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Publisher Name: International Research Organization for Life & Health Sciences (IROLHS)

Registered Office: L 214, Mega Center, Magarpatta, Pune - Solapur Road, Pune, Maharashtra, India – 411028. Contact Number: +919759370871.

Designed by: Tulyasys Technologies (www.tulyasys.com)

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Contents

ORIGINAL ARTICLES

- Hematological Abnormalities in Early and Advanced HIV Infection Patients
M Bhanu Kumar, T Thippeswamy, R Shankar, C Prathima 1
- Centric Relation in Asymptomatic Hypodivergent and Hyperdivergent Skeletal Pattern
Subhash Chandra, Ajoy Kr Shahi 6
- Clinical Assessment of Airway and Its Correlation with Laryngoscopy Grading
Neeraj Narang, Inder Dev Ashahiya, Sheetal Panwar, Rekha Mahendra 13
- Pulmonary Function in Type 2 Diabetes Mellitus: Correlation with Body Mass Index and Glycemic Control
Preetam R Acharya, Monalisa D'Souza, R Anand, Shashidhar M Kotian 18
- Factors Affecting Visual Outcome in Phacolytic Glaucoma
J Samuel Cornelius Gnanadurai, Elfride Farook Sanjana, M Radhakrishnan 24
- Association between Dyspnea, Forced Expiratory Volume in 1s, and Body Mass Index in Chronic Obstructive Pulmonary Disease
C Sabir, M Sanjeev Kumar 28
- Prevalence and Risk Factors of Peripheral Vascular Disease in Diabetic Foot Lesions
Venkata Nagateja Mucherla, Lingaraju Narasimaiah 32
- Comparative Study of Gabapentin in Combination with Valacyclovir and Valacyclovir Alone in Herpes Zoster
Sujata Singh, Anju Madhwar, Jitendra Pal Singh 37
- Occurrence and Antimicrobial Susceptibility Pattern of Methicillin-resistant *Staphylococcus aureus* and Methicillin-resistant Coagulase-Negative Staphylococci Isolated from Different Clinical Specimens from the Patients Hospitalized in Teerthanker Mahaveer Medical College and Research Centre, Moradabad, India
Raees Ahmed, Sudhir Singh, Umar Farooq, Amit Kumar Bharti, Navdeep Kaur 41

- Evaluation of Patient Satisfaction Based on Communication Skills of Dentists in Mumbai City: A Cross-Sectional Questionnaire Based Survey
Megha Rambhia, Kosha Shah, Purvi Bhate, Dheeraj Kalra, Haveri Rajeev 48
- Abdominal Surgical Site Infection Occurrence and Risk Factors in Krishna Institute of Medical Science, Karad
Hemant B Janugade, Basavaraj K Nagur, Kruthika R Sajjan, Sangeeta B Biradar, Jignesh K Savsaviya, Mahesh Reddy 53
- Role of Ultrasonography in Molar Pregnancy Coexisting with Viable Fetus: A Prospective Study
Madhavilatha Routhu, Swapna Chouhan 57
- Evaluation of Cervical Lesions: A Prospective Study
Ranu Jain, Rowena Walker, Lalit Jain, Jitendra Kumar Jatav 63
- Assessment of Matrix Metalloproteinase-1 and its Tissue Inhibitor of Metalloproteinase-1 in Pre-eclampsia
Madhur Gupta, Suresh Chari 70
- Comparison of Menopausal Symptoms and Quality of Life after Natural and Surgical Menopause
Neha Mahajan, Dinesh Kumar, Perveena Fareed 74
- Clinico-etiological Profile and Predictors of Outcome in Acute Encephalitis Syndrome in Adult
Rakesh Kumar Shahi, P Nigam 78
- Comparative Study of Knowledge, Attitude and Practices toward Contraception among Tribal and Non-Tribal Wives of Eligible Couples in a Rural Area of Assam
Mintu Dewri Bharali, Rupali Baruah, Jutika Ojah 84
- Comparison of Z-Plasty and Limberg Flap Techniques in Management of Sacrococcygeal Pilonidal Sinus
B D Manjunath, A Prem Kumar, N Nischal, Ramya Ramachandra 90
- Rapid Laboratory Techniques in Diagnosis of Malaria in a Tertiary Care Hospital, Chennai
B Santhy, T Ravichandran, C P Ramani, P Sumathy, A Heber 94

- Evaluating Facial Esthetics by Relating Upper and Lower Lips with E-plane:
A Short Clinical Photographic Study
Nikhil Asawa, Nilesh Bulbule, Dilip Kakade, Riddhi Shah 100
- Refractive Errors of Patients between 20 and 40 Years and its Correlation
with Axial Length
R Kumaraswamy, N Sivakumar, Heber Anandan, Mahammad Khaja Ramiz Uddin 104
- Comparative Study of Dermatoglyphic Patterns of Diabetes Mellitus and
Diabetic with Hypertension Patients of Hilly Region
Anju Bala, Arvind Deswal, P C Sarmah, Bidita Khandelwal, Binod Kumar Tamang 108
- Isolation of Pathogenic Aerobic Organism from the Blood of Septicemic
Neonates and the Susceptibility of Isolates to Various Antibiotics Attending
in TMMC & RC, Moradabad, India
Navdeep Kaur, Umar Farooq, Sudhir Singh, Amit Kumar Bharti, Raees Ahmed, Komal Singh 113
- Clinico-Pathologic Study of Exfoliative Dermatitis in Patients Visiting a
Tertiary Care Centre in South India
G Mahabaleshwar, Kashinath Nayak, Maria Kuruvila, Radha R Pai 119
- Obstetrical and Perinatal Outcome in Rhesus Antigen Negative Pregnancy
Shradha, B Moitra, Archana Kumari, P B Sahay 124
- Morbidity Pattern in the Inmates of Residential Ashram in Rural Dakshina
Kannada District, Karnataka
Diwakar Kumar Singh, S Nanjesh Kumar 130
- Prevalence of Prostatic Intraepithelial Neoplasia in Patients Diagnosed as
Benign Prostatic Hyperplasia Underwent Transurethral Resection of the
Prostate at a Rural Teaching Hospital, India
M V Munireddy, H Girish, K Krishna Prasad, Harsha Rajareddy 134
- Contrast-enhanced Computed Tomographic Evaluation of Acute Pancreatitis:
An Exploratory Study
U S Vinayaka, G Ravichandra, K Devadasa Acharya, K N Muralidhara 139

- Evaluation of Dexmedetomidine-0.5 µg/kg and 1 µg/kg in Blunting the Responses to Laryngoscopy and Intubation
Bansal Rachit, H S Nanda, Kashyap Mahesh 147
- Prevalence of Multidrug-Resistant and Extensively Drug-Resistant *Proteus*, *Providencia* and *Morganella* Species in Burn Wound Infection
Naz Perveen, S Krishan Prakash, Tanisha Bharara 154
- Comparative Study between General Anesthesia and Combined General Anesthesia with Spinal Anesthesia in Laparoscopic Cholecystectomy
H K Sale, Vitthal J Shendage, Sarita Wani 157
- Evaluation of Peripheral Arterial Disease of Lower Extremity by Doppler Imaging
Choudhary Vivek Anant, Patil Saurabh Shrinivas, Shah Vaibhav Ramesh 163
- Maternal and Fetal Outcome in Pregnancy with Fibroids: A Prospective Study
Muthuramu Poovathi 169
- Non-stress Test and Vibroacoustic Stimulation Test in High-risk Pregnancies and its Relation to Perinatal Outcome
Pradip Sambarey, Daksha Mrutyunjay Bilagi 173
- Solitary Extramedullary Plasmacytoma of Nasal Cavity: An Emerging Differential Diagnosis of Nasal Masses
A Maheshwari, R Panigrahi, S Mahajan 178
- Routine Internal Sphincterotomy with Hemorrhoidectomy: A Prospective Study
S Harish, R Raxith Sringeri, G Ajay 182
- Clinico-Etiological Profile and Outcome of Neonatal Respiratory Distress
Sayid M Barkiya, Venugopal N, Veena Kumari 189
- Membranoproliferative Glomerulo Nephritis Common Glomerular Disease - Changing Pattern of Biopsy Proven Renal Disease in a Tertiary Care Hospital
S Himamani 193

- Clinico-Epidemiological Profile of Esophageal Cancer in Kashmir
Syed Arshad Mustafa, Saquib Zaffar Bandy, Manzoor Ahmad Bhat, Aamir Rashid Patigaroo, Abdul Waheed Mir, Kulwant Singh Bhau 197
- Efficacy of Oral Vitamin K Compared to Injectable Vitamin K in Neonates
N Venugopalan, T Vanaja 203
- Maternal and Perinatal Mortality and Morbidity in Hypertensive Disorder Complicating Pregnancy
C K Rajamma, P Sridevi 206
- Panorama of Pleomorphic Adenoma in a Series of Patients Presented over a Period of 5-year
Pawan Bhat, Sachan Bhat, Deepa Hatwal, Sheela Chaudhri 210
- Effect of Intrathecal Fentanyl with Bupivacaine on Maternal Hemodynamics and Fetal Outcome during Cesarean Section: A Comparative Study with Two Different Doses
Roopesh Kumar, Pradeep Sahi, Anshul Jain, Hema Shobhne 214
- Distal Polyneuropathy in Type 2 Diabetes Mellitus in and Around Jabalpur, Madhya Pradesh, India
H S Patel, Sandeep Kumar Jain 218
- Effects of Aerosolized Levosalbutamol Verses Salbutamol on Serum Potassium Level and Heart Rate in Children with Acute Exacerbation of Asthma
Sayid M Barkiya, Veena Kumari, Venugopal N, Abdul Aseez 223
- Prevalence of Smoking and Smokeless Forms of Tobacco Use In Adults More Than 18 Years in an Urban Area
Sushrit A Neelopant, Girija S Ashtagi 228
- Recurrence Rate in Post Irradiated T1 and T2 Supraglottic and Glottic Carcinoma of the Larynx
T Santhi, K V Rajan 233
- Maternal and Perinatal Outcomes in Cases of Acute Renal Failure in Pregnancy and Puerperium in Tertiary Care Centre
Alka Patankar, Rajendra Wakankar, Snehal Raut 239

- Effect of 0.5% Bupivacaine Versus 0.75% Ropivacaine - Onset, Duration and Quality of Brachial Plexus Block through Supraclavicular Approach
Srihari Babu Gonuguntla 244
- Ultrasound Guided Fine-Needle Aspiration Cytology of Liver Lesions: A Prospective Study
Shashi Bhushan Tailor, Dharm Chand Kothari 249
- Comparative Study of Titrated Oral Misoprostol Solution and Oxytocin to Induce Labor Conducted at Kannur Medical College
K M Asokan, Smitha Santhosh 255
- Routine Elective Induction of Labor by 38-39 Weeks Advantages and Safety Concerns
Haridas Govinda Warriar, K M Asokan 259
- REVIEW ARTICLES**
- A Step toward Precision: A Review on Surgical Guide Templates for Dental Implants
Amrita Pawar, Sangam Mittal, Ricky Pal Singh, Rabbpreet Bakshi, Varun Sehgal 262
- Applications of 3-D Printing in Orthodontics: A Review
Shahnaz Mahamood, Maimoona Abdul Khader, Hashim Ali 267
- CASE REPORTS**
- Linear Syringocystadenoma Papilliferum with Unusual Presentation: A Rare Case Report
Bansode Shubhada, Kanade Umesh, Chaware Suresh, Ghatale Renuka 271
- Retroperitoneal Ancient Schwannoma: A Benign Tumor
Y V Narayanswamy Chetty, M R Sreevathsa, Sam Koruth, Sajith Krishnan 274
- Neurenteric Cyst of Posterior Mediastinum in an Infant: A Case Report
Mohammad Rafique Bagwan, S Mahesh Reddy, Chandrashekhar Z Pardeshi, Shruti Panicker, Karan Kumar 280
- Guillain-Barre Syndrome after General Anesthesia for Endoscopic Retrograde Cholangiopancreatography: A Case Report
K S Smitha, Manjunath Patil, A Sreenivas Babu 284

Fallopian Tube Prolapse: An Unusual Complication of Surgical Drainage Site <i>Muthuramu Poovathi, Ethirajan Kalarani</i>	287
Angioleiomyoma of Broad Ligament: A Rare Variant of Leiomyoma <i>A L Hemalatha, D N Nanjundaswamy, Swati Sahni, Amita Kumari</i>	290
Meckel's Diverticulum as Bleeding Per Rectum in Adult Male: A Rare Presentation <i>K B Rathore, W F Masih, S K Goyal</i>	293
Chondroid Syringoma: A Rare Case Series of Cutaneous Adnexal Neoplasm <i>Sapna Goel, Shilpa Bairwa, Mahak Sharma, Pooja Kanwat</i>	296
Management of Ruptured Hepatic Subcapsular Hematoma in Hemolysis, Elevated Liver Enzymes, Low Platelets Syndrome: A Case Report <i>Sangita Ramteke, Snehalata Suresh, Dipeeka Dharmale, Surangana Agrawal</i>	299
Chronic Uterine Inversion Secondary to Submucous Fibroid: A Rare Case Report <i>Archana Kumari, Anubha Vidhyarthi, K M Salini</i>	302
CASE PICTORIAL	
Rapid Intraventricular Clot Dissolution with Enoxaparin in Ischemic Cardiomyopathy <i>Vaibhav Ingle, Aneeta Datey, Anand Verma, Zubin Gandhi</i>	305

Hematological Abnormalities in Early and Advanced HIV Infection Patients

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Abstract

Background: Hematological abnormalities in patients with HIV infection are common. These hematological abnormalities include anemia, leukopenia, thrombocytopenia, and sometimes pancytopenia with variable bone marrow abnormalities.

Methodology: A study was conducted from March 2008 to April 2010 in a tertiary care center-JSS Hospital, Mysore, Karnataka. The patients admitted to the Department of Medicine and Dermatology wards with the diagnosis of HIV infection as per standard WHO criteria were included in the study. A detailed history, physical examination, and relevant investigations were conducted. Data were collected using a pre-tested proforma to meet the objectives of the study.

Results: A total of 100 HIV-positive patients were included in the study and were assigned into either Groups A and B. Group A patients included HIV-positive patients with CD4 counts > 200 cells/cumm, and Group B included HIV-positive patients with CD4 counts < 200 cells/cumm. 50 patients were included in each group. Most of these patients (about 60%) were in the highly reproductive age group (21-40 years) and were predominantly males (78%). The common symptoms among these patients were fever (79%), weight loss (64%), and oral thrush (24%). Anemia was the most common laboratory abnormality seen in both the groups with 70% in Group A and 84% in Group B. Leukopenia was seen in 10% of patients in Group A and 60% of patients in Group B. Thrombocytopenia was seen in 32% cases among Group A and 78% cases among Group B.

Conclusion: In patients with HIV infection, the frequency and severity of hematological manifestations including hypocellular bone marrow increased with the decline in CD4 counts. This might lead to a significant impact on clinical outcome and patient's quality of life. Hence, all the HIV patients should also be investigated for hematological abnormalities and treated accordingly.

Key words: AIDS, CD4 counts, Hematological abnormalities, HIV

INTRODUCTION

HIV infection targets mainly the immune system and hence hematological abnormalities are among the most common clinicopathological features. These hematological abnormalities vary from anemia, leukopenia, and thrombocytopenia including bone marrow dysplasia. The pathophysiological basis for these hematological

abnormalities may include impaired hematopoiesis, immune-mediated cytopenias, and/or coagulopathies especially in the advanced stage of the disease.^{1,2}

HIV destroys the T-cell lymphocytes which in turn disables the immune system to defend the body against diseases and malignancies. This will also lead on to various devastating opportunistic infections paralleling the declining immunity. Peripheral blood picture findings are highly variable depending on the clinical severity of immunodeficient state.³

In general, hematological abnormalities progress in frequency and severity with the progression of the disease from the asymptomatic HIV carrier state to the advanced state of the disease.⁴ About 15% of asymptomatic HIV

Access this article online



www.ijss-sn.com

Month of Submission : 12-2015

Month of Peer Review : 01-2016

Month of Acceptance : 01-2016

Month of Publishing : 02-2016

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carriers have mild anemia. The prevalence of anemia increases from 30% to 40% in those with the early disease to 75-90% in advanced patients. It may be still higher in HIV-infected infants and children.⁵

Granulocytopenia with or without lymphopenia occurs in approximately 8% of asymptomatic HIV carriers and as many as 70-75% of children and adults with AIDS. While anemia and granulocytopenia tend to occur concomitantly with a severity that parallels the course of the HIV infection, thrombocytopenia can occur independently of other cytopenias and at all stages of HIV infection. Isolated thrombocytopenia may be the first manifestation of HIV infection.^{6,7}

The accurate measurement of CD4 cell counts is essential for the assessment of immune system of HIV-infected person as the pathogenesis of AIDS is largely attributable to the decrease in CD4 lymphocyte counts. CD4 counts help to categorize the HIV-infected patients from mild to severe form of the disease and in turn guide the treatment. It also depicts the patient's predisposition to various opportunistic infections.

Among the neoplastic complications, Kaposi's sarcoma is the most common neoplasm in patients with AIDS, occurring with a 700 fold increase in HIV-infected patients compared with age-matched, non-infected controls.⁸ Other malignancies commonly seen in patients with AIDS are non-Hodgkin's lymphoma, seminoma, and non-melanoma skin cancer.⁹

The combined effect of the above alterations in hematological parameters will significantly compromise patient's quality of life who are already overburdened by the treatment of primary viral infection, secondary infections, and neoplastic complications. These hematopoietic abnormalities, in turn, lead to poor tolerance to therapies necessitating dose reductions, alteration of drug regimens, or interruption of therapies.

METHODOLOGY

A total of 100 patients detected to be HIV-positive as per the WHO criteria attending the Department of Medicine and Dermatology, JSS Hospital, Mysore during the period of March 2008-April 2010 were enrolled for the study. These patients were assigned into either Group A (HIV-positive patients with CD4 count > 200 cells/cumm) or Group B (HIV-positive patients with CD4 count < 200 cells/cumm).

Inclusion Criteria

HIV-positive patients as per the WHO criteria irrespective of their anti-retroviral treatment status, attending the

Department of Medicine/Dermatology, JSS Hospital, Mysore.

Exclusion Criteria

1. Patients with previously known hematological disorders
2. Congenital hematological disorders
3. Age <18 years
4. Pregnant woman
5. Critically ill patients.

Data were collected using a pre-tested proforma to meet the objectives of the study. The purpose of the study was carefully explained. Informed and written consent was obtained from all the patients prior to the study.

Detailed history, general, and systemic examination was conducted with emphasis on signs suggesting hematological system involvement such as pallor, clubbing, jaundice, edema, glossitis, lymphadenopathy, koilonychia, angular stomatitis, petechiae, and hepatosplenomegaly.

The investigations included complete hemogram with peripheral blood picture, bone marrow cytology, and CD4 cells count by Flow cytometry by a standard technique using Becton-Dickinson FAC Scan.

Statistical Analysis

Descriptive statistics was expressed as mean \pm SD (range). Results were compared using Chi-square test of significance. A $P < 0.05$ was considered statistically significant.

The study was carried out after obtaining permission from the Institutional Ethics Committee.

RESULTS

The patients were divided into two groups according to their CD4 counts: Group A (HIV-positive with CD4 counts >200 cells/cumm) and Group B (HIV-positive with CD4 counts <200 cells/cumm). Out of the 100 patients studied, 50 patients were included in each group.

Age and sex distribution: Most of the patients were males in the age group of 21-40 years (74%). The mean age of the patients in the present study was 33.8 years. In the Group A patients, males were predominant in the age group of 31-40 (50%), whereas females were predominantly in the age group of 21-30 (50%). In Group B patients, most of the patients were males and in the age group of 31-40 years (44.75%), whereas females were predominantly in the age group of 41-50 (66.67%) (Table 1).

Table 1: Age and sex distribution pattern in early and advanced HIV groups

Age in years	Group A (CD4 counts >200 cells/mm ³) n=50			Group B (CD4 counts <200 cells/mm ³) n=50		
	No. of males (%) n=40	No. of females (%) n=10	Total (%)	No. of males (%) n=38	No. of females (%) n=12	Total (%)
<20	0	1 (10)	1 (2)	0	0	0
20-30	10 (25)	5 (50)	15 (30)	3 (7.89)	1 (8.33)	4 (8)
31-40	20 (50)	2 (20)	22 (44)	17 (44.75)	2 (16.67)	19 (38)
41-50	5 (12.5)	1 (10)	6 (12)	15 (39.47)	8 (66.67)	23 (46)
51-60	4 (10)	1 (10)	5 (10)	2 (5.26)	1 (8.33)	3 (6)
>60	1 (2.5)	0	1 (2)	1 (2.63)	0	1 (2)
P value	Age and gender P=0.05 (S) overall P=0.000			Age and gender P=NS overall P=0.00		

Symptoms and Signs: Predominant symptoms in Groups A and B were fever (78% and 80%) and weight loss (62% and 66%). Predominant signs in Group A were pallor (70%) and adenopathy (8%), whereas in Group B was pallor (80%) and oral candidiasis (44%) (Table 2).

Peripheral blood picture: Anemia was the most common sign, about 77% of them had hemoglobin below 13 g% and about 6% had hemoglobin below 6 g%. Cytopenias of all peripheral blood cells have been observed in patients with HIV infection (Table 3).

The most common type of anemia in Group A (CD4 counts > 200 cells/cumm) was normocytic normochromic anemia and normocytic hypochromic anemia, while in Group B (CD4 counts <200 cells/cumm) it was normocytic normochromic anemia and pancytopenia.

Leukopenia was seen in 10% cases of Group A and 60% cases of Group B patients. Thrombocytopenia was seen in 32% and 78% cases of Groups A and B, respectively.

Bone marrow cellularity: Bone marrow picture was hypercellular in 64% and 68%; normocellular in 36% and 20% of Groups A and B patients, respectively, while it was hypocellular in 12% of Group B patients. In addition, megakaryocytic dysplasia was seen 2 cases of Group A and 7 cases of Group B patients. Marrow eosinophilia was seen in 2 cases (4%) of Group A and 4 cases (8%) cases of Group B (Table 4).

