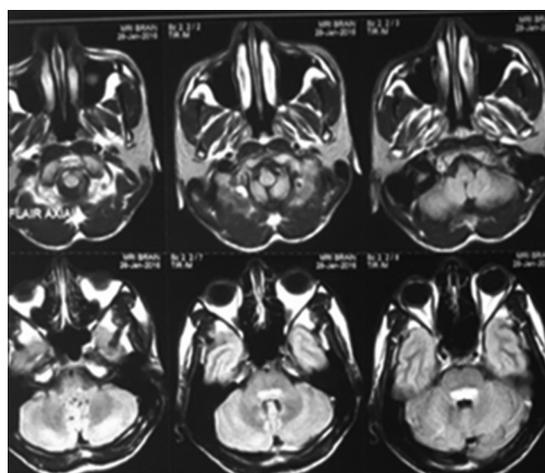


Figure 4: Magnetic resonance imaging brain showing hyperintense spot in right maxillary sinus

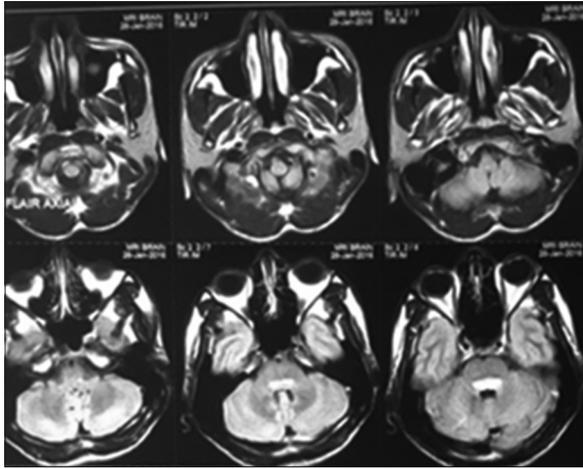


Figure 5: Magnetic resonance imaging brain with infarct in dorsal pons and midbrain

The patient was put on oral anti-coagulants clopidogrel 75 mg and ecosprin 75 mg, B6, folic acid, Vitamin B12 supplementation by the neurologist. The patient was advised limited physical activity, vegetarian diet with plenty of green leafy vegetables, a low sulfur and low protein diet.

The patient had clinically normal cardiovascular system but was advised echocardiogram.

On follow-up, at 3 weeks, the diplopia had resolved, the patient reported a general sense of well-being.

DISCUSSION

Diagnosis of gaze palsy is indeed a challenging task. This is a masquerade of a serious neurological disorder, probable yet to have full-blown manifestation. It is imperative that only a high index of suspicion can lead to prompt referral and mitigate life-threatening complications. Less than 10% of the patients with pontine lesions present with negligible motor deficits but predominantly sensory syndrome, disorders of eye movement or vestibular symptoms.¹

Homocysteinemias are seven biochemically and clinically distinct disorders characterized by abnormally elevated concentrations of sulfur-containing amino acid derivative homocysteine in blood and urine. Classic homocystinuria/homocysteinemia, familiar to the ophthalmologist is the most common form: Caused by the reduced activity of pyridoxal phosphate-dependent enzyme cystathionine β synthetase. The enzyme is required for the formation of cystathionine by condensation of homocysteine with serine. Most cases present between 3 and 5 years of age with ectopia lentis, mental retardation; marfanoid habitus and osteoporosis are some of the associated features. Life-threatening

vascular complications occur during the 1st decade of life. Diagnosis is established by elevated methionine and free homocysteine levels.

Type I or classic homocystinuria with autosomal recessive inheritance is an entity well recognized by ophthalmologists and is associated with early degeneration of zonules due to the deficiency of cysteine (present in high quantities in zonules) is the cause of early loss of accommodation and lenticular subluxation. Ectopia lentis is seen in more than 95% of untreated cases. Secondary angle closure due to papillary block may occur. Marfanoid habitus but infrequent arachnodactyly. Neurodevelopmental delay, mental handicap, psychiatric disturbances, and osteoporosis are the usual associations. Thrombosis in any vessel at any age - Post-operative/post-partum. Treatment involves oral pyridoxine, folic acid, and Vitamin B12 to reduce plasma homocysteine and methionine levels. Pathogenesis is attributed to decreased hepatic activity of cystathionine beta-synthetase, resulting in systemic accumulation of homocysteine and methionine.² Iris atrophy, optic atrophy, cataract, corneal opacity, myopia, and RD are known to occur in congenital homocystinuria.³ Furthermore, maculopathy and retinal degeneration have been noted.⁴

Most of the literature emphasizes the inferonasal subluxation of the lens as the major ocular manifestation. Early-onset progressive myopia with ectopia lentis and systemic association - myopia plus are high alert signs of homocysteinemia. Skeletal, vascular and central nervous system (CNS) manifestations are the other well-established associations.⁵ Neurodegeneration and epilepsy are known CNS complications.⁶ Although in some cases, CNS involvement in the form of mild proprioceptive deficits and sensory neuropathy, extra pyramidal signs, normal acoustic function and central motor system were reported. MRI changes noted were focal white matter gliosis, generalized cortical atrophy, and cortical infarct only in one case.⁷ In the present case, the central motor system was involved, in the form of a supranuclear gaze palsy.