DISCUSSION

Hematological abnormalities and impaired immune status represent one of the common causes of mortality in HIV-infected patients. This hematological status worsens with the progression of the disease.

In the present study, the age of the patients ranged from 19 to 62 years. 60% of these patients were in the highly productive age group of 21-40 years. There was an overall

Table 2: Symptoms and Signs in early and advanced HIV groups

Symptoms and signs	No. (%)		
	Group A (CD4 counts >200 cells/mm ³) (n=50)	Group B (CD4 counts <200 cells/mm ³) (n=50)	Total (n=100)
Fatigue	17 (34)	24 (48)	41 (40)
Fever	39 (78)	40 (80)	79 (79)
Weight loss	31 (62)	33 (66)	64 (64)
Jaundice	03 (06)	05 (10)	08 (08)
Dyspnea	04 (08)	10 (20)	14 (14)
Anorexia	08 (16)	20 (40)	28 (28)
Cough	06 (12)	18 (36)	24 (24)
Diarrhea	02 (04)	03 (06)	05 (05)
Palpitation	06 (12)	05 (10)	11 (11)
Pallor	35 (70)	40 (80)	75 (75)
Clubbing	01 (02)	11 (22)	12 (12)
Icterus	03 (06)	05 (10)	08 (08)
Oral thrush	02 (04)	22 (44)	24 (24)
Adenopathy	04 (08)	18 (36)	22 (22)
Edema	01 (02)	03 (06)	04 (04)
Petechiae	01 (02)	02 (04)	03 (03)

male predominance (78%) which is in accordance with a study done by Sharma *et al.* (79.7%).¹⁰ Females were much younger with 54% of them in the age group of 21-30 years.

The most common symptoms were fever (79%), weight loss (64%) followed by fatigue (41%). The most common signs were pallor (75%) and oral thrush (24%). The increased frequency of these symptoms and signs could possibly be due to the severity of the illness, and the majority of patients were in WHO clinical Stages III and IV.

The anemia was the most common hematological finding, about 77% of them had hemoglobin below 13 g% and about 6% were having hemoglobin below 6 g%. This incidence was in accordance with previous studies of Rajeev *et al.* (75%).¹¹ When hemoglobin (Hb)% is correlated to CD4 counts, in the Group A patients, about 70% of cases had Hb% <13 g%, whereas in Group B, 84% of cases had Hb% <13 g%. Morphologically the most common type of anemia was normocytic normochromic

Table 3: Hb, TLC, neutrophils, lymphocyte, and platelets counts in relation to CD4 counts in early and advanced HIV groups

Type of test	Unit no. of cells	No. (%)		
		Group A (CD4 counts >200 cells/mm ³) (n=50)	Group B (CD4 counts <200 cells/mm ³) (n=50)	Total (n=100)
Hb in g%	<6	03 (06)	03 (06)	06
	6-9	12 (24)	18 (36)	30
	9-13	20 (40)	21 (42)	41
	>13	15 (30)	08 (16)	23
P value	Hb and CD4 count P=0.34, overall P=0.000			
TLC (×1000 cells/mm ³)	≤4	05 (10)	30 (60)	35
	4-11	39 (78)	18 (36)	57
	>11	06 (12)	02 (04)	08
P value	TLC and CD4 count P=0.00, overall P=0.00			
Neutrophils (%)	≤50	03 (06)	04 (08)	07
	50-70	40 (80)	39 (78)	79 (14)
	>70	07 (14)	07 (14)	
P value	Neutrophils and CD4 count P=0.925, overall P=0.00			
Lymphocyte (%)	≤ 20	13 (26)	25 (50)	38
	20-40	30 (60)	15 (30)	45
	>40	07 (14)	10 (20)	17
P value	Lymphocytes and CD4 count P=0.009, overall P=0.002			
Platelets (in lakhs/mm ³)	<1	04 (08)	20 (40)	24
	1-1.5	12 (24)	19 (36)	31
	>1.5	34 (68)	11 (22)	45
P value	Platelets and CD4 count P=0.00 (S), overall P=0.032			

Hb: Hemoglobin, TLC: Total leukocyte count

Table 4: Bone marrow picture in relation to CD4 counts in early and advanced HIV groups

Bone marrow cellularity	No. (%)		
	Group A (CD4 counts >200 cells/mm ³) (n=50)	Group B (CD4 counts <200 cells/mm ³) (n=50)	Total (%) (n=100)
Hypocellular	0 (0)	06 (12)	06
Normal	18 (36)	10 (20)	28
Hypercellular	32 (64)	34 (68)	66
P value	Bone marrow and CD4 count P=0.015, overall P=0.00		

type followed by normocytic microcytic and the least being pancytopenia.¹¹

Leukopenia was prevalent in 35% of the patients. Leukopenia was seen in 10% cases of Group A and 60% cases of Group B. Lymphocytopenia was seen in 26% cases of Group A and 50% cases of Group B. Neutropenia was seen in 6% of cases of Group A patients and 8% cases of Group B. According to Zon *et al.*, the incidence of leukopenia range from 57% to 85% in patients with fully

developed AIDS, whereas it was <5% in asymptomatic seropositive patients presenting with leukopenia.¹² However, according to Castella *et al.*, the incidence of granulocytopenia was around 75% probably because of influence from anti-retroviral therapy along with the disease itself.¹³

The prevalence of thrombocytopenia (platelet count below 1.5 lakhs/mm³) was 24%. This is in accordance with studies of Murphy *et al.* (30%) and Zon *et al.* (40%). In a multi-centric AIDS cohort study of 1500 HIV-positive individuals, 6.7% had platelet counts <1.5 lakhs/mm³ on at least one semiannual visit. In the present study, thrombocytopenia was seen in 36% cases of Group A patients and 78% cases of Group B patients.^{14,15}

Bone marrow study in Group A cases showed hypercellularity in 64% and was normocellular in 36%. Whereas in Group B, 68% were hypercellular, 20% normocellular, and 12% were hypocellular. In number of earlier studies bone marrow is hypercellular in early stages of the disease and hypocellular later on as disease advance. In addition, there were 2 cases of megakaryocytic dysplasia in Group A and 7 cases in Group B. Megakaryocytic dysplasia has become increasingly recognized in patients with fully developed AIDS patients and also in isolated thrombocytopenia according to van der Lelie *et al.*¹⁶ Furthermore, in the present study, marrow eosinophilia was seen in 4% cases of Group A patients and 22% cases of Group B patients. However, according to Zon *et al.* and Delacretaz F *et al.*, marrow eosinophilia is common and has been reported in 9% and 61% of patients with AIDS.^{17,18}

CONCLUSION

In the present study, the most common hematological manifestations found were anemia, leukopenia, and thrombocytopenia. The frequency and severity of these hematological manifestations increased with the decline in CD4 counts and have got a significant impact on clinical outcomes and patients quality of life. Hence, all patients should be investigated for hematological abnormalities and treated accordingly to reduce the morbidity and mortality.

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How to cite this article: Kumar BM, Thippeswamy T, Shankar R, Prathima C. Hematological Abnormalities in Early and Advanced HIV Infection Patients. *Int J Sci Stud* 2016;3(11):1-5.

Source of Support: Nil, **Conflict of Interest:** None declared.

Centric Relation in Asymptomatic Hypodivergent and Hyperdivergent Skeletal Pattern

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Abstract

Introduction: Orthodontists have always believed in the appropriate positioning of mandibular condyle in relation to the temporal fossa when teeth are in maximum intercuspation. In addition, studies focusing on the relation between facial configuration and temporomandibular disorders (TMD) indicate an association of hyperdivergency with TMD.

Objective: The main objective of this study was to evaluate and compare the centric relation and centric occlusion in asymptomatic subjects with hyperdivergent and hypodivergent facial skeletal type. The hypothesis of this study was that condylar displacement was greater and more frequent in the hyperdivergent facial type.

Materials and Methods: Two groups of 35 subjects, each representing the extremes in facial type, were randomly selected and matched for age. Mounted casts and the mandibular position indicator instrumentation were used to measure and compare the amount of condylar distraction between the 2 groups in the horizontal and vertical planes. The total amount of change between the 2 groups was examined using a statistical *t*-test.

Result: Condyles in the hyperdivergent group, on average, were deflected backward 3.6 times greater than hypodivergent group.

Conclusion: The findings of this study demonstrated significantly greater condylar displacement for hyperdivergent group in the horizontal dimension.

Keywords: Centric relation, Hyperdivergent face type, Hypodivergent face type, Mandibular position indicator

INTRODUCTION

Orthodontists have always believed in the appropriate positioning of mandibular condyle in relation to the temporal fossa when teeth are in maximum intercuspation (MI). The condyle has to be positioned superiorly and anteriorly against the articular eminence, with the articular disc interposed between the two. This position is called centric relation. It is at this centric relation position of the condyle that the teeth should have MI (centric occlusion). Therefore, ideally, centric relation should coincide with centric occlusion.¹

The aim of all orthodontic treatment should be to match centric relation and centric occlusion, which is difficult to achieve with orthodontics. Since CR is the most consistent and reproducible positional reference, accurate studies of dental and maxilo-mandibular relationship are dependent on CR assessment.² Previous studies have shown that posterior mandibular displacement leads to temporomandibular disorders (TMD)³ and morphological changes.⁴ In addition, studies focusing on the relation between facial configuration and TMD indicate an association of hyperdivergency with TMD.^{5,6} Several studies have been done to establish relationship between facial morphology and condylar position.⁷⁻¹¹

Since the condyle position can be widely influenced by occlusion, it is of paramount importance to determine its displacement in three-dimensional.¹²⁻¹⁴ Conventional radiograph does not provide accurate information in this regard. Mandibular position indicator (MPI) and similar

Access this article online



www.ijss-sn.com

Month of Submission : 12-2015

Month of Peer Review : 01-2016

Month of Acceptance : 01-2016

Month of Publishing : 02-2016

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tools have been introduced to allow quantification of the three-dimensional displacement of the condyle.¹⁵⁻¹⁷

The significance and clinical relevance of identifying and integrating condylar displacement in orthodontic diagnosis and treatment planning, when it surpasses a threshold of 2 mm in the horizontal or vertical axis has been established. Accurate diagnosis requires the assessment of occlusal interferences and skeletal relationships, without the influence of the neuromuscular system. Despite reasonable evidence of facial configurations being more prone to articular instability, data related to the subject is scarce and conflicting.

Stringent and worms studied the relationship between skeletal pattern and internal derangement. They found a greater incidence of internal derangement in the dolichofacial skeletal pattern.¹⁸

Girardot reported a more significant condylar displacement in hyperdivergent facial morphologies, whereas Burke *et al.* found diminished upper articular joint spaces in the same facial type.^{7,11} Gidarakou found there was an increase in the mandibular plane angle (GoGn to SN) and an increase in the gonial angle of the mandible (Ar-Go-Me) to be associated with increased temporomandibular joints (TMJ) internal derangement.⁸ In contrast, Hidaka *et al.* found no relationship between facial type and condylar position.¹⁹

Therefore, the aim of this observational study was to clarify the above mentioned conflicting findings and throw more light on the relationship between facial type and condylar position.

The main objective of this study was to evaluate and compare the condylar position between CR and CO in asymptomatic subjects with hyperdivergent and hypodivergent facial skeletal type. The hypothesis of this study was that condylar displacement was greater and more frequent in the hyperdivergent facial type.

MATERIALS AND METHODS

The research protocol was reviewed and approved by the Ethical Committee of the Institute. Condylar position was studied in two groups of 35 subjects each representing the extremes in facial type. The subjects were patients who reported to our institution. Based on the study criteria, we included individuals, who were between 16 and 30 years of age and facial skeleton characteristics as measured cephalometrically. Age was a criterion for selection since the intention was to study young adult subjects having completed growth. Facial skeleton type was determined by

the Jarabak rotation index. Subjects were considered to be hyperdivergent if the posterior-anterior face height ratio (sella-gonion/nasion-menton) was 59% or less and mean mandibular plane angle was 34° or more. Subjects were considered to be hypodivergent if the posterior-anterior face height ratio (sella-gonion/nasion-menton) was 65% or more and mean mandibular plane angle was 16° or less.

Patients were excluded if they had missing permanent teeth except third molars, grossly carious teeth, restorative treatment, mobile teeth due to advanced periodontitis, crossbite or open bite, functional mandibular deviation due to occlusal interference, previous orthodontic treatment, history, clinical signs and symptoms of TMDs as determined by patient's clinical history and clinical examination, previous TMD treatment, evident dental or facial asymmetry, congenital skeletal deformity such as cleft lip and palate, and history of trauma or surgery to the TMJ. In addition, patients were excluded if they had Class III malocclusion and Class II div2 malocclusion. It was felt these factors could significantly affect condylar length and/or the occlusion, which could, in turn, distort data gathered for the study.

The records utilized included clinical history to evaluate TMJ dysfunction, clinical examination, lateral cephalometric radiograph in centric occlusion, and orthopantomogram, articulator mounted study casts in centric relation. Cephalometric measurements made were the mandibular plane angle (GoGn-SN), anterior facial height, posterior facial height, $PFH \times 100 / AFH$ (Jarabak's ratio).

Irreversible hydrocolloid material was used to make the impression. The impressions were poured in white dental stone. The cast was trimmed without allowing water to splash onto its tooth surfaces, which could partially dissolve them.

A single operator was involved in all the clinical and laboratory experiments. A single arbitrary face bow and SAM[®] 2P articulator were used for mounting the stone casts (Velmix; Kerr[®] Manufacturing Co., Romulus, MI, USA) with the CR wax records (DeLar Bite Registration Wax; DeLar[®] Corporation, Lake Oswego, OR, USA). Horizontal and vertical CD was evaluated using a single MPI and MI wax records (Moyco[®] Industries Inc., Philadelphia, PA, USA).

Maxillary cast was mounted in the articulator using the arbitrary face bow. The mandibular casts were mounted to the maxillary using a modified Roth power centric bite registration record. The MI records were obtained before CR registration, by asking the patient to bite firmly with the teeth in MI. After being chilled in ice water, record accuracy was checked in the mouth. For CR registration,

Roth's power centric technique was performed immediately after neuromuscular deprogramming with the patient relaxed and reclined at 45°. Two cotton rolls were interposed between the dental arches for a minimum of 10 min. CR bite registration was performed in two stages. With the softened wax, the anterior section was obtained by guiding the mandible during closure to avoid protrusion. The cusps responsible for premature inter-arch contact were maintained 2 mm apart. Next, the anterior wax was hardened in ice water and then interposed between the arches simultaneously with the posterior softened wax section to accomplish the registration. The mandible was guided during the closure, and when the anterior teeth fit into the corresponding anterior wax indentations, the patient was asked to bite firmly. With this technique, as the posterior wax section was softened, muscular strength helped to adjust the vertical intra-articular condylar position.^{20,21}

Each MPI recording was measured 3 times. The average of the 2 of 3 closest measurements was recorded.

Statistical Analysis

A statistical report was created from MPI measurements to compare the magnitude and direction of the condylar axis movement from CR to CO in hypodivergent (Group 1) and hyperdivergent (Group 2) groups. A Student's *t*-test was performed for comparison of the magnitude of MPI measurements.

RESULTS

X indicates the horizontal displacement of condyles. Positive values indicate protrusive movement of condyles, and negative values indicate retrusive condylar movement.

Z indicates the vertical displacement of condyles. Positive values indicate the superior displacement of condyles and Slavicek terms it as compression. Negative values indicate the inferior displacement of condyles, Slavicek terms it as a distraction.

Y indicates transverse condylar movement. Positive values indicate left the condylar movement, and negative values indicate condylar movement to the right side.

Table 1 summarizes the comparison between the 2 groups in X, Z, and Y coordinates.

Anteroposterior Dimension

Figure 1 shows mean condylar shift in X axis for Group 2 was 1.13 mm, which was 1.7 times greater than corresponding 0.65 mm for hypodivergent group, which was significant statistically.

Table 1 shows the comparison between the two groups. The mean forward movement of condyle was 0.95 mm and 0.63 mm for Groups 1 and 2, respectively, which was not significant statistically.

Figure 2 shows mean backward movement of condyle was -0.44 mm for Group 1 and -1.59 mm for Group 2 which was statistically significant (*P* < 0.0001). Thus, condyles in

Table 1: Mean values for the condylar deflection in three-dimensional for hypodivergent and hyperdivergent facial type

CD	Mean±SD		T value, df	P value
	Group 1	Group 2		
X (-)	0.44±0.38	1.53±0.95	6.762, 78	0.0001
X (+)	0.95±0.91	0.63±0.84	1.407, 58	0.1649
Z (-)	1.25±0.61	1.59±0.80	2.461, 108	0.0154
Z (+)	0.37±0.46	0.66±1.06	1.062, 28	0.2975
(X)	0.65±0.70	1.13±1.00	3.287, 138	0.0013
(Y)	0.39±0.41	0.38±0.19	0.1291, 68	0.8976
(Z)	0.99±0.70	1.46±0.89	3.386, 138	0.0009

SD: Standard deviation, CD: Condylar displacement

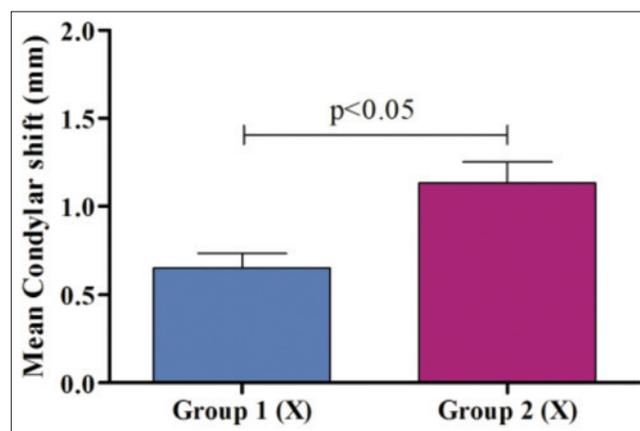


Figure 1: A comparison of total horizontal condylar displacement for the 2 groups

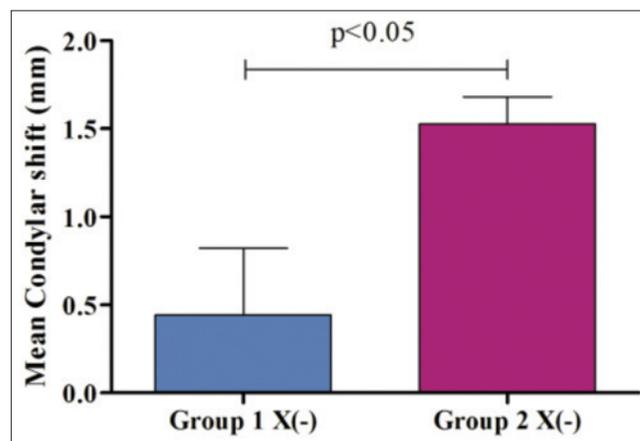


Figure 2: A comparison of backward condylar displacement for the 2 groups

hyperdivergent group, on average, were deflected backward 3.6 times greater than hypodivergent group.

Vertical Dimension

Figure 3 shows mean vertical displacement (Z axis) for Group 2 was 1.46 mm, which was 1.3 times greater than corresponding 0.99 mm for Group 1, the difference was significant statistically (Table 1).

Figure 4 shows mean distraction for Group 1 was -1.25 mm as compared to corresponding -1.59 mm for Group 2, which was significant statistically.

The mean compression was 0.37 mm for Group 1 as compared to 0.66 mm for Group 2, which was not statistically significant.

DISCUSSION

Various studies^{8-11,22-24} have shown that association exists between the internal derangement and facial morphology. These studies serve to illustrate identified

association between facial morphology and localized TMJ disturbances. The orthodontist should be aware that young growing individuals experiencing TMJ internal derangement may not have significant signs and symptoms at an early age; later as they grow older, they may become symptomatic.²²

Ideally, although CR and CO should be coincident, this is not frequently seen even in subjects with normal occlusion as they most often exhibit a small discrepancy.¹

To overcome the drawbacks of radiographs and other imaging techniques, articulator mounted models have been advocated by many clinicians to study the relationship of the condyle to the glenoid fossa.^{1,17,25-27}

Authors, such as Roth,^{1,26,27} Slavicek,^{17,28} Okeson,²⁵ Dawson,³⁰ Utt²⁹ Rosneer, and Goldberg,³¹ have advocated the use of diagnostic study models mounted in CR to make a complete diagnosis and establish the goal of optimal functional occlusion. Okeson advocates the use of mounted casts since the protective reflexes of the neuromuscular system may prevent detection of interferences clinically.²⁵

Instruments such as the MPI are valuable adjuncts to diagnostic casts mounted on an articulator as it provides information concerning changes between CO and CR at the level of the condyles.^{28,29} The MPI is used to measure the CR-CO discrepancy as the assessment is done in three-dimensional of space.^{27,28} The MPI allows for a simple and non-invasive technique for comparing clinically captured CR and CO position through the displacement of the opening and closing axis position of the patient. The MPI represents the opening and closing axis of the mandible that passes through both condyles; therefore, movement of the axis represents the movement of the condyles.

The “power centric” interocclusal registration as proposed by Roth was recorded in this study.¹ This technique makes use of the patient’s own power closure muscles to seat the condyles as closely as possible to the CR with the condyles centered transversely and seated against the articular disks anteriorly and superiorly within the fossa. This method eliminates the operator error often encountered in attempts to manipulate the patient’s mandible to CR. Since the patient is applying all the pressure, it is less likely to exceed the physiologic limits of the system.

Reproducibility of Roth powers centric bite registration technique was investigated by Wood and Elliott²⁰ and by Schmitt, Kulbersh *et al.*³² and by Wood and Elliott.³³ The result showed that there were no statistically significant differences ($P > 0.05$) within each operator or between

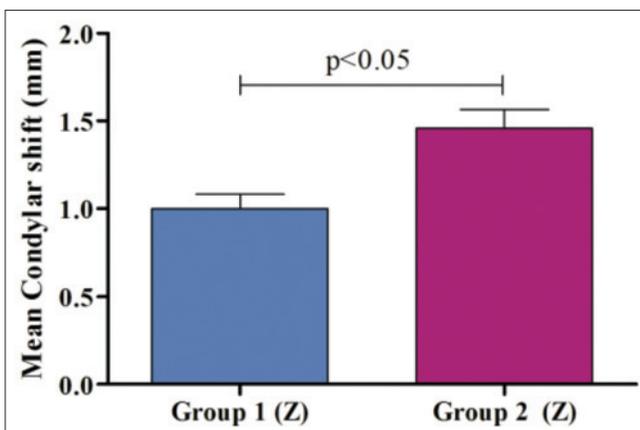


Figure 3: A comparison of total vertical condylar displacement for the 2 groups

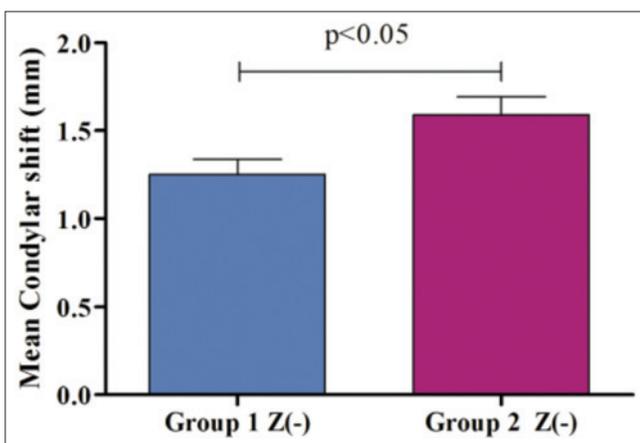


Figure 4: A comparison of condylar distraction for the 2 groups

operators; the Roth CR bite registration with Blue Delar wax is highly reproducible.

Wood and Korne³³ showed that recording condylar displacement with MPI device is highly reproducible.

Horizontal Condylar Displacement

The data showed that the hyperdivergent subjects had greater displacement of the condyle in the horizontal dimensions. Mean condylar shift in X-axis for the hyperdivergent group was 1.13 mm, which was 1.7 times greater than corresponding 0.65 mm for hypodivergent group which was statistically significant.

The displacement of condyle in X-axis can be subdivided into forward (+X) and backward (-X) components. The mean forward movement of condyle (+X) was 0.95 mm and 0.63 mm for Groups 1 and 2, respectively, which was not significant statistically. This was the only parameter in which greater displacement was seen in hypodivergent group. This finding is in contrast with the Girardot's²⁰ study where he found more forward displacement in the hyperdivergent group. The mean backward movement of condyle (-X) was -0.44 mm for Group 1 and -1.53 mm for Group 2 which was statistically significant ($P < 0.001$). Thus, condyles in the hyperdivergent group, on average, were positioned backward 3.6 times greater than hypodivergent group. Of all the dimensions totaled and compared, this one showed the greatest difference between the 2 groups. Thus, one might suspect the amount of backward condylar displacement for the hyperdivergent patient, on average, will be about thrice that of the hypodivergent patient. When the 2 groups were compared concerning anterior or posterior deflection of the condyle, it was found that the greatest movement occurred to the posterior in the hyperdivergent group.

This finding was similar to Girardot's data.¹¹ Girardot's study showed a similar overall and posterior displacement in the horizontal plane. In Girardot's study, backward displacement in the hyperdivergent group was 1.6 times greater than backward displacement recorded for hypodivergent group.

This supports Roth's²⁶ concept of a molar fulcrum and may be important since posterior displacement of the condyle away from the eminence would theoretically compromise joint stability and/or function. It has been hypothesized²⁴ that displacement of the condyle away from the eminence may be detrimental to joint health and/or stability since there is subsequent loss of juxtaposition between the condyle, disc, and eminence. The posterior aspect of the mandibular fossa is quite thin and apparently not meant for bearing stress. It has been demonstrated that when an occlusal condition causes a condyle to be positioned

posterior to musculoskeletally stable position, the posterior border of the disc can be thinned.

Vertical Dimension

Mean vertical displacement (Z axis) for Group 2 was 1.46 mm, which was 1.5 times greater than corresponding 0.99 mm for Group 1. The difference between two groups is significant statistically, did show more displacement in the vertical plane in the hyperdivergent group than in the hypodivergent group.

Girardot's study¹¹ reported a similar difference between hyperdivergent and hypodivergent group, but the mean vertical displacement was higher in his study for both groups. The mean vertical condylar displacement in the hyperdivergent group was 1.7 mm and 1.2 mm in hypodivergent group. Higher mean displacement reported by Girardot can be attributed to the difference in subject selection.

Girardot did not exclude the subject if there had been a restorative treatment or orthodontic treatment or patient had Class II div2 malocclusion. Orthodontic treatment mechanics such as cervical headgear and long Class II elastics that cause extrusion of molars will make the fulcrum worse.^{1,26} These factors would distort the data gathered from these subjects showing greater condylar distraction from CR to MI.

Stringert and Worms¹⁸ found hyperdivergent facial types to have a greater frequency of internal derangement than hypodivergent facial types. They suggested this might be a consequence of degenerative changes within the TMJ or as they said, "for some reason, persons with hyperdivergent characteristics are more prone to internal derangements."

The displacement of the condyle in the vertical plane can be subdivided into compression (+) and distraction (-) components.

The mean distraction for Group 1 was -1.25 mm as compared to corresponding -1.59 mm for Group 2, this was significant statistically. The mean compression was 0.37 mm for Group 1 as compared to 0.66 mm for Group 2, which was not statistically significant.

Ideally, in the present study, it would have been better if all subjects had worn a mandibular repositioning splint for 6 months prior obtaining CR records.

Medio-Lateral Dimension

The mean displacement between two groups was almost the same. Mean transverse displacement for Group 1 was 0.39 mm and for Group 2 was 0.43 mm. Thus, displacement in both the groups was minimal and below the 0.5 value. Utt²⁸ in his study

has indicated that values >0.5 mm in the Y plane is clinically significant. Since the subjects in the study were asymptomatic, this would explain for decreased value in Y plane.

The comparative differences in condylar shift between two facial types became even more conspicuous when measuring the number of condyles that were displaced to the extreme (2 mm or more). The number of hyperdivergent joints shifting 2 mm or more in the horizontal plane (X) numbered 15 as compared to 3 in hypodivergent. In the vertical plane (Z), 6 condyles in hypodivergent group were displaced to extreme as compared to 15 in the hyperdivergent group. Nine joints in hyperdivergent group only show 2 mm or more displacement in both horizontal and vertical plane. Since the subjects in this study comprised of asymptomatic individuals, the majority of them had MPI readings <2 mm. It was stated that subjects with 2 mm or more displacement should undergo muscle deprogramming prior to active Orthodontic treatment.²⁹

For the orthodontist desiring to treat to the upward and forward or seated condylar position, this study is helpful because it shows most pretreatment patients will have a centric relation to centric occlusion discrepancy. The information gathered from mounted casts can have a profound effect on treatment planning. The data gleaned from this study is particularly valuable because it indicates the clinician can generally assume condylar distractions will be much greater in hyperdivergent facial patterns than in hypodivergent ones. Certainly each case must be evaluated separately, but the clinician is better prepared for diagnosis with this knowledge.

CONCLUSION

It was hypothesized that hyperdivergent group would exhibit greater condylar displacement than the hypodivergent group. The findings of this study demonstrated significantly greater condylar displacement for the hyperdivergent group in the horizontal dimension. In vertical dimension condylar distraction was 1.5 times greater in the hyperdivergent group. There was no significant difference between the two groups in transverse dimension.

Therefore, if condylar displacement is not considered during assessment of orthodontic cases, the risk of misdiagnosis is high, being significantly higher in patients with the hyper divergent facial pattern.

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How to cite this article: Chandra S, Shahi AK. Centric Relation in Asymptomatic Hypodivergent and Hyperdivergent Skeletal Pattern. *Int J Sci Stud* 2016;3(11):6-12.

Source of Support: Nil, **Conflict of Interest:** None declared.

Clinical Assessment of Airway and Its Correlation with Laryngoscopy Grading

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Abstract

Background: Difficult intubation is a major concern for the anesthesiologist and becomes more serious when it is unexpected. The preoperative assessment for recognition of difficult airway in advance is the best method of preventing damage caused by the inability to maintain the airway.

Aim: This study was carried out to evaluate the efficacy of clinical tests which can predict the difficult laryngoscopy and intubation in patients undergoing elective surgery requiring general anesthesia. Then to compare and correlate the laryngoscopic grading obtained with the findings of airway assessment tests.

Materials and Methods: A total 250 adult patients of age group 18-70 years of either sex of ASA Class I and II, undergoing elective surgery for various procedures requiring general anesthesia with endotracheal intubation were included in this study. Preclinical evaluation is carried out by measuring body mass index, modified Mallampati test (Samsoon and Young) and Patils Thyromental test. These tests were then correlated with laryngoscopic grading as per Cormack and Lehane. Data are presented as the mean \pm standard deviation. Fisher's exact test and the Chi-square test were applied for the statistical analysis. Results having $P < 0.05$ were considered statistically significant.

Result: No method either individual or in combination with other, identifies all cases of difficult intubation. Modified Mallampati test a thyromental test were significantly correlate with laryngoscopic grading for difficult intubation.

Key words: Anaesthesia, Difficult intubation, Cormack Lehane Laryngoscopy Grading, Modified Mallampati test, Patils Thyromental Test

INTRODUCTION

The most vital element providing functional respiration is the airway. Difficulty in introducing the endotracheal tube through the laryngeal aperture is a major threat for an anesthetist. Failure to identify potential airway problems can lead to a paralyzed patient who can neither be ventilated nor intubated. Airway compromise is the most common cause of death or serious injury in anesthesia. Inadequate ventilation, esophageal intubation, and difficult tracheal intubation are the three main causes of serious injury or deaths that were identified in closed

claim analysis of American society of anaesthetists.¹ Prediction of difficult intubation is not a problem in obvious adverse orofacial and cervical anatomical factors such as short muscular neck, receding mandible, protruding upper incisor, temporomandibular joint arthritis or trismus, long high arched palate and increased alveolar mental distance or pathological factors such as ankylosing spondylitis of cervical spine, post burn neck contracture, fractures of mandible, maxilla and cervical spine, acromegaly, goiter, neoplasm of pharynx and larynx or congenital abnormalities such as micrognathia, pierre robin syndrome, cleft lip, and palate.^{2,3} However, several patients of normal appearance unexpectedly present great difficulty at intubation. Radiological techniques for prediction of difficult intubation are time consuming, costly and as such cannot be routinely employed.

So, the need for anatomical factors that can predict difficult intubation which are quick, easy, accurate and

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Month of Submission : 12-2015
 Month of Peer Review : 01-2016
 Month of Acceptance : 01-2016
 Month of Publishing : 02-2016

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can be routinely employed. Airway assessment, availability of resources (including personnel and equipment), and a preformulated plan have also lowered the incidence for difficult intubation.

The existing tests as Mallampati grading, Patils thyromental grading have been shown in various studies to have high false positive rate (when used alone).^{4,5} Thus, the aim of this study is to combine the reading of two tests to improve the predictability of difficult intubation.

MATERIALS AND METHODS

This study was conducted in the Department of Anesthesiology, NSCB Medical College Jabalpur. It involves the airway assessment of 250 patients of age group 18 years to 70 years of either sex, and who had to undergo either routine or emergency procedure requiring endotracheal intubation. Patients having obvious adverse anatomical, pathology or congenital factors are excluded from the study. Data were collected in a standard form and following main features of the patient were noted age, weight, body mass index (BMI), thyromental distance, oropharyngeal classification and laryngoscopic grading. Modified Mallampati test and Patils thyromental test were performed for airway evaluation. The thyromental distance was measured from the thyroid notch and mental prominence with neck fully extended. The measurement was made by a ruler scale.

These airway tests are then correlated to laryngoscopic grading (of Cormack and Lehane) using Macintosh laryngoscope of blade size 3. In this study, difficult endotracheal intubation is define as less than adequate exposure by direct laryngoscopy, i.e., Grade III and Grade IV, while Grade I and Grade II are considered adequate. The direct laryngoscopy is done in the sniffing position. (i.e., neck flexed and atlanto occipital joint extended).

To minimize uncertainty and inaccuracy of numerical grading system, schematic diagrams are provided for classification of the view of the oropharynx and of glottis, according to Mallampati as modified by Somsoon and a Young⁶ and to Cormack and Lehane classifications⁷ in Figures 1 and 2.

Same induction and intubation protocol was used in all patients. Various comparisons are made according to the data collected.

Statistics

Data are presented as the mean ± standard deviation and Fisher’s exact *t*-test and the Chi-square test were applied

in the statistical analysis. Results with *P* < 0.05 were considered statistically significant.

The statistical significance of the data was analyzed to assess the usefulness of these two anatomical factors in predicting the level of difficulty encountered during laryngoscopy and intubation and comparison of the efficacy of two factors combined with single factor.

RESULTS

The observations are based on the study conducted on 250 patients who required general anesthesia for their surgery.

Demographic data regarding age, sex, weight and height of the patients were comparable.

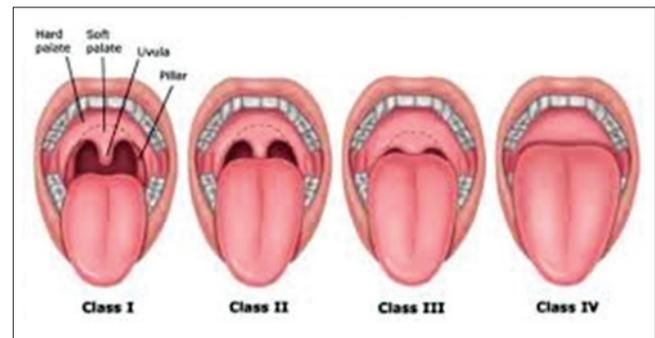


Figure 1: modified Mallampati classification

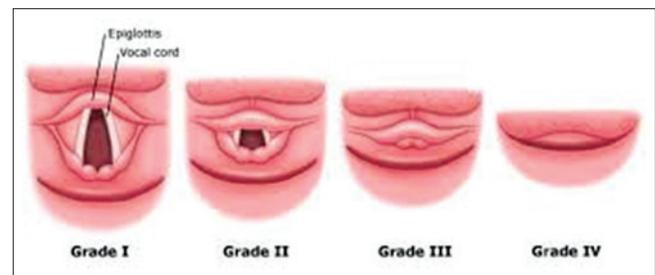


Figure 2: Cormack lahane laryngoscopic grading

Table 1: Distribution of patients according to BMI and thyromental distance

Parameter	No of patient	Total
BMI		250
18-25	234	
26-30	11	
31-35	5	
Thyromental distance		250
>6.5	167	
6.5-6	68	
<6.0	15	

BMI: Body mass index

Table 1 shows that 234 patients were of 18-25 (kg/mt²) BMI group and only 5 patients were in 31-35 (kg/mt²) BMI group. Out of 250 patients only 15 patients had thyromental distance of <6.0 cm.

Table 2 shows that out of 250, 172 patients had class I and 33 patients had class III airway, while according to Laryngoscopy grading 190 patients were in grade I and 11 patients in grade III.

According to table 3, 226 patients belong to BMI group of 18-25 (kg/mt²) which were categorised as easy, while only 4 patients in BMI group of 31-35 (kg/mt²) were in the easy subgroup of laryngoscopic grading.

According to Table 4, of 33 Class III airway patients, 2 patients had Grade I laryngoscopic view, whereas 8 patients had Grade III laryngoscopic view. Chi-square value was 118.63. Degree of freedom was 6 $P < 0.001$ (highly significant).

According to Table 5, of 68 patients of 6-6.5 cm thyromental distance group 46 patients had Grade I

laryngoscopic view while only 2 patients had Grade III laryngoscopic view. Chi-square value was 123.19. Degree of freedom was 4 $P < 0.001$ (highly significant). Table 6 shows statistical analysis of both tests.

DISCUSSION

Difficult intubation is a major concern for the anesthetist and becomes more serious when it is unexpected. Difficult laryngoscopy and intubation continue to cause morbidity and mortality associated with anesthesia. The reason for difficult laryngoscopies are not completely identified. Although the incident of difficult and failed tracheal intubation is comparatively low, unexpected difficulties and poorly managed situation may produce life-threatening conditions such as cerebral damage or even death.

It is the unexpected difficult intubation that leads to disaster. Predicting problem at intubation should not be difficult where there is obvious pathology involving neck, maxilla-facial, pharyngeal, and laryngeal structures, whether or not this is associated with specific medical condition or congenital syndromes. However, several patients of apparently normal appearance unexpectedly present great difficulties at intubation. A study of anatomical factors in these patients should improve ability to predict and manage a potential failed intubation. The importance must be stressed of correct positioning of head and neck during direct laryngoscopy in order to achieve alignment of axis of mouth, pharynx, and larynx to permit tracheal intubation. The position of flexion of lower cervical spine

Table 2: Distribution of patients according to modified Mallampati class and Cormack and Lehane grading of laryngoscopy

Parameter	I	II	III	IV	Total
Class of airway	172	43	33	2	250
Laryngoscopy grading	190	49	11	0	250

Table 3: Relationship of BMI distribution and grade of laryngoscopy

BMI (kg/mt ²)	No. of patients laryngoscopy grading		Total
	Easy I and II	Difficult III and IV	
18-25	226	8	234
26-30	9	2	11
31-35	4	1	5
Total	239	11	250

BMI: Body mass index

Table 4: Relationship between class of airway and grade of laryngoscopy

Class of airway	No. of patients	Grade of laryngoscopy (no. of patients)				IV
		I	II	III		
Class I	172	157	15	0	0	
Class II	43	30	10	3	0	
Class III	33	2	23	8	0	
Class IV	2	1	1	0	0	
Total	250	190	49	11	0	

Table 5: Relationship of thyromental distance and laryngoscopy grading

Thyromental distance (cm)	No. of patients	No. of patients on laryngoscopy grading			
		I	II	III	IV
>6.5	167	138	29	0	0
6-6.5	68	46	20	2	0
<6.0	15	5	1	9	0
Total	250	189	50	11	0

Table 6: Predictive value of Airway classification and Thyromental distance

Statistical analysis	Airway classification (%)	Thyromental distance (%)
Sensitivity	72.72	100
Specificity	88.0	69.87
PPV	22.85	19.25
FPR	11.29	30.12
FNR	27.27	0

PPV: Positive predictive value, FPR: False Positive Rate, FNR – False Negative Rate

combined with extension of the head at atlanto-occipital joint has been well described.^{8,9}

The incident of airway difficulty in the general surgical population varies greatly depending on its degree. A Grades II or III laryngoscopic view requiring multiple attempts and or blades is relatively common and occurs in 100-1800 of 10000 patient or 1-8%. As the degree of difficulty increase to definite Grade III laryngoscopic view, then the incidence is generally slightly less and ranges from 100 to 400 of 10000 patients or 1-4%. The incidence of failed tracheal intubation is still less and ranges from 5 to 35 of 10000 patients or 0.05% to 0.35%; the high and low ends of this range are associated with obstetric and other surgical patients, respectively.³

It is clear that unexpected airway difficulty occurs commonly, that some cases of anticipated difficulty are simple to manage, and that better routine predictors of airway difficulty are needed.

There was small number of patients in whom difficulty in laryngoscopy and intubation is encountered even though they are not affected by any of these conditions. Radiographic technique to measure posterior depth of mandible or atlanto-occipital distance are expensive, time consuming and as such cannot be routinely employed.^{10,11} It is therefore desirable to develop a clinical method which is applicable and objective for detecting cases in whom laryngoscopy and intubation is likely to be difficult. Various preoperative methods have been described to detect difficulty in intubation such as modified Mallampati test, Patils Thyromental distance test and Wilson's score.

This study is conducted on 250 adult patient admitted for various surgical procedure who required endotracheal intubation for general anesthesia, to evaluate the efficacy of two pre operative clinical tests i.e., modified Mallampati test and Patils thyromental distance as anatomical factors in predicting difficult laryngoscopy and endotracheal intubation by using both tests in combination.

The present study showed no statistical significance between age, sex and difficulty in laryngoscopy. Similar studies showed no significant difference in age and sex ratio of patients in two groups of easy and difficult laryngoscopies.^{12,13}

This study showed significant relationship between BMI and difficulty in laryngoscopy. This correlated well with other studies.^{12,13} The most important factors determining ease of examination was the posterior depth of mandible.¹⁴ Other factors of importance were an increase in the anterior depth of mandible and reduction in the distance between the occiput and spinous process of c1 vertebra.¹⁰

Mallampati hypothesized that the size of the base of the tongue, as assessed by visualization of oropharyngeal structures could be used as a clinical test to predict subsequent difficulty at laryngoscopy and intubation. When tongue is maximally protruded in seated patient, there is concealment of faucial pillars and uvula by the base of the tongue and if the base of tongue is disproportionately large, it overshadows the larynx, rendering the exposure of the larynx by direct laryngoscopy poor and difficult.¹⁵

Evaluation of difficulty in laryngoscopy was carried out on the basis of gradation criteria described by Cormack and Lehane.⁷ Grades I and II were considered adequate exposure (easy laryngoscopies) and Grades III and IV inadequate exposure (difficult laryngoscopies).

In this study, there were 95.6% of patients who had easy laryngoscopic grading while there were 11% of patients who had difficult laryngoscopic grading. The reason for wide variation in reported incidence of difficult laryngoscopy may be related to confusion regarding grading system of view documented by anesthesiologist, i.e., whether it was initial view or best view on laryngoscopy.¹⁶ It is seen that external laryngeal pressure, changing laryngoscope blades and changing neck position can alter the view at laryngoscopy.^{3,12}

In our study, thyromental distance a of ≤ 6 cm was considered to predict a difficult laryngoscopy and obtained a sensitivity of 100% and specificity of 69.87%. This distance reflects the ease of displacement of the tongue by the laryngoscope blade by giving an estimate of mandibular space.

Difference in proportion may be because of different methods of measuring thyromental distance followed in these studies. There is variation in measurement of thyromental distance because of inside versus outside of mentum and full extension of neck versus neutral head position. Lewis *et al.*¹⁷ observed that it is preferable to perform the test in the sitting position with the head in extension and distance measured from the inside of the mentum to thyroid cartilage. There is much variation in the size of fat pad on the bony point of the skin (outer mentum).

In this study, comparative analysis of class of airway and level of difficulty in laryngoscopy as predicted, the incidence of difficult laryngoscopy was extremely high in patients with Class III or IV airway and very low in patients with Class I or II airway. Statistically, there was significant correlation between airway class and laryngoscopy grades.