The other forms of homocystinuria, including adult onset types, may be due to the (1) Defective Methionine synthase enzyme, (2) reduced availability of 2 co-factors 5- methyl tetrahydrofolate and methycobalamin.⁸ Hyper homocysteinemia or increased free homocysteine levels in seen in heterozygotes for the genetic defects results coronary, cerebrovascular, peripheral arterial disease and deep vein thrombosis in adult life, such as this case. Vitamin supplements are helpful in reducing the plasma homocysteine levels.⁹ Increased risk of coronary artery disease, stroke, and thromboembolism, Alzheimer's disease, schizophrenia, cognitive deficiency, osteoporosis,

venous thrombosis, pregnancy-related complications are associated with hyper homocysteinemia. Vitamin B6 supplementation is found effective in such cases. Patient was given supplementation of B6.¹⁰

Vascular occlusions in young adults may be associated with systemic genetic, biochemical disorders. However, there are no specific Indian studies to understand the association between cerebrovascular occlusions and disorders with biochemical abnormalities as a part of a genetic syndrome or otherwise. An interesting fact is that, in contrast to the west, a much higher incidence of 52-84% prevalence of homocysteinemia has been reported in Indian studies, among the general population.¹¹

Others are more common and are treated with folate, Vitamin B12 and in selected cases as in methionine synthase deficiency, methionine, avoiding excess plasma accumulation of homocysteine.¹² Furthermore, elevated plasma levels of homocysteine are strong, graded, independent risk factor for stroke, myocardial infarction, and other vascular events.²

CONCLUSION

This case presented a unique challenge because of its unusual presentation and incidental detection of homocysteinemia. It is atypical because of the adult onset and the absence of other features of congenital homocysteinemia (except for marfanoid habitus) on one hand; the CNS manifestations and presentation almost a decade earlier for classical adult onset type, on the other

hand. The patient is on regular follow-up: Advised more investigations, once he is able to afford them. The high risk of cardiovascular disease was explained to the patient. A karyotyping, examination of family members may give a better insight to the understanding of this biochemical abnormality.

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Mesothelial Cyst of Left Round Ligament, Misdiagnosed as a Left-sided Ovarian Cyst Presenting with Pain Abdomen: A Rare Case Report

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Abstract

The mesothelial cysts of the round ligament of the uterus are a rare pathology. They are usually misdiagnosed as inguinal hernias or as an adnexal mass. Mesothelial cysts are considered as developmental disorders. Ultrasound and computed tomography scan help in the diagnostic workup. Most of the cysts are asymptomatic. If the cyst is symptomatic or grows in size over time, they may be treated by surgical excision and the nature of lesion can be confirmed by histopathology. A 35-year-old female patient, Para 4 Living 4, the female patient presented to outpatient department with complaint of excessive flow during menstrual cycle for the past 2 cycles and pain abdomen since 15 days.

Key words: Mesothelial cyst, Ovarian cyst, Round ligament

INTRODUCTION

A mesothelial cyst of the round ligament is a rare cause of inguinal mass or an adnexal mass.¹⁻⁴ The literature between 1980 and 2013 reveals 10 cases only.^{3,4} Establishing an accurate pre-operative diagnosis based on clinical features is challenging.^{2,5} Mesothelial cyst is usually asymptomatic or tends to produce pain, discomfort or sensation of heaviness and bulging.^{1,2} A mesothelial cyst may be associated with an inguinal hernia in 30-40% of cases.^{5,6} The imaging studies help in the diagnostic workup.

CASE REPORT

A 35-year-old female patient, Para 4 Living 4, the female patient presented to outpatient department with complaints of excessive flow during menstrual cycle for the past 2 cycles and pain abdomen since 15 days. The patient had h/o ovarian cyst for the past 4 years, which

was treated conservatively in various private hospitals over a period of 2-year, but the cyst did not resolve. The above history was supported by previous ultrasound reports, which showed left ovarian cyst of 4 cm × 5 cm. The patient was married for the past 20 years; her last child was 6 years old. All the children delivered at home. She was not using any contraception methods. Her past menstrual cycles were regular and normal. However, her present cycles were regular but excessive flow lasting for 6-7 days associated with clots and dysmenorrhea.

Examination

On examination, the patient was moderately built and nourished.

The vitals were stable. On systemic examination, the respiratory and cardiovascular systems were within normal limits. On per abdomen examination, there was tenderness in the left iliac fossa. There was no palpable mass. There was no guarding and rigidity. On per speculum examination, cervix and vagina appeared normal. On per vaginal examination, the uterus was normal in size and fornices were free and non-tender.