The modified Mallampati test has high false positive rate of 11.29% and high false negative rate of 27.27%. In this study,

thyromental distance versus difficulty in laryngoscopy, the sensitivity, specificity and positive predictive value was found out to be 100%, 69.87% and 19.25% respectively. Our result also in corroboration with other studies.^{13,14,18,19}

In this study, comparative analysis of thyromental distance and level of difficulty in laryngoscopy showed that incidence of difficult laryngoscopy was extremely high in patients with distance of 6 cm or less and very low in patients with thyromental distance more than 6.5 cm. statistically, there was significant correlation between the thyromental distance and laryngoscopy grades.

This test also has a high false positive rate of 30.12%.

When both the thyromental distance test and modified Mallampati test are used in combination in the patient, the specificity for detection of cases of difficult laryngoscopy has greatly increased as compared to the results of single test and therefore the false positive rate will also decrease.

Analysis of the present study showed that when both tests are positive in a patients, is taken as predictor of difficult intubation, specificity has greatly improved and false positive rate has decrease significantly.

CONCLUSION

Thus, we concluded that there was correlation between BMI and difficulty in laryngoscopic view. When the two tests are used in combination, then specificity increase, sensitivity remain same, false positive results decrease and false negative results increase. Neither the single test nor the combination of two tests is 100% sensitive or specific. These predictive tests either used alone or in combination can be used as useful adjunct to the pre anesthetic checkup to detect those cases in whom laryngoscopy and intubation

is likely to be difficult but they should not be relied on absolutely.

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How to cite this article: Narang N, Ashahiya ID, Panwar S, Mahendra R. Clinical Assessment of Airway and Its Correlation with Laryngoscopy Grading. *Int J Sci Stud* 2016;3(11):13-17.

Source of Support: Nil, **Conflict of Interest:** None declared.

Pulmonary Function in Type 2 Diabetes Mellitus: Correlation with Body Mass Index and Glycemic Control

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Abstract

Introduction: The lung with its large surface area and extensive vasculature is postulated to be one of the “target organs” for damage in diabetes mellitus (DM). However, changes in lung function occurring in Type 2 Diabetes Mellitus (Type 2 DM) have not been well-characterized in previous studies.

Purpose: To study the pulmonary function abnormalities in patients with Type 2 DM and to find correlations with duration, body mass index, glycemic control, and nephropathy.

Materials and Methods: This prospective study was conducted among Type 2 DM patients attending the diabetic clinic of a medical college hospital. 124 non-smokers with Type 2 DM, not suffering from respiratory allergies and who did not have any acute or chronic pulmonary diseases were included. Body mass index (BMI) was calculated for all patients. Glycemic control was assessed by measuring glycosylated hemoglobin (serum HBA1c). Spirometry and measurement of diffusing capacity by single-breath method (DLCO-SB) was done in all the patients. The presence of diabetic glomerulopathy was determined by checking urine samples for microalbuminuria in a subset of patients.

Patients were divided into subgroups based on BMI, HBA1c levels, duration of DM and data analyzed using ANOVA and Student's unpaired *t*-test. SPSS version 17.0 was used for statistical analysis.

Results: A statistically significant reduction was seen in diffusing capacity with increasing duration of DM ($P < 0.05$). Statistically insignificant reductions were observed in forced expired volume in 1 s (FEV1), forced vital capacity (FVC), peak expiratory flow rate, (PEFR) forced expiratory flow (FEF 25%-75%) in patients with >20 years of DM in comparison to their counterparts with <10 years of DM; FEV1/FVC was found to be unimpaired in DM.

Conclusions: Type 2 DM is associated with a reduction in diffusing capacity with increasing duration of disease. This reduction was not limited only to patients with microalbuminuria. BMI and level of glycemic control did not affect lung functions in diabetic patients.

Key words: Diffusing capacity, Pulmonary function, Type 2 diabetes mellitus

INTRODUCTION

Diabetes mellitus (DM) is an important universal public health problem. The World Health Organization estimates

that about 347 million people worldwide have diabetes with a global average prevalence of approximately 10%.¹ India is witnessing an epidemic of DM and is referred to as the diabetes capital of the world. It is estimated that by 2025, there will be nearly 70 million people with diabetes in India, meaning, every 5th diabetic in the world would be an Indian.²

DM is known to cause widespread metabolic, hormonal and microvascular abnormalities as well as disturbances in the functioning of many organ systems such as the kidneys, retinae, nerves, and the cardiovascular system.³

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Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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The presence of abundant connective tissue in the lung and an extensive microcirculation raises the possibility that the lung may be an important “target organ” in diabetic patients. However, studies evaluating lung functions in Type 2 DM in the past have observed conflicting results with few reporting only minimal changes and others observing marked (and possibly clinically significant) abnormalities in various lung function parameters.

The underlying mechanism appears to be a microangiopathy brought in by the non-enzymatic glycosylation of various scleroproteins that form the matrix of the lung.³ There have been several studies putting forth many reasons for the impaired lung function seen in diabetics.⁴⁻⁸ One study by Chance *et al.* revealed that diabetic microangiopathy can involve alveolar tissue and capillaries in the body, leading to restriction of lung volume and alveolar gas transport, as was recorded by the reduced diffusing capacity of the lung for carbon monoxide, as well as its components: membrane diffusing capacity and pulmonary capillary blood volume.⁹ Irfan *et al.* reported in their study that diabetic patients had significant hypertriglyceridemia and concluded that dyslipidemia might have played a role in the pathogenesis of decreased lung functions in diabetic patients.¹⁰

The present study attempts to assess the lung function in Indian patients with Type 2 DM and to correlate their lung function with duration of DM, glycemic control, body mass index (BMI), and diabetic nephropathy, keeping in mind, the conflicting observations reported from studies carried out in this area earlier.

MATERIALS AND METHODS

The study was conducted over a period of 2-months among a total of 124 patients with Type 2 DM attending the diabetic clinic of a medical college hospital using convenient sampling technique. Approval was taken from the Institutional Ethics Committee and was as per the Helsinki Declaration.

Adults with Type 2 DM as diagnosed by the treating physician, having no respiratory symptoms at the time of enrollment and willing to participate were included after taking a written informed consent. Health status was decided by a detailed history followed by a thorough clinical examination. Smokers, patients with respiratory allergies and patients suffering from acute or chronic pulmonary diseases were excluded from the study.

Anthropometric Measurements

Height and weight of all subjects were recorded and BMI calculated as weight (kg) divided by height (meters) squared.

Biochemical Investigations

Glycemic status of subjects was determined by:

1. Fasting blood sugar by glucose oxidase and peroxide method after 12 h of fast
2. Postprandial blood sugar by glucose oxidase and peroxide method after 2 h of meal
3. Glycosylated hemoglobin (HbA1c) using high-performance liquid chromatography.

In addition, a urine sample was tested for microalbuminuria as a surrogate marker for diabetic nephropathy in a subset of patients ($n = 80$).

Pulmonary Function Test and Lung Diffusing Capacity (DLCO)

Pulmonary function parameters recorded included forced vital capacity (FVC), forced expired volume in 1 s (FEV1), peak expiratory flow rate (PEFR), FEV1/FVC ratio and forced expiratory flow (FEF 25-75%) which were measured using the Collins Eagle Spirometer (Ferraris Respiratory, UK). Spirometry was performed using the closed circuit method by first asking the subjects to inhale completely and rapidly with a pause of <1 s at total lung capacity (TLC) followed by a “blast” of exhalation which was continued until the end of test criteria were met. Acceptability and repeatability criteria as laid out in the ATS/ERS document on standardization of lung function testing were strictly followed.¹¹ The variables were recorded both in absolute volume as well as percent predicted based on regression equations.

DLCO was measured using the single-breath method by the same system using 0.3% CO, 0.3% CH₄, 21% O₂ and balance N₂ by volume.

Subgroups

For the purpose of data analysis the BMI, HBA1c, duration of diabetes were divided into the following subgroups:

- The BMI is stratified into:
 - <18.5 underweight
 - 18.5-24.9 normal
 - 25-29.9 overweight
 - ≥ 30 obese
- HBA1C is subdivided into:
 - 6-7.5-good control
 - >7.5-poor control
- Duration of diabetes is further classified as:
 - <10 years
 - 10-20 years
 - >20 years

Statistical Analysis

Results were tabulated using Microsoft Excel 2007 and analyzed using descriptive statistics. Further statistical evaluation of the data was performed using the ANOVA

and student's unpaired *t*-test. A statistical package, SPSS version 17.0 was used to do the analysis with $P < 0.05$ considered as statistically significant.

RESULTS

A total of 124 patients were enrolled in the present study, with mean age of the study population being 56.57 ± 11.58 years (Range: 20-74 years). The male:female ratio was found to be 61:63. The average duration of DM was found to be 7.69 years. The mean body mass index and HBA1c of the study group were 25.31 ± 3.21 and 8.175 ± 1.6 , respectively (Table 1).

Table 2 summarizes the correlation between the lung function parameters and duration of DM. All pulmonary function parameters except FEV1/FVC, that is, FEV1, FVC, PEFR, FEF 25-75%, and DLCO were reduced in patients with duration of diabetes >20 years as compared to diabetics with duration <10 years. However, only one parameter - diffusing capacity shows a statistically significant decline ($P = 0.008$) with increasing duration of disease. The reduction observed in other pulmonary function parameters was statistically insignificant ($P > 0.05$).

Table 1: Demographics of study population

Parameter (units)	Frequency (percent)
Sex	
Male	61 (49.2)
Female	63 (50.8)
BMI (kg/m ²)	
<18.5	-
18.5-24.9	57 (45.96)
25-29.9	59 (47.58)
>30	8 (6.45)
HBA1c (%)	
6-7.5	58 (46.77)
>7.5	66 (53.23)
Disease duration (years)	
1-10	80 (64.51)
11-20	42 (33.87)
>20	2 (1.61)
Treatment	
Oral hypoglycemic agents	92 (74.1)
Insulin	32 (25.8)

BMI: Body mass index

Table 3 illustrates the lack of correlation between body mass index and pulmonary function parameters observed in the present study.

No correlation was observed between level of glycemic control (HBA1c) and pulmonary function parameters as shown in Table 4.

Microalbuminuria and its relationship with pulmonary function parameters are shown in Table 5. Patients with microalbuminuria ($n = 80$) did not show any significant deviations when their lung functions were compared against predicted values.

DISCUSSION

Studies analyzing pulmonary function in Type 2 DM patients have observed mixed results, with some studies observing minimal changes and others showing abnormalities in lung volumes, pulmonary mechanics, and diffusing capacity. A meta-analysis of pulmonary function in diabetes by Bram van den Borst *et al.* concluded that there is a modest but statistically significant restrictive impairment in lung function irrespective of BMI, smoking, diabetes duration, and glycemic control.⁶ The Framingham heart study which involved 3254 participants showed that in subjects with diabetes there is a larger reduction in FVC than FEV1 and the larger FEV1/FVC values suggests a restrictive physiology.¹² Reduced lung volumes and airflow limitation, the severity of which relates to glycemic control were the key findings of the Fremantle Diabetes Study, one of the largest community-based prospective study in Western Australia involving Type 2 diabetics.⁵ Studies in Asian population have also observed a predominantly restrictive impairment.^{10,13-15} However, Sinha *et al.* showed that except DLCO, there were no differences in other pulmonary function parameters like FEV1, FVC, and PEFR in Type 2 diabetic patients as compared to their control group.¹⁶ Benbassat *et al.* also concluded that lung functions including diffusing capacity are preserved in patients with DM.¹⁷ In the present study, the significant reduction observed in diffusion capacity (DLCO) with reduction in FEV1, FVC, PEF and FEF 25-75% and a

Table 2: Duration of diabetes and pulmonary function parameters

Duration of diabetes (years)	FEV1 (L) FEV1 (% Pred.)	FVC (L) FVC (% Pred.)	FEV1/FVC	PEF (L/m) PEF (% Pred.)	FEF 25-75%(L/s) FEF25-75% (% Pred.)	DLCO (ml/min/mmHg) DLCO (% Pred.)*
<10	2.13±0.65 (81.8±14.35)	2.51±0.71 (83.4±13.64)	80.54±9.90	6.54±1.77 (97.12±19.02)	2.32±0.95 (69.21±22.62)	21.51±6.34 (91.41±22.19)
10-20	2.26±0.66 (83.67±11.65)	2.7±0.76 (86.64±13.26)	82.16±6.23	8.45±10.19 (100.64±14.43)	2.54±1.05 (73.64±26.44)	24.53±6.14 (98.36±20.24)
>20	1.81±0.61 (87.5±28.99)	2.17±0.84 (85.5±28.99)	81.91±1.42	5.49±0.28 (91.00±5.65)	1.70±0.35 (57.5±16.26)	13.87±6.04 (71.00±35.35)

* $P=0.08$, FEV1: Forced expired volume in 1 s, FVC: Forced vital capacity, PEF: Peak expiratory flow, FEF: Forced expiratory flow, DLCO: Diffusing capacity

Table 3: Body mass index and pulmonary function parameters

Body mass index	FEV1 (L) FEV1 (% Pred.)	FVC (L) FVC (% Pred.)	FEV1/FVC	PEF (L/m) PEF (% pred.)	FEF 25-75% (L/s) FEF25-75% (% pred.)	DLCO (ml/min/mmHg) DLCO (% Pred.)
Normal	2.17±0.72 (81.54±14.77)	2.57±0.83 (82.6±14.75)	80.84±6.00	6.79±1.82 (96.03±15.29)	2.24±1.01 (66.28±23.63)	22.6±6.20 (95.75±22.69)
Overweight	2.16±0.58 (84.03±12.47)	2.56±0.59 (87.29±12.49)	81.31±11.15	7.54±8.69 (99.94±19.41)	2.54±0.92 (75.76±24.01)	22.17±6.48 (91.92±20.48)
Obese	2.23±0.78 (78.38±14.28)	2.66±0.89 (78.00±10.88)	81.54±4.99	7.14±1.90 (101.00±17.40)	2.28±1.25 (62.13±18.30)	22.82±9.03 (88.13±28.02)

P>0.05, FEV1: Forced expired volume in 1 s, FVC: Forced vital capacity, PEF: Peak expiratory flow, FEF: Forced expiratory flow, DLCO: Diffusing capacity

Table 4: HBA1c and pulmonary function parameters

HBA1c	FEV1 (L) FEV1 (% Pred.)	FVC (L) FVC (% Pred.)	FEV1/FVC	PEF (L/m) PEF (%Pred.)	FEF25-75%(L/s) FEF 25-75% (% Pred.)	DLCO (ml/min/mmHg) DLCO (% Pred.)
6.5-7.5	2.09±0.60 (81.00±12.58)	2.51±0.66 (83.47±13.54)	80.04±11.13	6.55±1.83 (97.98±15.93)	2.32±0.89 (69.31±23.11)	22.77±6.24 (93.28±22.30)
>7.5	2.24±0.69 (83.86±14.53)	2.62±0.78 (85.47±13.86)	82.05±5.86	7.71±8.21 (98.42±18.85)	2.43±1.06 (71.59±24.70)	22.10±6.77 (93.58±21.83)

P>0.05, FEV1: Forced expired volume in 1 s, FVC: Forced vital capacity, PEF: Peak expiratory flow, FEF: Forced expiratory flow, DLCO: Diffusing capacity

Table 5: Micro-albuminuria (n=80) and pulmonary function parameters

Urine for Microalbuminuria+ve	FEV1 (L) FEV1 (% Pred.)	FVC (L) FVC (% Pred.)	FEV1/FVC	PEF (L/m) PEF (%Pred.)	FEF 25-75%(L/s) FEF 25-75% (% Pred.)	DLCO (ml/min/mmHg) DLCO (% Pred.)
n=80	2.17±0.66 (82.52±13.68)	2.57±0.73 (94.53±13.69)	81.11±8.75	7.17±6.13 (98.22±17.48)	2.38±0.98 (70.52±23.9)	22.41±6.48 (93.44±21.96)

P>0.05, FEV1: Forced expired volume in 1 s, FVC: Forced vital capacity, PEF: Peak expiratory flow, FEF: Forced expiratory flow, DLCO: Diffusing capacity

preserved FEV1/FVC ratio (albeit not up to statistically significant levels) in diabetic patients of duration >20 years points to a subclinical restrictive impairment. The likely reason for the lack of a statistically significant reduction in the said parameters could be because we compared the values with predicted values and did not compare the results with a matched control group.

One significant observation in the present study was an impairment of DLCO, which was more prominent with increasing duration of diabetes in patients with Type 2 DM. This observation is in agreement with findings of a previous study by Mori *et al.* who reported that pulmonary diffusing capacity correlated negatively with the duration of diabetes.¹⁸ However, the present study did not show a statistically significant correlation between the reduction in DLCO and renal microangiopathy as assessed by microalbuminuria. Agarwal *et al.* reported a significant reduction in diffusing capacity in patients with Type 2 DM with microangiopathy - microalbuminuria and/or retinopathy. No difference was observed in the other spirometric values.¹⁹ Another study by Sinha *et al.* showed a significant reduction in pulmonary diffusing capacity in Type 2 DM Asian Indian patients with any or a combination of microangiopathy(ies) (retinopathy, nephropathy, and peripheral neuropathy).¹⁶ Our findings are in agreement with previous studies by Benbassat *et al.*

and Pinar Celik *et al.* which did not find any correlation between reduced diffusion capacities in diabetics with other chronic complications.^{16,20} Fuso *et al.* and Ozmen *et al.* taking note of these conflicting observations regarding the effect of DM on diffusing capacity opined that the usual clinical method of measuring DLCO, i.e., the Single-breath method may not be sensitive enough to detect pulmonary vascular angiopathy and have proposed measuring the CO transfer capacity in both seated and supine positions, i.e., measurement of posture related variation in DLCO to increase the sensitivity and diagnostic utility of the test.^{21,22}

The pathophysiological mechanism responsible for the reduction in diffusion capacity is believed to be multifactorial. Chronic hyperglycemia, as reflected by elevated HBA1c seen in 53.23% of our patients, leads to non-enzymatic glycosylation of collagen and elastin present in the extracellular matrix of the lung. The structural result of these biochemical alterations is a thickening of the alveolar epithelial basal lamina and a nodular fibrosis in the lung.^{23,24} Microangiopathy occurring in the small vessels of the lung may lead to thickening of the capillary endothelial basement membrane and decrease alveolar microvascular perfusion. Other postulated mechanisms include changes in surfactant and its actions and decreased affinity of HbA1c to carbon monoxide.

The present study failed to show any correlation between glycemic level and pulmonary function parameters. The average duration of disease in our patients was 7.69 years, whereas HBA1C is more predictive of short-term glycemic control. Previous studies by Mori *et al.*¹⁸ and Pinar Celik *et al.*²⁰ have also reported a similar lack of association between this index of diabetes control and lung function. Since HbA1C reflects the glycemic control over the previous 3-4 months, it improper to conclude that control of blood glucose level in diabetics has no bearing on pulmonary functions on the basis of this result alone. Davis *et al.*,⁵ Dennis *et al.*,²⁵ and McKeever *et al.*²⁶ in their studies have reported that diabetics with inadequate glucose control have a lower pulmonary function as compared to those with adequate control.

The present study had a few limitations. First, the spirometry values in our patients were compared against predicted pulmonary function determined from age, gender and body habitus instead of using a control group without DM. Second, we were unable to include static lung volume measurements such as residual volume (RV), total lung capacity (TLC), and functional residual capacity (FRC) in the present study since we lacked equipment to record the said parameters. Reduction in measured volumes would have helped to further confirm our observation of subclinical restriction seen in long-standing diabetics. Third, although we had a good number of patients, yet our results cannot be extrapolated to a vast country like India with different ethnic groups. Probably a multicentric prospective study including population representation from different parts of the country and a longer follow-up period would address this issue. Fourth, we used microalbuminuria as a marker of nephropathy since the test is easily done on outpatient basis. However, for microalbuminuria to signify diabetic nephropathy it needs to be persistent. Probably, a better marker would be a 24 h urine albumin excretion which is, however, difficult to use in an outpatient setting. Moreover, a large number of our patients were already on angiotensin converting enzyme (ACE) inhibitors causing microalbuminuria levels to be less than expected. Studies using 24 h protein excretion and taking ACE-inhibitors use into consideration needs to be done to correlate lung function and renal damage more accurately in diabetic patients.

CONCLUSION

The present study hints at the possibility of a restriction in lung function in patients with long-standing Type 2 DM. However, this impairment was not manifest as clinical symptoms in these patients and did not correlate with body habitus or degree of glycemic control. The observed

reduction in diffusing capacity (DLCO) was not restricted only to patients with microalbuminuria. Further studies using a non-diabetic control population and recording static lung volume measurements (RV, TLC, FRC) would be needed to confirm our observation.

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How to cite this article: Acharya PR, D'Souza M, Anand R, Kotian SM. Pulmonary Function in Type 2 Diabetes Mellitus: Correlation with Body Mass Index and Glycemic Control. *Int J Sci Stud* 2016;3(11):18-23.

Source of Support: Nil, **Conflict of Interest:** None declared.

Factors Affecting Visual Outcome in Phacolytic Glaucoma

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Abstract

Introduction: The occurrence of phacolytic glaucoma is not an infrequent event in India. This problem is especially common in rural India owing to the delay in getting the cataract removed.

Aim: To clinically evaluate the presenting features, management, factors affecting the visual outcome and post-operative control of intraocular pressure (IOP) in phacolytic glaucoma.

Materials and Methods: 50 patients with phacolytic glaucoma who presented to Ophthalmology Department, Sri Ramachandra Medical College during March 2010 - September 2011 were included in the study. All the patients underwent extracapsular cataract extraction.

Results: Phacolytic glaucoma occurs mainly in the age group of 50-70 years with a female preponderance. 46% of patients presented with hand movements, 40% with perception and projection of light, 14% with a defective projection of light. The mean pre-operative IOP was 44 mmHg. Iritis (34%) was the most common post-operative complication followed by hyphema (2%). A best corrected visual acuity of 6/12 or better was attained in 66% of patients. Out of 14% of patients presenting with a defective projection of light, only 2% had poor visual recovery (<6/60) due to glaucomatous disc damage. 66% of patients who presented within 10 days of onset of acute symptoms had a good visual outcome of 6/12 or better. All patients (100%) who presented after 10 days of onset of symptoms attained a final visual acuity of 6/18 or worse. There is good post-operative control of IOP in all the cases with a mean post-operative IOP of 14 mmHg.

Conclusion: The post-operative visual prognosis is good in phacolytic glaucoma. There is good post-operative control of IOP in all cases. Defective projection of light does not indicate a poor visual prognosis and is not a contraindication for cataract surgery. There is a definite correlation between duration of symptoms and final visual acuity.

Key words: Extra capsular cataract extraction, Phacolytic glaucoma, Visual outcome

INTRODUCTION

Cataractous lenses manifest a number of changes such as protein modification, lipid disturbances, and lens electrolyte imbalance.¹ There is increased the formation of heavy molecular weight (HMW) protein aggregates characterized by linkage of the polypeptide chains through disulfide bonds formed as a result of oxidation of

thiol groups on the protein.² This leads to an increase in the water insoluble fraction of protein. The lens fibers are broken down into coarse angular fragments and then into smooth eosinophilic globules (Morgagnian globules). As degeneration proceeds, proteins coagulate, lipids, crystals of cholesterol, tyrosine, leucine, and deposits of calcium carbonate and phosphate are formed.² Subsequent events depend largely on the state of the capsule. (1) If the capsule becomes impermeable by thickening and proliferation of the epithelium, water, and solutes are retained, and the nucleus is found floating in richly proteinaceous, milky fluid containing the coagulated end products of cortical degradation (Morgagnian cataract).¹ (2) If the capsule remains permeable, the imbibed water and soluble products of degeneration diffuse away and the lens shrinks. The leaking lens protein is ingested

Access this article online



www.ijss-sn.com

Month of Submission : 12-2015

Month of Peer Review : 01-2016

Month of Acceptance : 01-2016

Month of Publishing : 02-2016

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by macrophages which block the trabecular meshwork leading to secondary open angle glaucoma (phacolytic glaucoma).¹ The pathogenesis in phacolytic glaucoma is the release of soluble lens protein into the aqueous through microscopic defects in the lens capsule. However, theories vary as to how this protein leads to elevated intraocular pressure (IOP). It has been postulated that macrophages laden with phagocytized lens protein block the trabecular meshwork to produce elevated IOP. This theory has been supported by the demonstration of macrophages in the aqueous and trabecular meshwork of eyes with phacolytic glaucoma.² An alternative theory is that HMW soluble protein from the lens directly obstructs the aqueous outflow.² HMW protein is known to increase in the cataractous lens and has been demonstrated in the aqueous of eyes with phacolytic glaucoma in quantities sufficient to obstruct aqueous outflow.²

Aim of Study

The study aims to clinically evaluate the presenting features, management, and visual prognosis of phacolytic glaucoma. The study also aims to study the risk factors which determine the final visual outcome and the post-operative control of IOP.

MATERIALS AND METHODS

50 patients with phacolytic glaucoma who presented to the Ophthalmology Outpatient Department of Sri Ramachandra Medical College during the period March 2010 to September 2011 were included in the study. Patients with primary glaucoma, prior ocular hypotensive treatment, and glaucoma due to dislocated lens were excluded from the study. All patients were examined in detail, and glaucoma workup was done. A detailed history, including presenting complaints, duration of symptoms, cataract surgery in the other eye, was taken. All the patients were subjected to a detailed slit lamp examination. Fundus examination, IOP measurement by applanation tonometry and gonioscopy were done in all cases. Phacolytic glaucoma was diagnosed by the presence of corneal edema, deep anterior chamber with a variable content of cells and flare, floating chunks of white lens material and the presence of hypermature morgagnian cataractous lens and IOP above 21 mmHg.¹ Preoperatively, an attempt was made to control the IOP with oral acetazolamide 250 mg 4 times a day, oral glycerol 30 ml 3 times a day, and topical timolol 0.5% eye drops twice a day. In patients who have IOP >30 mmHg, 100 ml of 20% mannitol was given intravenously on the day of surgery. Pre-operative topical betamethasone 0.1% eye drops 6 times a day was used to reduce the inflammation. After obtaining informed consent and explanation of

relatively guarded visual prognosis, the patients were operated under local anesthesia. Planned extracapsular cataract extraction (ECCE) was done followed by posterior chamber intraocular lens implantation³ in all cases except those with aphakia in the other eye or vitreous disturbance during surgery.

Surgical Technique

Fornix-based conjunctival flap was raised. A partial thickness groove was made at the limbus from 10 to 2'o clock position. The anterior chamber was entered with a no 11 bard parker blade. The gradual entry into anterior chamber by a grooved limbal incision helps to avoid sudden decompression.³ Anterior chamber was then thoroughly irrigated with balanced salt solution to remove the leaked lens material. A capsulotomy was carried out gently with a bent 26 gauge needle. Care was taken during capsulotomy to avoid zonular rupture. Vigorous irrigation of the anterior chamber and instillation of viscoelastics facilitated the completion of capsulotomy. The limbal incision was then extended laterally either way to approximately 120°. The nucleus was expressed out by pressure-counter pressure method. The residual cortical matter was aspirated with a simcoe cannula. After ensuring the posterior capsular integrity, a posterior chamber intraocular lens of appropriate power was implanted in the capsular bag.³ The corneoscleral incision was closed with 10.0 ethicon interrupted sutures. Post-operative medication for all patients consisted of topical corticosteroids 6 times a day and a short acting cycloplegic twice a day. Topical corticosteroids were gradually tapered off over 6 weeks. On the third post-operative day, patients were subjected to slit lamp examination, and visual acuity was assessed. After 6 weeks, best corrected snellen visual acuity was assessed. The post-operative IOP was also measured by applanation tonometer. Good IOP control was defined as IOP < 21 mmHg without the need for any anti glaucoma medication. Post-operative visual acuity ≥ 6/12 was considered as a good visual outcome.

RESULTS

Age Incidence

30-40 years	2 (4%)
41-50 years	5 (10%)
51-60 years	18 (36%)
61-70 years	18 (36%)
70 years	7 (14%)

Lens Status in Fellow Eye

Immature cataract	15 (30%)
Mature cataract	3 (6%)
Aphakia	3 (6%)
Pseudophakia	29 (58%)

Modes of Clinical Presentation

Deep anterior chamber with flare	50 (100%)
Lens matter in anterior chamber	2 (4%)
Pseudohypopyon	4 (8%)

Pre-operative IOP

<40 mmHg	14 (28%)
40-60 mmHg	32 (64%)
>60 mmHg	4 (8%)

Pre-operative Visual Acuity

Hand movements	23 (46%)
Perception/projection of light	20 (40%)
Defective projection	7 (14%)

Surgical Complications

Vitreous disturbance	1 (2%)
Iritis	17 (34%)
Hyphema	1 (2%)

Best Corrected Visual Acuity (6 Weeks)

≥6/12	33 (66%)
6/18-6/24	11 (22%)
6/36-6/60	5 (10%)
<6/60	1 (2%)

Duration of Symptoms and Visual Outcome

Duration	≥6/12	6/18-6/60	<6/60
≤5 days	28 (56%)	3 (6%)	0
6-10 days	5 (10%)	9 (18%)	0
>10 days	0	4 (8%)	1 (2%)

DISCUSSION**Age Incidence**

The majority of the patients (72%) were between 50 and 70 years of age. Earlier studies⁴ have also indicated that phacolytic glaucoma occurred more commonly with increasing age probably due to the aggregation of high molecular weight protein over time.

Sex Incidence

There were 22 (44%) males and 28 (56%) females in the study. It is possible that phacolytic glaucoma is more common in females because of socio-economic constraints, but the fact that the prevalence of cataract itself is more common in females than in males should be considered. This finding was consistent with data from Punjab study in India⁵ and Framingham eye study.

Clinical Presentation

The majority of the fellow eyes were pseudophakic (58%) with satisfactory vision. So, it is possible that they ignore the cataract in the other eye which has become hyper mature. This is consistent with the findings of previous studies.⁴

All patients (100%) presented with a deep anterior chamber and a variable amount of flare. In 92% of patients, the pre-operative IOP was <60 mmHg. The mean pre-operative IOP was 44 mmHg. 7 (14%) patients had a defective projection of light.

Surgery

46 (92%) patients underwent ECCE with posterior chamber intraocular lens implantation. The remaining 4 (8%) patients underwent ECCE alone (because of aphakia in the other eye in 3 cases and posterior capsular rent with a vitreous disturbance in 1 case). There was a significant increase in the incidence of post-operative iritis in phacolytic glaucoma patients.⁶ The inflammation was controlled with frequent topical corticosteroids and cycloplegics. The iritis cleared completely within 4 weeks in all the cases without any sequelae.

Visual Outcome

A best corrected visual acuity of 6/12 or better was taken as good visual outcome. 66% of patients had a good visual outcome. The post-operative visual prognosis in phacolytic glaucoma was good which correlates with previous studies.⁴ One patient had poor visual recovery (<6/60) due to glaucomatous disc damage.

Pre- and Post-operative Visual Acuity

There was no significant correlation between pre-operative and post-operative visual acuity. Out of 7 patients presenting with the defective projection of light, 3 patients attained ≥6/12, 3 patients attained 6/18-6/24. Only one patient had poor visual recovery (<6/60) due to glaucomatous disc damage. The defective projection of light may be due to sudden rise in IOP that caused optic nerve ischemia leading to conduction defects.⁷ Thus, even in patients with the defective projection of light, there is still a good chance of excellent visual recovery post-operatively provided the patient presents early. This correlates with previous studies.⁸ 28 (56%) patients who presented within 5 days and 5 (10%) patients who presented between 6 and 10 days had a good post-operative visual outcome (≥6/12). All the patients who presented after 10 days attained a post-operative visual outcome of 6/18 or worse. This shows a definite correlation between duration of symptoms and final visual outcome which is in agreement with previous studies.^{4,6} So, if a patient arrives at a late stage, guarded visual prognosis must be explained to the patient before surgery.^{9,10}

Post-operative IOP

The mean post-operative IOP was 14 mmHg. The IOP showed a dramatic decline in all the cases after surgery and none of the patients required any anti glaucoma medication. This is in accordance with previous studies.⁸

CONCLUSION

Phacolytic glaucoma occurs mainly in the age group of 50-70 years with a female preponderance. The fellow eye is pseudophakic (58%) in the majority of cases. 46% of patients presented with hand movements, 40% with perception and projection of light, and 14% with the defective projection of light. All cases (100%) presented with deep anterior chamber and flare, 8% presented with milky fluid in the anterior chamber, and 4% with lens matter in the anterior chamber. The mean pre-operative IOP was 44 mmHg. Posterior capsular rent with vitreous disturbance occurred in 2% of patients. The most common post-operative complication was iritis (34%) followed by hyphema (2%). Iritis was managed successfully with topical corticosteroids and cycloplegics. 66% of patients attained a good post-operative visual acuity of 6/12 or better. There is no definite correlation between pre-operative and post-operative visual acuity. Out of 7 patients presenting with the defective projection of light, only 1 patient had poor visual recovery (<6/60) due to glaucomatous disc damage. The defective projection of light does not indicate a poor visual prognosis and is not a contraindication for surgery. There is a definite correlation between duration of symptoms and final visual acuity. 66% of patients who presented within 10 days of onset of acute symptoms had a good visual outcome of 6/12 or better. All patients (100%) who presented after 10 days of onset of symptoms attained a final visual acuity of 6/18 or worse. There is good post-operative control of IOP in all the cases

with a mean post-operative IOP of 14 mmHg. Visual rehabilitation is better with posterior chamber intraocular lens implantation. Hence, planned ECCE with posterior chamber intraocular lens implantation is the surgery of choice in phacolytic glaucoma. The few intraoperative and post-operative complications which occurred in this study could be reduced by doing small incision cataract surgery.

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How to cite this article: Gnanadurai JSC, Sanjana EF, Radhakrishnan M. Factors Affecting Visual Outcome in Phacolytic Glaucoma. *Int J Sci Stud* 2016;3(11):24-27.

Source of Support: Nil, **Conflict of Interest:** None declared.

Association between Dyspnea, Forced Expiratory Volume in 1 s, and Body Mass Index in Chronic Obstructive Pulmonary Disease

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Abstract

Introduction: Low body mass index (BMI) in chronic obstructive pulmonary disease (COPD) is associated with poor prognosis, morbidity, and mortality. Low BMI is also associated with low respiratory strength, higher grade of breathlessness, and lower forced expiratory volume in 1st s (FEV1) values.

Aim: The present study was done to assess whether there was any difference in the grade of breathlessness and FEV1 among underweight, normal weight, and overweight COPD patients.

Materials and Methods: The study was conducted at a teaching hospital in north Kerala on 45 COPD patients of both sexes selected on the basis of BMI. The data were collected from June 2014 to August 2015 using standard operating procedures.

Results: In this study, FEV1% <50% was found to be higher in the underweight group of COPD patients (55.55%). Number of patients with a higher grade of breathlessness was higher in the underweight group of patients 66.66%.

Conclusion: BMI should be assessed in all cases of COPD as a low BMI is associated with lower FEV1, who in turn is associated with poor prognosis and mortality.

Key words: Body mass index, Chronic obstructive pulmonary disease, Dyspnea, Forced expiratory volume in 1st s

INTRODUCTION

The association between low weight for height and advanced disease in patients with chronic obstructive pulmonary disease (COPD) is a common clinical observation.¹ Low body mass index (BMI) is associated with increased morbidity, mortality, and poor prognosis.

Various studies have provided evidence that COPD is often associated with significant extrapulmonary abnormalities, the so-called systemic effects of COPD.² As in other chronic inflammatory diseases, weight loss, muscle wasting, and tissue depletion are commonly

seen in COPD patients. Selective wasting of fat-free mass coupled with impaired respiratory and peripheral muscle function and reduced capacity for exercise occur in COPD patients.

There is an enhanced sensation of dyspnea in the underweight emphysematous COPD patients. Although the origin of dyspnea is multifactorial, a reduced diffusion capacity of carbon monoxide and respiratory strength are at least in part responsible for the enhanced sensation of dyspnea in this group of patients.

Studies have shown that low BMI is associated with more severe airflow obstruction as shown by low forced expiratory volume in 1st s (FEV1). BMI, airflow obstruction, dyspnea, and exercise capacity index which predict the mortality in COPD patients include the degree of pulmonary impairment (FEV1), BMI, degree of breathlessness, and distance walked in 6 min. Some recent studies have shown that most malnourished patients had a severe degree of breathlessness.

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Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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MATERIALS AND METHODS

15 COPD patients each in underweight, normal weight, and overweight categories, both males and females were selected from the in-patients and out-patients in the Chest and Tuberculosis Department of a Teaching Hospital of North Kerala.

Objectives

1. To assess whether there is any difference in the grade of breathlessness among underweight, normal weight, and overweight COPD patients
2. To study the distribution of FEV1 values among underweight, normal weight, and overweight COPD patients.

Inclusion Criteria

Mild, moderate, and severe cases of COPD patients of both sexes who are strictly adhering to the prescribed treatment and follow-up.

Exclusion Criteria

1. Pneumonia
2. Bronchial asthma
3. Interstitial lung diseases
4. Neuromuscular and skeletal disorders affecting respiratory system
5. Other structural lung disease
6. Diabetes mellitus, hypothyroidism, and hyperthyroidism
7. Cardiovascular diseases such as left ventricular failure secondary to hypertension and coronary artery diseases.

Evaluation

Evaluation of each patient included:

- Vital data regarding name, age, sex, and BMI
- Present history regarding a cough, fever, breathlessness
- Past history included duration of breathlessness, number of exacerbations, number of hospitalizations
- Medication history
- Family history
- Personal history (Table 1).

Investigations

Radiological evaluation to assess the changes associated with COPD and to rule out other structural lung diseases.

Electrocardiography to assess right ventricular changes and to rule out left ventricular strain and ischemic heart disease.

Pulmonary Function Test

Pulmonary function test was performed with an electronic flow sensing spirometer that met the accuracy criteria of

the American Thoracic Society. Only those participants who demonstrated two acceptable quality maneuvers that were reproducible within the 5% of the largest value were included in the present study.

Anthropometric Measurements

Measurement of height was made using a clinical stadiometer in bare feet. Body weight was measured with a calibrated precision scale. BMI, defined as weight in kilograms divided by square of height in meters was calculated. Patients were grouped into underweight, normal weight, and overweight according to the WHO classification for the Asian population. Those with BMI <17.5 were categorized as underweight, BMI between 17.5 and 22.99 as ideal weight and 23-27.99 as overweight.

RESULTS

Grade of Breathlessness (Modified Medical Research Council) and BMI - Wise Distribution

Table 2 and Figure 2 reveals that the maximum number of patients having Grade IV breathlessness was in the underweight group. Maximum number of patients having Grade III breathlessness was in the normal weight group. Maximum number of patients with Grade II breathlessness was in the overweight group.

Spirometry and BMI - Wise Distribution

Maximum number of patients with an FEV1 <30% was in the underweight group while no patient in the normal and overweight group had FEV1 <30%. The maximum number of patients with an FEV between 30% and 50% was also in the underweight group (Table 3 and Figure 3).

Table 1: MMRC grading of breathlessness

Grade	Degree of breathlessness related to activity
1	Not troubled by breathless except on strenuous exercise
2	Short of breath when hurrying on a level or when walking up a slight hill
3	Walks slower than most people on the level, stops after a mile or so, or stops after 15 min walking at own pace
4	Stops for breath after walking 100 yards, or after a few minutes on level ground
5	Too breathless to leave the house, or breathless when dressing/undressing

MMRC: Modified Medical Research Council

Table 2: BMI and grade of breathlessness

BMI	I	II	III	IV	V
Underweight <17.5 kg/m ²	0	1	8	5	1
Normal weight 17.5-22.99 kg/m ²	0	3	9	2	0
Overweight >23-27.99 kg/m ²	0	9	6	1	0
Total	0	13	23	8	1

BMI: Body mass index

Table 3: BMI and FEV1 values

BMI	FEV1 (act/predicted) (%)			
	>80	50-80	30-50	<30
Underweight <17.5 kg/m ²	0	5	7	3
Normal weight 17.5-22.99 kg/m ²	0	11	4	0
Overweight 23-27.99 kg/m ²	0	11	4	0

BMI: Body mass index, FEV1: Forced expiratory volume in 1 s

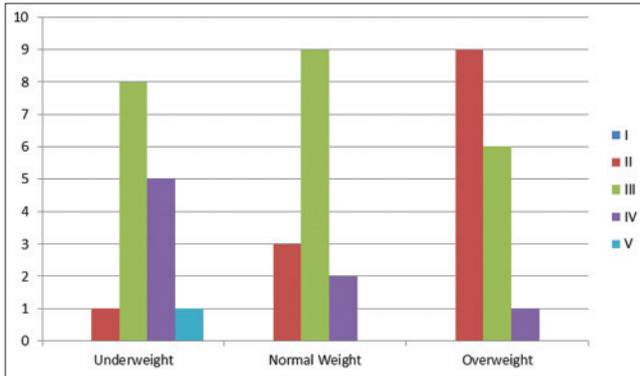


Figure 1: Body mass index and grade of breathlessness

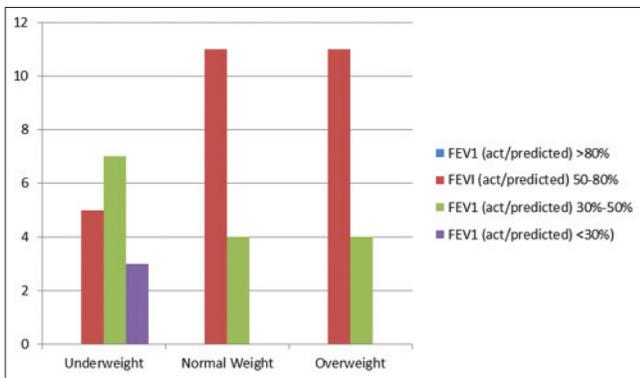


Figure 2: Body mass index and forced expiratory volume in 1 s values

DISCUSSION

The patients with a higher grade of breathlessness were in the underweight group. Studies have shown that patients with COPD who are distinguished as pink puffers (emphysematous), low diffusion capacity, and weight loss are indeed more dyspneic than normal weight patients with COPD.³

Although the origin of dyspnea is multifactorial, reduced diffusion capacity and respiratory muscle strength are at least in part responsible for the enhanced sensation of dyspnea in the underweight COPD patients.⁴

Various studies have provided evidence that COPD is often associated with significant extrapulmonary abnormalities, the pathogenesis and clinical manifestations of COPD are

not restricted to pulmonary inflammation and structural remodeling.⁵

The systemic effects of COPD include oxidative stress, altered circulating levels of inflammatory mediators, acute phase proteins, and impaired endogenous oxidant-antioxidant imbalance. Furthermore, altered circulating levels of several cytokines and adhesion molecules have been observed.⁶

Selective wasting of fat-free mass coupled with impaired respiratory and peripheral muscle function and a reduced capacity for exercise occur in COPD patients.⁷

Recent studies have shown that best correlation of BMI was with FEV1 in COPD patients.⁸ Most malnourished patients had the most severe airflow obstruction. The present study also shows that more severe degree of obstruction was present in the underweight group. Maximum number of patients with the FEV1 (act/predicted) <30% was in the underweight group. The maximum number of patients with FEV1 (act/predicted) between 30% and 50% were also in the underweight group.

The FEV1 is essential for the diagnosis and quantification of respiratory impairment resulting from COPD. The rate of decline in FEV1 is also a good marker of disease progression and mortality.

Risk factors such as low FEV1, presence of hypoxemia or hypercapnia, short distance walked in a fixed time, a high degree of functional breathlessness, and a low BMI are associated with poor prognosis.

It was hypothesized that a multi functional grading system that assesses the respiratory, perceptive, and systemic effects of COPD would better characterize the illness and predicts outcome.

Four factors that predict the risk of death in COPD were identified:⁹

- BMI (B)
- The degree of airflow obstruction
- Functional dyspnea (D)
- Exercise capacity (E) assessed by 6 min walk test.

These variables were integrated into a multidimensional index.