Investigation

Routine blood investigations and ultrasonography (USG) of the whole abdomen were advised.

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The ultrasound report showed uterus was anteverted, normal in size and echotexture, endometrium 10 mm. The left ovary was enlarged with cystic changes 45 mm × 55 mm, thin-walled, unilocular. The right ovary was normal.

Management

As the patient was young and the size of the cyst was less than 5 cm, the patient pain subsided by analgesics and the general condition was stable, and the patient was treated conservatively, and cyclical oral contraceptive pills were advised for 3 months. The patient was reviewed after 3 months and USG was done on day 2/day 3 of the cycle.

The ultrasound showed the persistence of left ovarian cyst 55 mm × 65 mm. As the patient was symptomatic and pain abdomen was persistent, laparotomy was advised.

Intraoperative Findings

The uterus was bulky, with left ovary was enlarged 4 cm × 3 cm × 2.5 cm with the hemorrhagic cyst. The fallopian tube showed a paratubal cyst 1 cm × 1 cm. A cyst of 7 cm × 4 cm × 3 cm was seen in the broad ligament (Figure 1). On exploration and blunt dissection, the cyst was traced laterally and was originating in the left round ligament. The cyst was unilocular, filled with straw color fluid, lined by paper thin wall and was excised separately (Figure 2). Total abdominal hysterectomy with left salphingo-oophorectomy was done as the patient had menorrhagia with pelvic inflammatory disease with the left ovarian hemorrhagic cyst. The specimen was sent for histopathology. The post-operative period was uneventful, and patient recovered completely.

Histopathology Report

Section of the separate cyst showed flattened cells lining the cyst wall with thickened and dilated blood vessels underlying a fibrocollagenous stroma-mesothelial cyst of round ligament. Histopathology of the uterus and left adnexa showed chronic cervicitis with nabothian cyst with paratubal cyst.

DISCUSSION

The round ligament extends from the uterus, through the inguinal canal, and ends in the region of mons pubis and labia major. Embryologically, this is the female counterpart of gubernaculum testis and is predominantly composed of smooth muscle fibers, connective tissue, vessels, and nerves with a mesothelial coating.

The round ligament cyst is the same disease as a cyst of Nuck's canal and is inclusion of embryonic mesenchymal elements or remnants during the development of the round ligament.¹

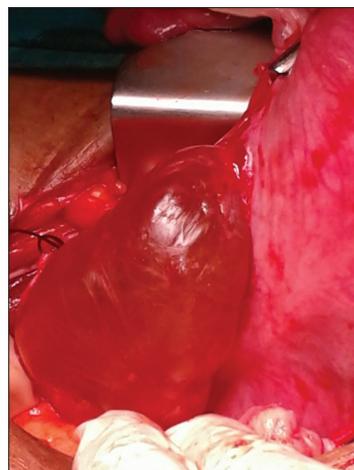


Figure 1: Thin-walled, straw colored fluid filled cyst in the left-sided round ligament

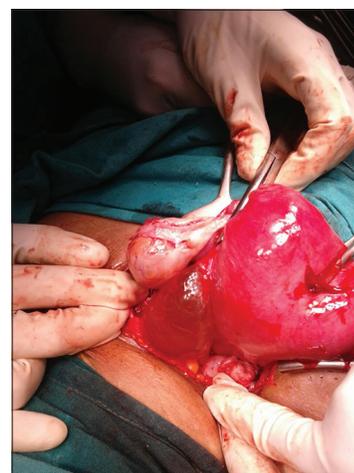


Figure 2: The relationship of the round ligament cyst, to uterus and left adnexa

The cyst of mesothelial investment of round ligament is lined with a single layer of flat, cuboidal cells.^{1,2} Clinically, a mesothelial cyst of the round ligament is usually misdiagnosed as the inguinal hernia or adnexal mass because of its anatomic location and relatively rare occurrence.¹⁻³ Other unusual tumors involving the round ligament has been reported in the literature like ovarian cyst, endometriosis, leiomyoma, rarely leiomyosarcoma.^{4,5}

CONCLUSION

Although rare, a mesothelial cyst of the intraperitoneal round ligament should be included in the differential diagnosis of the inguinal mass or adnexal mass in the female patient. Computed tomography scan or an ultrasound would be a useful tool in the diagnosis as they demonstrate a peristaltic cystic mass. The definitive diagnosis is usually made intraoperatively and is further confirmed histologically.²

Given the benign nature of the disorder, a reasonable option would be to observe the asymptomatic patient with serial ultrasound examinations. The cyst that becomes symptomatic/grow in size is better treated by surgical excision.^{3,5} Following excision prognosis is excellent, and no recurrence have been reported.^{5,6}

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