CONCLUSION

BMI should be assessed in all cases of COPD as a low BMI is associated with lower FEV1, which in

turn is associated with poor prognosis and mortality. A lower BMI is also associated with a higher grade of breathlessness and treating physician should be more alert in evaluating and treating these groups of patients.

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How to cite this article: Sabir C, Kumar MS. Association between Dyspnea, Forced Expiratory Volume in 1 s, and Body Mass Index in Chronic Obstructive Pulmonary Disease. *Int J Sci Stud* 2016;3(11):28-31.

Source of Support: Nil, **Conflict of Interest:** None declared.

Prevalence and Risk Factors of Peripheral Vascular Disease in Diabetic Foot Lesions

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Abstract

Introduction: Diabetic foot problems are common throughout the world, resulting in major medical, social, and economic consequences for the patients, their families, and society. Ischemia (peripheral vascular disease [PVD]) and peripheral neuropathy contribute to its etiopathogenesis. Of the two primary etiopathogenic factors, PVD represents only potentially preventable and correctable variable.

Aim: The aim of the study is to check prevalence and risk factors of PVD among the patients with diabetic foot lesions.

Materials and Methods: It was a cross-sectional study done in the Department of Surgery, PESIMSR Kuppam, a tertiary care centre from 2011 to 2013. The diagnosis of PVD and the risk factors will be studied at the same time.

Results: A total of 140 Type 2 diabetes patients with foot lesions were studied. 14 patients were diagnosed to have PVD among which 13 (92.9%) are males and 1 (7.1%) patient was a female. Mean age of the patients with concomitant diabetes and PVD is 56.4 years (standard deviation \pm 8.1). The mean hemoglobin A1c in the study population was 9.2 ± 2.4 with claudication (71.4%), rest pain (14.3%) or absent/feeble lower limb distal arterial pulses are a more likely presentation.

Conclusion: The prevalence of PVD is multi-fold higher in patients with diabetes with smoking, hyperglycemia, hypertension, dyslipidemia, as major risk factors. Ankle, brachial pressure index, is useful in identifying PVD and it needs further evaluation by an arterial color Doppler and digital subtraction angiography.

Key words: Ankle brachial pressure index, Claudication, Diabetic foot lesions, Peripheral vascular disease

INTRODUCTION

In India, the prevalence of foot ulcers in diabetic patients in the general population is 3%, which is much lower than reported in the western world.¹ With increasing prevalence of unhealthy lifestyles and aging of the Indian population, it is no surprise that diabetes mellitus is reaching epidemic proportions, and this comes along with its colossal socioeconomic and medical burden. Diabetic foot lesions represent a common morbid end point of this metabolic derangement associated with significantly poor functional outcomes and limb loss. Ischemia (peripheral vascular disease [PVD]) and peripheral neuropathy contribute to

the etiopathogenesis of the diabetic foot lesions when superimposed by injury or infection. Of the two primary etiopathogenic factors, PVD represents only potentially preventable and correctable variable. A low ankle/arm index is a good marker of vascular events and may be diminished without presenting symptomology (silent PVD).² The epidemiology of PVD has rarely been studied in non-European population. PVD is a major cause of morbidity and mortality especially affecting the elderly population. The prevalence of PVD is multi-fold higher in patients with diabetes compared with the age of sex-matched non-diabetic patients, and this may be because of hyperglycemia, hypertension, hyperlipidemia, platelet factors, and other factors that are increased in diabetic foot patients. The impact of PVD on the natural history of diabetic foot lesions has been extensively studied in Caucasian populations where it is prevalent in significant numbers. Recent estimates by the World Health Organization (WHO) show that India already has the largest number of diabetic patients in any given country, and this trend will continue in the future. Unfortunately,

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Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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there is very little epidemiological data on PVD in migrant Indians or individuals from the Indian subcontinent.

Epidemiology

In India, the prevalence of foot ulcers in diabetic patients in the general population is 3%, which is much lower than reported in the western world.

Up to 25% of patients with diabetes will suffer from a foot ulcer during their lifetime.³

Approximately 50% of diabetic foot ulcers become infected, and 20% of these require amputation.⁴

About 60% of all non-traumatic amputations occur in those with diabetes. After a major limb loss, 50% of contralateral limbs develop a serious lesion. After the index amputation, 9-17% of patients experience a second amputation within the same year. 25-68% of amputees have their contralateral extremity amputated within 5 years.⁵

In the world, at least one amputation for every 30 s is done for patients with Type II diabetes mellitus.⁶

MATERIALS AND METHODS

It was a cross-sectional study done in the Department of Surgery, PESIMSR, Kuppam, a tertiary care centre from 2011 to 2013. The diagnosis of PVD and the risk factors were studied at the same time. All patients with diabetic foot lesions were included in the study and other non-diabetic foot lesions including traumatic, neuropathic, and infective ulcers were excluded from the study.

Detailed history and clinical examination were done in all patients with diabetic foot lesions and history of PVD mainly on the presence of claudication pain and absent foot pulses, etc.

The ankle brachial pressure index (ABPI) was calculated in every patient, the criterion for diagnosing PVD is ABPI <0.9. All patients examined evaluated, and data of risk factors were collected.

RESULTS

Table 1 shows that 2.14% of the study population was between 31 and 40 years, 20% was between 41 and 50 years, 54% was between 51 and 60 years, 45% was between 61 and 70 years, 8% was between 71 and 80 years, and 2% was between 81 and 90 years. The maximum number of patients are in the age group of 51-60 years.

Table 2 shows 10% of the study population had PVD.

Table 3 shows 10 (71.4%) out of 14 PVD and 10 (7.9%) out of 126 non-PVD patients had a history of claudication pain (*P* < 0.0001) which means that the patients presenting with complaints of claudication pain have more chances of having PVD.

Table 4 shows 2 (14.3%) out of 14 PVD and 3 (2.4%) out of 126 non-PVD patients had rest pain.

Table 5 shows the mean ABPI in the PVD group of patients is 0.81 ± 0.20 in the right leg, and it is 0.94 ± 0.15 in the

Table 1: Age and sex distribution among the study population

Age (years)	Female	Male	Total patients (%)
31-40	2	1	3 (2.14)
41-50	10	18	28 (20)
51-60	19	35	54 (38.5)
61-70	16	29	45 (32.14)
71-80	2	6	8 (5.7)
81-90	0	2	2 (1.4)
Total (%)	49 (35)	91 (65)	140

Table 2: Distribution of pvd among the study population

Patients with	Number of patients	Percentage
PVD	14	10
Non-PVD	126	90
Total	140	100

PVD: Peripheral vascular disease

Table 3: Claudication pain among study population

Claudication pain	PVD (%)	Non-PVD (%)	Total
Yes	10 (71.4)	10 (7.9)	20
No	4 (28.6)	116 (92.1)	120
Total	14	126	140

PVD: Peripheral vascular disease

Table 4: Rest pain among study population

Rest pain	PVD (%)	Non-PVD (%)	Total
Yes	2 (14.3)	3 (2.4)	5
No	12 (85.7)	123 (97.6)	135
Total	14	126	140

PVD: Peripheral vascular disease

Table 5: Distribution of ankle brachial pressure index among the study population

ABPI	Right	Left
0.3-0.59	1	0
0.6-0.89	9	4
0.9-1.2	125	126
>1.2	5	9

ABPI: Ankle brachial pressure index

left leg. Whereas in the non-PVD group, it is 1.07 ± 0.08 in the right leg and 1.07 ± 0.08 in the left leg.

Table 6 shows 7 (50%) out of 14 PVD and 37 (29.4%) out of 126 non-PVD patients have the habit of smoking ($P = 0.11$).

Table 7 shows 5 (35.7%) out of 14 PVD and 29 (23%) out of 126 non-PVD patients were hypertensive. With a $P = 0.29$.

Table 8 shows 10 (71.4%) out of 14 PVD and 42 (33.3%) out of 126 non-PVD patients had dyslipidemia.

DISCUSSION

Diabetes is a chronic complex metabolic disease which results in the inability of the body to maintain and use carbohydrates, fats, and proteins. Most people (95% of all cases) have a form of diabetes known as non-insulin dependent diabetes or Type 2 diabetes. Diabetic foot is defined, based on the WHO criteria as infection, ulceration and/or destruction of deeper tissues associated with neurological abnormalities and various degrees of PVDs of the lower limb.⁷ It is one of the most serious complications of diabetes. Approximately 50% of all non-traumatic amputation are performed on diabetics for complications of diabetic foot like non-healing ulcers and gangrene PVD is a common associated condition in patients with Type 2 diabetes. In west around 14%⁸ of the patients with Type 2 diabetes suffer from PVD, but in India, these figures vary between 4% and 15%.^{9,10} It is one of the major causes

of morbidity, mortality, and severe disability in diabetes. Peripheral atherosclerosis observed in patients with the diabetic is typically more distal in distribution and often more extensive.¹¹ The vessels involve being distal popliteal, the tibial, and metatarsal vessels of lower limbs are most commonly and severely affected.¹²

Diabetic atherosclerosis has also been described as extraordinary diffuse, multi-segmental, and often involving collateral vessels.¹³

Early diagnosis and treatment allow up to 80% of patients with diabetic foot problems to have some form of surgical or endovascular revascularization.¹⁴

Histologically, atherosclerosis in the diabetics is indistinguishable from that in the non-diabetic.¹⁵ Intimal atherosclerosis and medial calcific stenosis (MCS) are both commonly found in the diabetic. The latter condition, MCS is also called Monckeberg's arteriosclerosis, has been found in some studies to occur with increased frequency in the diabetic population.¹⁶ It involves progressive degeneration and calcification of the tunica media of muscular arteries.

The three main factors leading to diabetic foot ulceration - Neuropathy¹⁷ microangiopathy and large vessel disease - gives rise to a similar array of abnormalities of microvascular function - limited vasodilatory reserve, impaired postural vasoconstriction, impaired pressure regulation, and maldistribution of blood flow.

In the majority of cases, the diabetic foot is classified as neuro-ischemic. It is the combination of the two fundamental factors of neuropathy and PVD rather than either factor alone which contributes to the clinical problem of the diabetic foot.

Other factors also contribute to foot ulceration. These include loss of joint position sense, limitation of joint mobility, foot deformity, high plantar foot pressures, and the presence of callus underweight bearing areas. These alone do not cause foot ulceration.

The symptoms of PVD in diabetic patients are similar to those of any other patient group:¹⁸

1. Intermittent claudication
2. Rest pain
3. Ischemic loss of tissue - ulceration.

Diabetes with PVD has a poorer lower limb function than those with PVD alone, attributed to diabetic neuropathy differences in exertional leg symptoms and greater risk of cardiovascular diseases in a patient with diabetes. Diabetics are at four times greater risk in developing PVD than the

Table 6: Smoking among study population

Smoking	PVD (%)	Non-PVD (%)	Total
Yes	7 (50)	37 (29.4)	44
No	7 (50)	89 (70.6)	96
Total	14	126	140

PVD: Peripheral vascular disease

Table 7: Hypertension among study population

Hypertension	PVD (%)	Non-PVD (%)	Total
Yes	5 (35.7)	29 (23)	34
No	9 (64.3)	97 (77)	106
Total	14	126	140

PVD: Peripheral vascular disease

Table 8: Dyslipidemia among study population

Dyslipidemia	PVD (%)	Non-PVD (%)	Total
Yes	10 (71.4)	42 (33.3)	52
No	4 (28.6)	84 (66.7)	88
Total	14	126	140

PVD: Peripheral vascular disease

general population, the disease is more aggressive and has 5 times more chances of developing critical limb ischemia.

Assessment should be made to establish the degree of infection, ulceration gangrene, and ischemia, whether it requires treatment and if so the most appropriate treatment. Ischemia is a contributing factor in diabetic foot ulcer that must be recognized and treated to avoid prolonged hospital stay, spreading infection, and unnecessary amputation.

A key principle in treatment of PVD is a hemodynamic assessment of circulatory impairment which helps in deciding further course of treatment. In lower limbs, measurement of pressure plays a central role in assessing disease severity. Segmental pressure measurements in limbs can be used for localized and grade hemodynamically significant lesions, as well as overall degree of circulatory impairment. The single most useful index is ankle pressure which can be measured by handheld Doppler probe and a pressure cuff which is tied just above malleolus, the probe is positioned over dorsalis pedis or posterior tibial arteries to obtain a flow signal.

Normally, ankle brachial index is 1-1.2 but values of 0.6-0.9 are typical of claudication. 0.3-0.6 of rest pain and below 0.3 of incipient or actual gangrene.¹⁹ In some individuals at rest, occult disease may be uncovered if ABPI falls after exercise.

Toe pressure may be obtained by an appropriately sized cuff and use of photoplethysmograph probe on the pulp of distal digit. It is useful in patients with disease confined to the distal vessel are more commonly to help predict the likelihood of healing forefoot procedures ulceration or toe amputations toe pressure 30 mm Hg is predictive of healing in 90% of cases, a pressure 10 mm Hg is predictive of poor outcome. Toe pressure also gives an objective measurement of the extent of occlusive disease between ankle and toe. Normal toe-brachial index is 0.75 and index 0.25 represents severe occlusive disease.

Duplex scanning evaluation of aorta and iliac arteries employs the same 2-3 mHz transducers employed for evaluation of mesenteric and renal arteries. Patients are best studied after an overnight, initial posting is supine but right and left lateral decubitus positions may be helpful to accomplish a complete study. The evaluation proceeds along bifurcation and each iliac artery through the pelvis to groin. A 5 or 75 mHz transducer is typically used to study the femoral, popliteal, and tibial vessels. Evaluation of popliteal and tibial and popliteal arteries is best performed with a combination of prone and supine patient positioning. The tibial arteries are scanned from infrageniculate popliteal artery distally.

Color flow image is useful to identify all vessels initially and to search for regions of color flow disturbance indicative of stenosis.^{20,21} Subsequently, the technologist sweeps the pulse Doppler probe through all the segments. Representative images and Doppler velocity spectra are recorded in all regions. The technical adequacy of this examination for identification of all vessels exceeds 90% in most reports although evaluation of peroneal artery may be somewhat less successful.

Patients with atypical symptoms that might be due to ischemia can be examined to exclude the presence of significant arterial disease. The duplex scan also has a potential to find suitable distal revascularization targets when none is visualized by angiography.

Angiography

It must be stressed that angiography should only be performed if intervention is intended. It allows assessment of whether intervention is technically possible and enables a most appropriate form of treatment to be chosen.

Early diagnosis and treatment by specialized podiatric teams have reduced the rate of diabetes-related amputations by 50%. A podiatric team has following responsibilities to identify patients at high risk and monitor them and to treat patients with ulcers.

Treatment modalities include:

- A. Medical management
- B. Intervention
 1. Endovascular²²
 2. Surgical
 3. Amputation.

CONCLUSION

Peripheral arterial disease (PAD) is a common cardiovascular complication in patients with diabetes. The risk of developing PAD is much higher in patients with diabetes, and the disease is more severe and progresses more rapidly than in non-diabetic individuals. Moreover, the presence of PAD is a potent marker of increased cardiovascular risk. If PAD is identified on the basis of an ABI of -0.90 , its prevalence in patients with diabetes may be as high as 10%.

Because the major threat to patients with diabetes and PAD is from cardiovascular events, the primary therapeutic goal is to modify atherosclerotic risk factors. Risk factor management includes lifestyle modifications, treating associated conditions (diabetes, dyslipidemia, and hypertension), and preventing ischemic events with aggressive antiplatelet therapy such as clopidogrel. Pharmacologic therapies to improve symptomatic PAD

include cilostazol. A supervised exercise program or cilostazol are the preferred first treatment steps for the management of symptomatic PAD. Revascularization has an important role to play in the management of patients for whom risk factor modification and pharmacological treatment prove inadequate.

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How to cite this article: Nagateja, Lingaraju N. Prevalence and Risk Factors of Peripheral Vascular Disease in Diabetic Foot Lesions. *Int J Sci Stud* 2016;3(11):32-36.

Source of Support: Nil, **Conflict of Interest:** None declared.

Comparative Study of Gabapentin in Combination with Valacyclovir and Valacyclovir Alone in Herpes Zoster

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Abstract

Background: In herpes zoster, during the acute illness, the rash is often accompanied by intense pain in the majority of patients which can interfere with sleep and routine daily activities affecting the quality of life. Many studies have shown that gabapentin administered in acute phase reduces the incidence of post-herpetic neuralgia, but the evidence of its efficacy and safety in the acute phase is scarce.

Objective: The aim of the present study was to compare and evaluate the effects of adding gabapentin with valacyclovir and valacyclovir alone in the acute phase of herpes zoster.

Materials and Methods: A total of 40 patients were enrolled in the study and were divided into two groups. Group 1 ($n = 20$): Gabapentin given in successive escalating doses for 28 days + valacyclovir 1 g tds for 7 days. Group 2 ($n = 20$): Valacyclovir 1 g tds for 7 days. Efficacy of the therapy was assessed by the time needed for healing of rash and improvement in pain intensity which was evaluated by using a 10 cm visual analog scale (VAS) at each visit, i.e., on the day of enrollment (0 day), 3, 7, 14, 21, and 28 days. A checklist was used to enquire about adverse effects at each visit. The results were analyzed using Student's *t*-test (paired and unpaired).

Result: The herpetic rash healed in about 5-8 days in both the groups. Improvement in VAS score was significantly higher in Group 1 at each visit except on days 3 and 7.

Conclusion: Gabapentin in combination with valacyclovir is safe and effective for the management of herpes zoster and the pain associated with it.

Key words: Gabapentin, Herpes zoster, Valacyclovir

INTRODUCTION

Herpes zoster results from reactivation of the varicella-zoster virus, which remains latent in the sensory ganglia after primary infection.¹ Unlike varicella (chickenpox), herpes zoster is a sporadic disease with an estimated lifetime incidence of 10-20%. The incidence of herpes zoster

increases sharply with advancing age, roughly doubling in each decade past the age of 50 years. During the acute illness, the rash is often accompanied by intense pain in the majority of patients that can be described as burning, deeply aching, tearing, electric shock-like or lancinating which can interfere with sleep and routine daily activities affecting the quality of life.²

Though in majority of cases, the zoster-associated pain resolves spontaneously with time, but as it is also the chief complaint for which patient seeks medical care, the pain management has important status in acute condition. Therefore, the treatment of herpes zoster should include drugs for managing pain in addition to controlling the acute viral infection. Antiviral agents, oral corticosteroids, and

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Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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adjunctive individualized pain management modalities are used to achieve these objectives.^{3,4}

Evidence-based strategies for the management of acute herpes zoster include the use of antiviral agents (acyclovir, famciclovir, and valacyclovir) with or without analgesics. These are effective in reducing the severity and duration of acute illness when given within 72 h of rash onset. In addition to this, some studies have also demonstrated that their use in immunocompetent patients is associated with significant improvements in the severity of the acute pain of herpes zoster.^{5,6}

Numerous treatment algorithms list trials of common analgesics such as ibuprofen or acetaminophen, topical treatment such as capsaicin cream or lidocaine patches, tricyclic antidepressants, or other antidepressants (e.g. amitriptyline hydrochloride, desipramine hydrochloride), and anticonvulsants (e.g., carbamazepine, gabapentin, lamotrigine) as first-line therapy for neuropathic pain.⁷⁻⁹ These medications may be used alone or in combination. The choice of medication should be directed toward the type of painful symptom described.

Gabapentin has been proposed as one of several first-line treatments for neuropathic pain, which is structurally related to gamma-aminobutyric acid, a pain-modulating neurotransmitter. Numerous studies have shown that gabapentin administered in acute phase reduces the incidence of post-herpetic neuralgia (PHN), but the evidence of its efficacy and safety in the acute phase is scarce. Therefore, the present study was planned with the objectives to compare and evaluate the effects of adding gabapentin with valacyclovir and valacyclovir alone in the acute phase.

MATERIALS AND METHODS

This was a prospective observational comparative study for the evaluation of efficacy and safety of gabapentin in combination with valacyclovir and valacyclovir alone for acute herpes zoster. The patients enrolled for the

study were adults aged 50 years or more, presenting with signs and symptoms suggestive of localized herpes zoster within 72 h of the onset of rash accompanied with at least moderate pain.

The exclusion criteria for the study were herpes zoster ophthalmicus, pregnancy, lactation, and patients who had received cytotoxic or immunosuppressive drug therapy within the 3 months before presentation. Patients who had received topical or systemic antiviral medications or immunomodulatory agents for varicella zoster virus infections, for example, interferon or capsaicin, within the previous 4 weeks and those receiving tricyclic antidepressant drugs or other pain medication immediately before presentation were also excluded.

A total of 40 patients fulfilling the inclusion criteria were enrolled in the study and were divided into two groups according to the medications they received.

Group 1 ($n = 20$): Gabapentin given in successive escalating doses starting from 300 mg HS for first 3 days, 300 mg BD for next 3 days, and finally 300 mg tds which were continued till 28th day of the study + valacyclovir 1 g 3 times daily for 7 days.

Group 2 ($n = 20$): Valacyclovir 1 g 3 times daily for 7 days.

Main outcome measures: Resolution of zoster-associated pain, rash healing, and safety of therapy.

Efficacy of the therapy was assessed by the time needed for healing of rash and improvement in pain intensity. Pain was evaluated by using a 10 cm visual analog scale (VAS) with the end points of 0 cm rated as no pain and the points of 10 cm as intolerable pain at each visit, i.e., on the day of enrollment (0 day), 3, 7, 14, 21, and 28 days.

A checklist was used to enquire about adverse effects at each visit by the patients.

Statistical Analysis

The results were analyzed using Student's *t*-test (paired and unpaired) and were expressed as mean \pm standard error.

RESULTS

Out of the 40 patients enrolled in the study, 22 were male and 18 were female (Figure 1). Demographic parameters and other baseline characteristics including age, sex, age, severity of rash, pain, and VAS score were similar in both the groups and there was no significant difference in any parameter (Table 1).

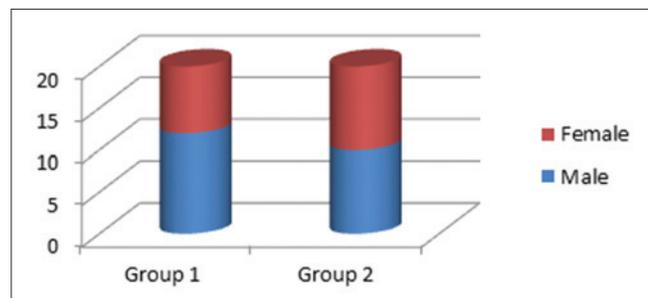


Figure 1: Sex distribution

The herpetic rash healed in about 5-8 days in both the groups. The average pain score was significantly reduced in both the groups after 28 days. Comparative analysis between the groups shows that improvement in pain score was more in Group 1 (Table 2). This difference was significant ($P < 0.05$) at all follow-up visits except for the first two visits, i.e. at 3 day and 7 day still the improvement was higher in Group 1 (Table 2).

Intragroup comparison shows that significant reduction in VAS score was seen after 7 days in Group 1 ($P < 0.05$) and it further improved and was maintained thereafter while in Group 2 significant reduction in VAS score ($P < 0.05$) was

observed only after 14 days and was maintained thereafter (Figures 2 and 3).

Table 3 shows the adverse effects encountered in different groups during follow-up visits. Adverse effects were more common among the patients who received the combination treatment. Most common adverse effect reported was sedation and dizziness in Group 1, but these side effects were tolerable, and none of the patients withdrew from the study because of adverse effects. Moreover, these adverse effects reduced both in incidence and severity with the duration of the study. In Group 2, the only complaint reported by the patients was gastrointestinal side effects.

Table 1: Demographic profile and disease characteristics at baseline

Characteristics	Group 1 (n=20)	Group 2 (n=20)	P value
Age			
Mean±SD	57.35±5.79	60.1±7.03	NS
Sex			
Male	12	10	NS
Female	8	10	NS
SES			
High	1	0	NA
Middle	18	18	NS
Low	1	2	NS
Diet			
Veg	7	8	NS
Non-veg	13	12	NS
Area of lesion			
Thoracic	6	6	NS
Lumbosacral	7	6	NS
Trigeminal	4	7	NS
Cervical	3	1	NS
Mean VAS score			
Mean±SD	7.45±1.39	7.25±1.45	NS

SD: Standard deviation, VAS: Visual analog scale, SES: Socioeconomic status, NS: Nonsignificant

Table 2: Comparison of VAS scores at each visit between Group 1 and Group 2

Days	Group 1	Group 2	P value
0	7.45±1.39	7.25±1.45	NS
3	6.55±1.23	6.6±1.27	NS
7	5.3±1.17	5.75±1.29	NS
14	3.45±1.14	4.25±1.55	<0.05
21	2.05±0.94	3.15±1.53	<0.05
28	1.15±0.87	2.35±1.46	<0.05

VAS: Visual analog scale

Table 3: Adverse drug effects

Drug effects	Group 1	Group 2
Sedation	15	0
Dizziness	11	0
Vertigo	8	0
Gastrointestinal side effects	4	5

DISCUSSION

The majority of patients with herpes zoster experience pain. Antiviral agents have been shown to decrease the duration of herpes zoster rash and the severity of pain associated with the rash.¹⁰ However, these benefits have only been demonstrated in patients who received antiviral agents within 72 h after the onset of rash. Moreover, antiviral agents may be beneficial as long as new lesions are

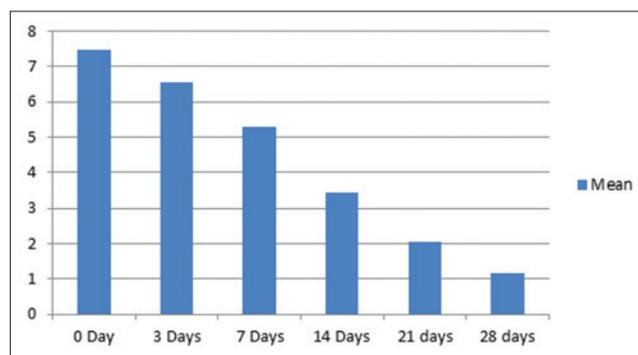


Figure 2: Mean visual analog scale score at each visit in Group 1

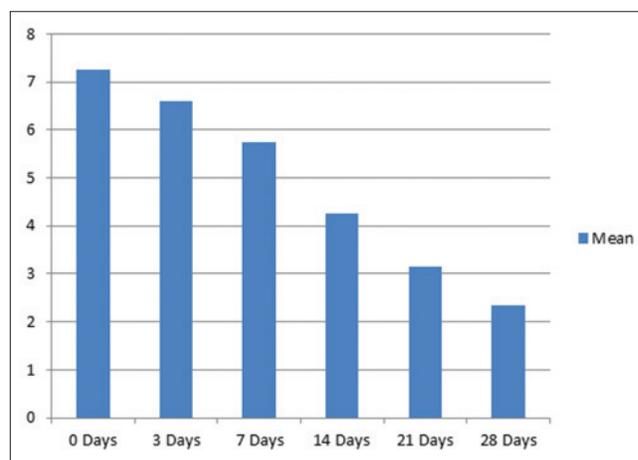


Figure 3: Mean visual analog scale score at each visit in Group 2

actively being formed, but they are unlikely to be helpful after lesions have crusted.

The primary treatment for acute zoster-associated pain includes narcotic and non-narcotic analgesics (both systemic and topical), neuroactive agents, and anticonvulsant agents. While the efficacy of these treatments for general neuropathic pain has been well established, only a few of these modalities have been evaluated specifically for acute zoster-associated pain in controlled studies.¹¹

The role of gabapentin in reducing the pain of PHN is well established.^{7,12,13} In most of the earlier studies, gabapentin was started after 30 days to 3 months from the onset of zoster. These studies showed significant role of gabapentin in the chronic pain of PHN. In our study, gabapentin was started within 72 h of rash onset. The results of the present study demonstrate that gabapentin in combination with valacyclovir was more effective ($P < 0.05$) in reducing the pain of acute herpes zoster when compared with valacyclovir alone. A study done by Sanjay Kanodia *et al.* observed that gabapentin in a dose of 600 mg is effective in acute herpetic neuralgia.¹⁴ In other study, Berry and Petersen observed 66% reduction of pain as compared to placebo by using single dose 900 mg of gabapentin.¹⁵ The results of our study are in accordance with the previous studies.

The present study shows that some patients experienced somnolence, dizziness, and gastrointestinal side effects in the gabapentin group but it was tolerable. Few earlier studies have also demonstrated the similar type of tolerability and safety profile, but the incidence of side effects was more in the present study.¹⁴ This variation could be because of the smaller sample size of our study.

Limitation of the Study

The sample size of the study was small, and it included only the elderly people, thus caution must be exercised while extrapolating the results.

CONCLUSION

The results of this study show that early initiation of gabapentin in combination with valacyclovir is safe and

effective for the management of herpes zoster and the pain associated with it. Further trials can be done in future enrolling more number of patients to confirm the findings of the present study.

ACKNOWLEDGMENT

The authors are thankful to the volunteer patients who have participated in the study.

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How to cite this article: Singh S, Madhwar A, Singh JP. Comparative Study of Gabapentin in Combination with Valacyclovir and Valacyclovir Alone in Herpes Zoster. *Int J Sci Stud* 2016;3(11):37-40.

Source of Support: Nil, **Conflict of Interest:** None declared.

Occurrence and Antimicrobial Susceptibility Pattern of Methicillin-resistant *Staphylococcus aureus* and Methicillin-resistant Coagulase-Negative Staphylococci Isolated from Different Clinical Specimens from the Patients Hospitalized in Teerthanker Mahaveer Medical College and Research Centre, Moradabad, India

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Abstract

Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant coagulase-negative staphylococci (MRCoNS) have been reported a public health problem globally. MRSA and MRCoNS are the most important infectious agent of the nosocomial infection, which is a major problem particularly in developing nations including India, where the burden of infectious diseases are high, and healthcare providing facilities are low. Rising percentage in the antimicrobial resistance of the methicillin-resistant staphylococci to the available anti-staphylococcal antibiotics is a growing problem in the Indian scenario.

Objective: This study was conducted to determine the occurrence and antimicrobial sensitivity pattern of MRSA and MRCoNS isolated from different clinical specimens.

Materials and Methods: MRSA and MRCoNS were identified among 400 staphylococcal isolates, isolated from various clinical specimens. All the isolates were identified as per Clinical and Laboratory Standards Institute guidelines and antimicrobial susceptibility pattern was determined by Kirby-Bauer disc diffusion method.

Results: A total of 400 staphylococcal isolates were processed, of which 347 isolates (86.75%) were coagulase-positive *S. aureus* and 53 isolates (13.25%) were CoNS, tested by both slide and tube coagulase test. Among 347 coagulase-positive *S. aureus*, 148 (42.65%) were MRSA, whereas among 53 CoNS, 28 (52.83%) were MRCoNS. Among MRSA isolates maximum resistance was seen with co-trimoxazole (91.89%) and least with vancomycin (0%). Among MRCoNS isolates maximum resistance was seen with both penicillin and co-trimoxazole (100%) and least with vancomycin (0%).

Conclusion: It is concluded that to preserve the value of vancomycin for the treatment of life-threatening staphylococcal infections in future, there is need of regular surveillance of MRSA and MRCoNS which is necessary for the appropriate guideline of antimicrobial therapy and to avoid the use of powerful antibiotics as initial infections.

Key words: Methicillin-resistant coagulase-negative staphylococci, Methicillin-resistant *Staphylococcus aureus*, Nosocomial infection, Vancomycin

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Month of Submission : 12-2015

Month of Peer Review : 01-2016

Month of Acceptance : 01-2016

Month of Publishing : 02-2016

INTRODUCTION

Staphylococci are Gram-positive cocci, arranged in grape-like clusters. They are non-motile, non-sporing, occasionally capsulated, and are facultative anaerobes that grow better

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under aerobic than anaerobic conditions. Staphylococci are classified as coagulase-positive *Staphylococcus aureus* and coagulase-negative staphylococci (CoNS).¹

S. aureus is one of the most important pathogen leading to cause diseases ranging from minor skin and soft tissue infections to life-threatening conditions.² CoNS previously considered as avirulent commensals have emerged as an important prevalent pathogen, especially as a cause of nosocomial infection.³ Bloodstream infections are the major causes of CoNS with increased morbidity and mortality.⁴

The term methicillin-resistant *S. aureus* (MRSA) and methicillin-resistant CoNS (MRCoNS) are used for the *S. aureus* and CoNS respectively, leads to the methicillin-resistance but now refers to a multi-drug resistant group and are susceptible only to glycopeptide antibiotics such as vancomycin.⁵

In the 1960s, methicillin was first introduced in human medicine for the treatment of infection caused by penicillin's resistant *S. aureus*.⁶ In 1961, in England, the first MRSA emerged.⁷

Methicillin-resistance among *S. aureus* and CoNS is caused by the *mecA* gene which encodes an altered penicillin-binding protein 2a with a low affinity for beta-lactam antibiotics including the penicillinase-resistant penicillin. A genetic element in which *mecA* gene is located called the staphylococcal cassette chromosome.⁸

The factors responsible for the emergence of resistant forms of staphylococci includes widespread use of antibiotics, prolonged hospital stay, lack of awareness, receipt of antibiotics before visiting the hospital, etc.⁹

MRSA and MRCoNS are considered as the most important cause of hospital-acquired infection (HAI) as well as community acquired infection (CAI) causing a wide range of diseases, leads to the increased mortality, morbidity, the length of hospital stay along with increased financial burden.¹⁰

Outbreaks of hospital-acquired MRSA are typically the result of nosocomial transmission of MRSA from patient to patient and colonized healthcare workers act as the reservoir for the spread of MRSA to uncolonized susceptible patients. Outbreaks of community-acquired MRSA reported worldwide.¹¹

The similar habitats are shared by MRSA and MRCoNS, both categories are colonizes to the anterior nares and different areas of skin and mucous membranes permanently

or transiently may play an important role as agents of subsequent bacteremia and some other infections.¹² It reported by Centers for Disease Control and Prevention that skin infections can be caused by MRSA among healthy newborns so health-care workers should be aware.¹³

Nosocomial or HAIs includes surgical wound infections, ventilator associated pneumonia, bacteremia associated with intravenous devices and other prosthetic materials such as cerebrospinal fluid (CSF) shunts, prosthetic joints, and the vascular graft. CAIs includes infections affecting the skin and soft tissue (e.g., boils, impetigo, cellulitis, and myositis), toxin-mediated disease (e.g., food poisoning and toxic shock syndrome), bones and joints infections, infections related to deep sites (e.g., endocarditis, abscess formation in liver, spleen and other sites) and infections related to the urinary tract and lungs.¹⁴

The treatment of infection caused by staphylococci has become very complicated due to the increasing resistance to various antibiotics, emphasize the need for better control of MRSA and other resistant bacteria for appropriate treatment within healthcare settings.

MATERIALS AND METHODS

Study Design

The study was conducted in Department of Microbiology, Teerthanker Mahaveer Medical College and Research Centre, Moradabad from March 2015 to February 2016.

The study included those patients from whom staphylococci have been isolated among different clinical samples submitted to Microbiology Laboratory for culture and sensitivity and excluded the specimens were staphylococci isolates have been considered contamination due to Laboratory or skin flora.

Isolation and Identification of Clinical Specimens

A total of 400 staphylococci isolates were obtained from various clinical specimens including pus, blood, urine, high vaginal swab (HVS), and CSF.

All the clinical specimens were collected from the patients, submitted to the microbiology laboratory for the sample processing according to standard protocols and the antimicrobial sensitivity was determined according to Clinical Laboratory Standard Institute (CLSI) guidelines.

BacT/alert culture bottles were used for the collection of blood and body fluids that are loaded in BacT/Alert three-dimensional (3D) system according to the manufacturer instructions. On the detection of growth in the BacT/alert 3D system, further sample processing was done.

Inoculation of all the clinical specimens and positively detected samples from BacT/alert 3D system was performed primarily on their respective culture plates and incubated aerobically at 37°C for 24 h. Further identification was carried out by conventional methods including colony characteristics, Gram-staining, catalase test, slide and tube coagulase test, growth on mannitol salt agar.

Antimicrobial Susceptibility Testing

The antibiotic susceptibility pattern of all the confirmed *S. aureus* and CoNS were determined by Kirby-Bauer disc diffusion method against the following antibiotics as per CLSI guidelines: Penicillin (10 µg), erythromycin (15 µg), clindamycin (2 µg), co-trimoxazole (25 µg), tetracycline (30 µg), levofloxacin (5 µg), gentamycin (10 µg), vancomycin (30 µg), linezolid (15 µg), oxacillin (1 µg), ciprofloxacin (5 µg), cefalexin (30 µg), rifampicin (5 µg), chloramphenicol (30 µg), ampicillin (10 µg), amoxy/clavulanic acid (20/10 µg), teicoplanin (30 µg), amikacin (30 µg), tobramycin (10 µg), amp/sulbactam (10/10 µg), and cefotaxime (30 µg).

Muller-Hinton agar used to perform all antimicrobial susceptibility tests, and the interpretation criteria were taken according to National Committee for Clinical Laboratory Standard (NCCLS).

Detection of MRSA and MR CoNS

Oxacillin (1 µg) disc diffusion method

The test was performed by Kirby-Bauer disc diffusion method by using 1 µg of oxacillin disc on Muller-Hinton agar plate incubated at 35-37°C for 24 h at. The interpretation criteria were taken according to (NCCLS) guidelines. If a zone of inhibition was <10 mm or any discernible growth within a zone of inhibition was used as an indicator for methicillin-resistant and ≥13 mm zone of diameter was indicative for methicillin susceptible.

Cefoxitin (30 µg) disc diffusion test

The isolated samples were subjected to cefoxitin disc diffusion test by using 30 µg discs. A suspension, equivalent to 0.5 McFarland standard was prepared from each strain. Then, a swab was taken and dipped into the suspension and lawn culture was done on MHA plate after that plate was incubated at 37°C for 18-24 h and zone of inhibition was measured.

An inhibition zone diameter of ≤21 mm was considered as cefoxitin resistant reported as methicillin-resistant and ≥22 mm was reported as cefoxitin sensitive indicating methicillin-sensitive.

Statistical Analysis

The data were recorded and analyzed using Microsoft Excel (2007 Version). Results are presented in frequency (number) and percentage (%).

RESULTS

In our study, 400 staphylococcal isolates were collected from various clinical specimens among the patients hospitalized in Teerthanker Mahaveer Medical College and Research Centre, Moradabad, Uttar Pradesh, India.

The highest percentage of staphylococcal isolates was obtained from pus samples (38%), followed by blood (33.5%), urine (24%), HVS (3%), and CSF (2%) (Figure 1) (Table 1).

Out of 400 staphylococcal isolates tested, 347 isolates (86.75%) were coagulase positive *S. aureus* and 53 isolates (13.25%) were CoNS, tested by slide and tube coagulase test. Among 347 coagulase positive *S. aureus*, 148 (42.65%) were methicillin-resistant, and among 53 CoNS, 28 (52.83%) were methicillin-resistant.

The occurrence of MRSA and MRCoNS were significantly variable among different clinical samples. Among 148 MRSA isolates highest percentage was obtained from blood 43.24% (64/148), followed by pus 35.13% (52/148), urine 18.24% (27/148), CSF 2.70% (4/148), and HVS 0.67% (1/148). Among 28 MRCoNS highest percentage was obtained from blood 46.42% (13/28), followed by pus 25% (7/28), urine 24% (6/28), and HVS 3.57% (1/28) (Figure 2) (Table 2).

Among 148 MRSA isolates, 72 (48.65%) were from male patients and 76 (51.35%) were from female patients. Among 72 MRSA isolated from male patients, maximum 27 (37.5%) were obtained from 0 to 10 age group whereas, among 76 MRSA isolated from female patients, maximum 24 (31.58%) were obtained from 21 to 30 age group.

Out of 28 MRCoNS isolates, 9 (32.14%) were from male patients and 19 (67.85%) were from female patients. Among 9 MRCoNS isolated from male patients, maximum 3 (33.33%) belonged to (0-10) age group whereas, among 19 MRCoNS isolated from female patients, maximum 6 (31.58%) belonged to (0-10) age group (Figure 3) (Table 3).

MRSA and MRCoNS isolates show different antimicrobial susceptibility pattern against agents of different classes.

Table 1: Distribution of staphylococcal isolates from different clinical specimens

Clinical specimens	Number of staphylococcal isolates	Percentage
Pus	152	38
Blood	134	33.5
Urine	96	24
HVS	12	3
CSF	6	2
Total	400	100

HVS: High vaginal swab, CSF: Cerebrospinal fluid

Table 2: Isolation of coagulase positive and coagulase negative staphylococci from various clinical specimens

Clinical specimens	Number of <i>S. aureus</i>	MRSA n (%)	MSSA n (%)	Number of CoNS	MRCoNS n (%)	MSCoNS n (%)
Pus	137	52 (35.13)	85 (42.75)	15	7 (25)	8 (32)
Blood	113	64 (43.24)	49 (24.62)	21	13 (46.42)	8 (32)
Urine	83	27 (18.24)	56 (28.14)	13	7 (25)	6 (24)
HVS	8	1 (0.67)	7 (3.52)	4	1 (3.57)	3 (12)
CSF	6	4 (2.70)	2 (1.01)	0	0 (00)	0 (00)
Total	347	148 (42.65)	199 (57.35)	53	28 (52.83)	25 (47.17)

MRSA: Methicillin-resistant *Staphylococcus aureus*, MRCoNS: Methicillin-resistant coagulase-negative staphylococci, HVS: High vaginal swab, CSF: Cerebrospinal fluid

Table 3: Age and sex distribution of MRSA and MRCoNS isolates

Age group	Total number of MRSA	Male	Female	Male-female ratio	Total number of MRCoNS	Male	Female	Male-female ratio
0-10	48	27	21	9:7	9	3	6	1:2
11-20	27	12	15	4:5	3	1	2	1:2
21-30	36	12	24	1:2	7	2	5	2:5
31-40	9	3	6	1:2	2	0	2	0:2
41-50	10	6	4	3:2	2	1	1	1:1
51-60	9	6	3	2:1	3	1	2	1:2
61-70	7	5	2	5:2	1	1	0	1:0
71-80	2	1	1	1:1	1	0	1	0:1
Total	148	72	76	18:19	28	9	19	1:2

MRSA: Methicillin-resistant *Staphylococcus aureus*, MRCoNS: Methicillin-resistant coagulase-negative staphylococci, HVS: High vaginal swab, CSF: Cerebrospinal fluid

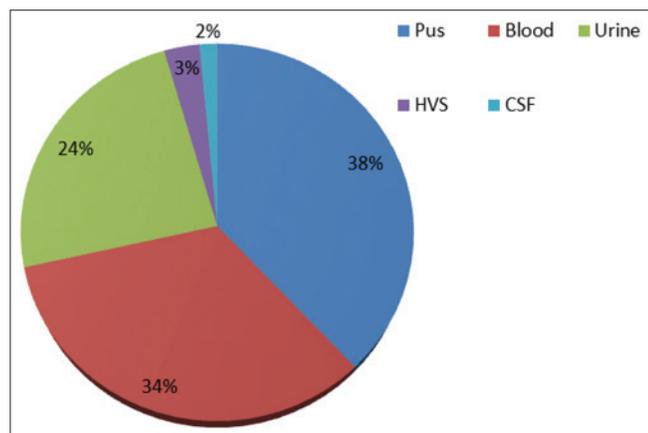


Figure 1: Distribution of staphylococci among different clinical specimens

It was observed that MRSA isolated from various clinical samples show highly variable drug resistant pattern whereas nearly similar drug resistant was shown by MRCoNS.

Among MRSA isolates maximum resistance was seen with co-trimoxazole (91.89%), followed by penicillin-G (89.19%) and least with vancomycin (0%), followed by linezolid (5.40%). Among MRCoNS isolates maximum resistance was seen with both penicillin-G and co-trimoxazole (100%), followed by amoxicillin (89.28%) and least with vancomycin (0%), followed by teicoplanin (10.71%) (Figure 4) (Table 4).

Table 4: Antimicrobial resistance pattern of MRSA and MRCoNS isolates

Antibiotics	MRSA (n=148)	MRSA (%)	MRCoNS (n=28)	MRCoNS (%)
Co-trimoxazole	136	91.89	28	100
Penicillin-G	132	89.19	28	100
Amoxicillin	132	89.19	25	89.28
Cefalexin	128	86.40	24	85.71
Ampicillin	127	85.87	25	89.28
Amoxy/clavulanic acid	121	81.67	24	85.71
Ciprofloxacin	116	78.38	21	75
Erythromycin	109	73.65	24	85.17
Ofloxacin	104	70.27	16	57.14
Levofloxacin	93	62.84	20	71.43
Gentamycin	88	59.46	16	57.14
Cefotaxime	80	54.05	21	75
Amp/Sulbactam	76	51.35	24	85.71
Clindamycin	71	47.97	20	71.43
Chloramphenicol	65	43.91	16	57.14
Tetracyclin	64	43.24	13	46.42
Tobramycin	53	35.81	23	82.14
Refampicin	40	27.03	16	57.14
Amikacin	24	16.22	11	39.28
Teicoplanin	15	10.13	3	10.71
Linezolid	8	5.40	5	17.86
Vancomycin	0	00	0	00

MRSA: Methicillin-resistant *Staphylococcus aureus*, MRCoNS: Methicillin-resistant Coagulase-Negative staphylococci

DISCUSSION

Among hospitalized patients *S. aureus* has been noted as the most important causative agent of wound infection.

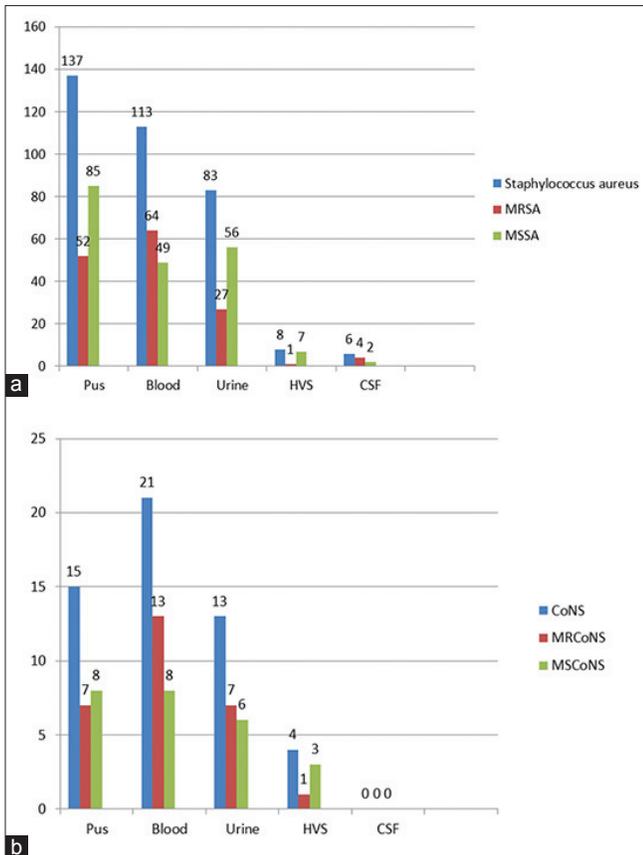


Figure 2: (a) Isolation of coagulase positive staphylococci from different clinical specimens, (b) isolation of coagulase negative staphylococci from different clinical specimens

CoNS are a group of an opportunistic pathogen that causes a wide range of diseases in hospitalized patients.¹⁵

The growing concern in the Indian scenario about the rapid increases in the resistance of *S. aureus* and CoNS to various antimicrobial agents. MRSA and MRCoNS have been recognized as the predominant pathogen among hospitalized patients with increased morbidity and mortality.¹⁶

The earlier studies were reported to MRSA of concern but during 1970s it became clear that the occurrence of methicillin resistance was higher in CoNS (MRCoNS) than in *S. aureus* (MRSA),¹⁷ in our study it has become true in a continuous manner. The present study shows low occurrence rate of MRSA, which is 42.65% than MRCoNS which is 52.83% reported that methicillin resistance seen in CoNS (MRCoNS) was higher than *S. aureus* (MRSA).

The occurrence of MRSA in different regions of India varies according to the INSAR (Indian Network of Surveillance of Antimicrobial Resistance) group,¹⁸ a multi-hospital based study in various part of India shown that

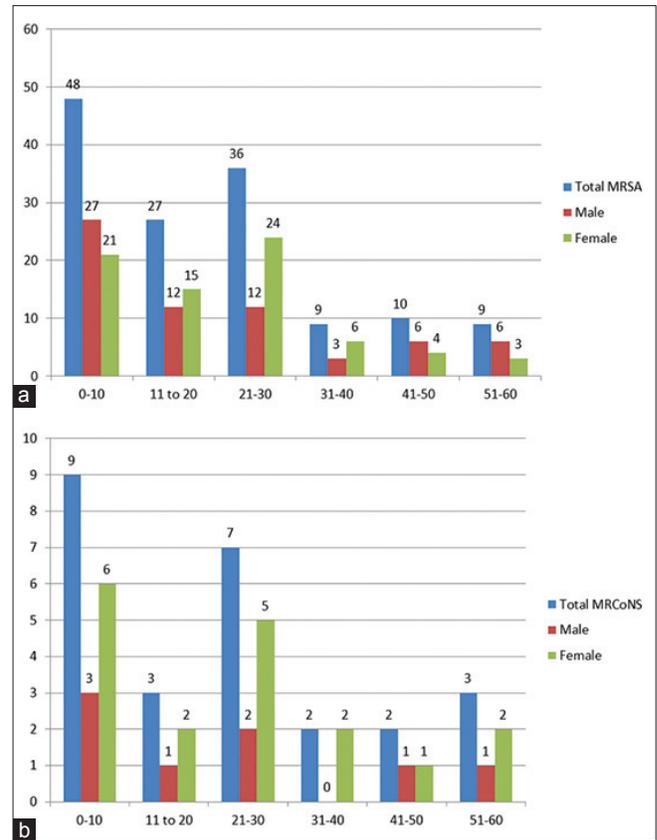


Figure 3: (a) Age and sex distribution of methicillin-resistant *Staphylococcus aureus* isolates, (b) age and sex distribution of methicillin-resistant coagulase-negative staphylococci isolates

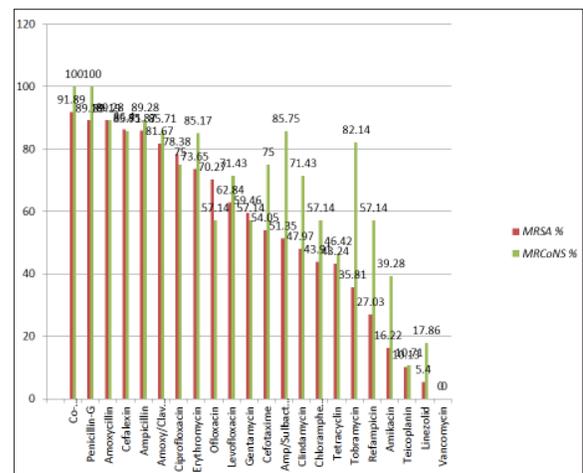


Figure 4: Antimicrobial resistance pattern of methicillin-resistant *Staphylococcus aureus* and methicillin-resistant coagulase-negative staphylococci isolates

the overall MRSA occurrence in India was 42% in 2008 and 40% in 2009.

In a study at Aligarh, India¹⁹ it was shown that 35.1% of *S. aureus* and 22.5% of CoNS isolates were resistant to methicillin which is low as compared to our study. Anila A. Mathew has reported an occurrence rate of MRSA of

about 34% in the clinical specimen and occurrence rate of MRSA in Eastern U.P. and AIIMS in New Delhi, were 54.85% and 44% respectively.²⁰ In our study MRSA was 42.65% which is accordance with the similar findings of MRSA in AIIMS, New Delhi.

Few studies from India has reported slightly higher occurrence rate of MRSA as compared to our study such as 46% by Arora *et al.*,²¹ from Amritsar, 48.72% by Deepa *et al.*,²² from Mysore, South India, 51.6% by Vidhani *et al.*,²³ from New Delhi, 54.85% by Anupurba *et al.*, from Banaras Hindu University.²⁴

In another study in Nagpur in November-1999 to October-2000, the rate of MRSA was 19.5% which is low as compared to this study.⁹ MRCoNS in our study was 52.83% which is average than other studies from India, ranging from 22.5 to 73.5%.²⁵

This variation in the occurrence of methicillin resistance among staphylococci is due to the various factors as the availability of healthcare facilities in a particular hospital, implementation, and monitoring of infection control policy, antimicrobial therapy that play a different role from hospital to hospital.

The occurrence of MRSA and MRCoNS were noted variable among different clinical specimens. Out of 148 MRSA and 28 MRCoNS, the highest percentage of MRSA 43.24% (64/148) and MRCoNS 46.42% (13/28) were obtained from blood. The similar findings also reported by Anbumani at Chennai,²⁶ according to which maximum isolates of MRSA were from blood specimen compared to pus. Our study shows that females are more susceptible to MRSA and MRCoNS infections than males.

In the present study, MRSA and MRCoNS represents variable drug resistant pattern. MRSA isolates shows the highest resistance to co-trimoxazole (91.89%) followed by penicillin-G (89.19%), whereas MRCoNS isolates shows the highest resistance to both penicillin-G and co-trimoxazole (100%). All tested MRSA and MRCoNS shows no resistance to vancomycin. These results agreed with many other studies in the world mentioned that vancomycin was the first drug of choice to methicillin-resistant staphylococci for example in the study done by Von Eiff *et al.*,²⁷ and by Calderon-Jaimes *et al.*²⁸

Most of the MRSA and MRCoNS showed multidrug resistance that makes difficult to treat the infection. Hence, it is necessary to evaluate the drug resistant pattern against MRSA and MRCoNS for controlling the nosocomial infections in an effective manner.

CONCLUSION

In our study, it is concluded that in our hospital the occurrence of methicillin resistance is higher in both *S. aureus* and CoNS that is worrisome in the present therapeutic scenario. Females are more susceptible to both MRSA and MRCoNS infections as compared to males.

According to our study, most of the MRSA and MRCoNS isolates shows the high level of resistance against widely used antimicrobial agents. Although both MRSA and MRCoNS show no resistance to vancomycin.

Vancomycin is the first drug of choice for the treatment of infections caused by MRSA and MRCoNS and to preserve its value we should avoid the use of vancomycin as initial treatment and save it for the treatment of life-threatening infections caused by staphylococci. Linezolid and teicoplanin also show low resistance to both MRSA and MRCoNS so they can also play an important role in the treatment of staphylococcal infections.

In this study, both MRSA and MRCoNS shows higher resistance to co-trimoxazole, penicillin-G, amoxicillin, cefalexin, ampicillin so these are less effective in the treatment of MRSA and MRCoNS infections.

As of multidrug-resistant nature of both MRSA and MRCoNS, the infection control committee of the hospital should want to recommend continuous surveillance of hospital-associated infection and want to take strict infection control policy to eradicate infections caused by MRSA and MRCoNS.

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How to cite this article: Ahmed R, Singh S, Farooq U, Bharti AK, Kaur N. Occurrence and Antimicrobial Susceptibility Pattern of Methicillin-resistant *Staphylococcus Aureus* and Methicillin-resistant Coagulase-Negative Staphylococci Isolated from Different Clinical Specimens from the Patients Hospitalized in Teerthanker Mahaveer Medical College and Research Centre, Moradabad, India. *Int J Sci Stud* 2016;3(11):41-47.

Source of Support: Nil, **Conflict of Interest:** None declared.

Evaluation of Patient Satisfaction Based on Communication Skills of Dentists in Mumbai City: A Cross-Sectional Questionnaire Based Survey

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Abstract

Background: Soft skills are skills people use to communicate, solve problems, lead and think creatively in contrast to hard skills, which are an object, machines, tools and are technically oriented. They help to organize, plan, and manage health care better. They are one of the key factors in successful dental practice. Soft skills increase confidence, professionalism, coordination, friendliness, and optimism in an individual to greater extent. The present study is designed to assess soft skills of dentists in Navi Mumbai.

Methods: The present study is a cross-sectional questionnaire-based study carried out in the month of July and August 2015 among the patients visiting the private clinic in and around Navi Mumbai. A sample size of the study was 420. Frequency and percentage of responses to each question were reported.

Results: The majority of the respondents (73%) felt that they were explained their treatment satisfactorily. Majority of respondents (94.5%) people felt sufficiently involved in their treatment but, 5.5% patients felt they didn't have a say in the treatment they received.

Conclusion: The present study showed that 73% dentist explained and answered patients' quires beyond the expectation of the patients. 76.1% felt that dentists met their expectations in being supportive and understanding their experience. It is a very necessary to understand the patient psychology and accordingly formulate a treatment that meets their requirements. By making our patients fully informed partners in the care we provide, we ensure that the gesture is returned by being loyal and continuing care with us.

Key words: Dentists, Navi Mumbai, Patient satisfaction, Soft skills

INTRODUCTION

A soft skill is the ability to make use of one's knowledge readily and effectively. One must have the ability to be discerning to be competent in one's skill. Skills can be learned and are essential in the everyday function of organizations. Soft or social skills are those personal values and interpersonal skills that determine a person's ability

to fit in a particular structure such as a project team or a company. Perrault defined soft skills as personal qualities, attributes or the level of commitment of an individual that sets him apart from other individuals who may have similar skills and experience.¹ The soft skills are skills people use to communicate, solve problems, lead and think creatively in contrast to hard skills, which are object, machines, tools and are technically oriented. As introduced, there is no definition based on the functionally soft skills. Soft skills are used in personal and professional life. The soft skills help to organize, plan, and manage the changes during the course of growing dental practice. Soft skills increase confidence, professionalism, coordination, friendliness, and optimism in an individual to greater extent. According to the survey of North America, organizational culture and motivational fit are more toward 31% and critical reasoning

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Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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and judgment with interpersonal behavior is 21% and 26%, respectively. Technical skills contribute around 12% and 10% of relevant experience.²

There are various types of soft skills like positive attitude which includes helping hand for personal relationship, positive and good approach for optimistic behavior; self-confidence which is a need to project a sense of calm and inspire confidence in others to build-up positive skill and energy; work ethics which includes highly motivated and dedicated persons to do their best work; teamwork which is a need to take a leadership role and form co-operative group or teams; good communication skills which says they should be good listeners, verbally active to communicate with colleagues, patients, customers and express their needs to the concerned personally; time management skills are essential to use time on job wisely. They should be able to work confidently on different projects and priorities the task accordingly; problem-solving skills teach to take the responsibility and initiative to creatively solve problems; flexibility and adaptability teaches to be strong enough to adapt to new situations and challenges to embrace the change and be open to accept the new ideas.²

Knowing the importance of soft skills in dentistry, which could affect the patient satisfaction, the present study was planned with objective to investigate the effect of soft skills of dentists on patient's perception of quality.

METHODS

The present study is a cross-sectional questionnaire-based study carried out in the month of July and August 2015, among the patients visiting the private clinic in and around Navi Mumbai. The patients were randomly selected. Prior to the start of study, necessary permissions were taken from the Head of Department, Institutional Research Board of YMT Dental College, Kharghar.

A questionnaire consisting of 10 questions was distributed among people who had visited private dental practitioners wherein one or more treatment was rendered by the dentist and not by the associates or consultants. They were met personally and a questionnaire was filled in the same meeting.

Sample Size

Since there was no prevalent data from the literature available, the sample size was determined using single proportion formula; where 50% was taken as the level of communication skill. Thus, the sample size determined was 384 for a population of 10,000-1,000,000 and hence, rounding to 400.

Pilot Study

Content, construct validity of questions was checked in a pilot study done on 25 randomly selected patients who visited the outpatient department at a dental college in Navi Mumbai. These 25 patients were not included in final study. After conducting the pilot study, a thorough discussion with an expert to check the inherent flaws in the designing of questionnaire, and corrections were made accordingly.

Data Collection

Patients above the age of 20 years, who were willing to participate and who gave a verbal and written consent to participate in the study were included in the present study. A participation was voluntary and anonymous. There were no limitations to inclusion of patients based on gender, caste, and religion and socio-economic status.

Instrument to assess soft skill was self-designed pretested questionnaire consisting of 10 questions. All questions were in English however during the time of interview communication was facilitated in local language by the investigators. The questionnaire was restricted to 10 questions to prevent patient fatigue and to get the most genuine response.

Statistical Analysis

The questionnaire forms which were collected back were screened for completeness. Any unfilled or partially filled forms were discarded. All forms which were to be included in the final analysis were numbered serially. All questions and options were coded numerically and data obtained was compiled on MS Office Excel Sheet 2010. Data were analyzed by Statistical Package for Social Sciences V22.0, IBM. Results are presented as frequency and percentage of responses to each question.

RESULTS

In the present study, a total of around 420 questionnaires were distributed and 402 were received back, giving a response rate of the survey was 95.14% (Table 1).

Among the respondent's, 315 (78.4%) responded that they were referred by a friend or relative, whereas only 32 (8%) said that they followed advertisements while selecting their dentists. About 46% patients visited dentists because they experienced pain followed by 19.2% went for routine check-up.

The majority of the respondents (73%) felt that they were explained their treatment satisfactorily, whereas only

Table 1: Responses of patients to various questions

Q. No	Questions	Options	Frequency	Percentage
1	How did you come to know about your dentist?	Via a friend or relative	315	78.4
		Friend and advertisements and hoardings	1	0.2
		Advertisements and hoardings	32	8
		Referred by another doctor	54	13.4
2	Reason for visiting the dentist	Pain	185	46
		General check up	77	19.2
		Gum problems	53	13.2
		Extraction	34	8.5
		Replacement of missing teeth	33	8.2
		Others	15	3.7
		Pain and check up	1	0.2
		Check up and gum problems	1	0.2
		Check up and extraction	1	0.2
		Check-up and others	1	0.2
		Extraction and replacement	1	0.2
3	Did the dentist explain your treatment answer your questions and listen to your concerns?	Beyond expectation	97	24.1
		Met expectation	293	72.9
		Below expectation	12	3
4	Did you feel your dentist was supportive and understood what you were trying to feel and experience?	Beyond expectation	87	21.6
		Met expectation	306	76.1
		Below expectation	9	2.2
5	Did you feel involved in your treatment?	Beyond expectation	88	21.9
		Met expectation	292	72.6
		Below expectation	22	5.5
6	Discomforts (if any) were they attended positively?	Beyond expectation	90	22.4
		Met expectation	271	67.4
		Below expectation	32	8.0
		None	9	2.2
7	On follow-up visits (if needed) how was care provided?	Beyond expectation	93	23.1
		Met expectation	276	68.7
		Below expectation	19	4.7
		None	14	3.5
8	Were you happy with how the staff/associates treated you?	Beyond expectation	87	21.6
		Met expectation	297	73.9
		Below expectation	18	4.5
9	Rate your experience	Excellent	67	16.7
		Very good	177	44.0
		Good	134	33.3
		Average	24	6.0
		Poor	0	0.0
10	Reason for dissatisfaction	Appointment time slots	40	10
		Multiple visits	84	20.9
		Longer waiting duration	80	19.9
		Overpriced treatments	61	15.2
		Appointment time slots and multiple visits	5	1.2
		Appointment time slots, multiple visits and longer waiting duration	1	0.2
		Multiple visit and longer duration	3	0.7
		Multiple visit, longer duration, and overpriced	1	0.2
		Multiple visit and overpriced treatments	5	1.2
		Longer waiting and overpriced	3	0.7
		Others	48	11.9
		Multiple visit and others	1	0.2
		None	70	17.4

minimum of 3% was not satisfied and 24% got more than what they expected.

A total of 306 patients (76%) felt that the dentist was supportive enough and understood them; however, the percent of people who were satisfied beyond expectation dropped to 21% (Q. No. 4).

The majority of respondents (94.5%) people felt sufficiently involved in their treatment but, 5.5% patients felt they did not have a say in the treatment they received. (Q. No. 5). Close to 89.8% patients felt their discomforts were taken care of during the treatment. The number of dissatisfied patients rises to 8% here and only 2% patients out of 402 experienced no discomforts (Q. No. 6).

On follow-up visits, 68.7% patients were provided care that met their expectations and 23.1% experienced care that was beyond their expectation but 5% were still not happy (Q. No. 7) Around 74% patients were happy by the way; they were greeted and treated by the staff and associates and 4.5% were unhappy (Q. No. 8).

About 44% (171/402) rated their experience as very good, followed by 33.3% (134/402) who said it was good, close to 17% said it was excellent and only minimum of 6% said it was average. None of the patients said it was poor (Q. No. 9).

Main reason for dissatisfaction noted were multiple visits at 20.9%, longer waiting durations at 20%, overpriced treatments at 15%, and appointment time slots of the dentist at 10%. However, 17% patients said there was no reason for dissatisfaction (Q. No. 10).

DISCUSSION

Health care today is becoming more patient centered and as a result patient's experience of care and assessment of satisfaction level have to be taken more seriously as it influences the treatment cooperation and leads to overall better prognosis and healthier relations on the long term.³ According to Holt and McHugh study, the main reason for changing dentist among many patients in their survey was dentist's interpersonal attributes⁴ and yet sufficient literature has not been recorded in this field and hence we decided to carry out a study highlighting the importance of soft skills of a dentist for having happy and satisfied patients.

Satisfaction is a person's feeling of pleasure or disappointment resulting from comparing a products perceived performance or outcome in relation to his or her expectation.⁵

Soft skills, a cluster of personality traits, as mentioned before are also a measure of one's emotional intelligence quotient and plays a vital role in contributing to the success of a practice.

The six basic expectations of a patient from their dentist are: Friendliness, empathy, efficiency and punctuality, control, options and alternatives and information.⁶

In our survey, we identified that a majority of patients go to a dentist only when recommendation comes by relative or a friend which is an indication of a past good experience with the dentist. A friendly and approachable dentist is always preferred over a rude or insensitive one.

Communication skills of a dentist in terms of explaining the treatment, answering questions and listening properly

to the patients concerns without interrupting them is also important. Barnes found the dentist's willingness to talk to patients and sensitivity expressed toward children to be important criteria in assessment.⁷

Since about 70% patients said that their needs meet expectations, it suggests that a considerable number of dentists did communicate well, however, there is still room for improvement, and we recommend spending more time with patients at their initial visit.

Empathizing with the patient and listening to them attentively will very often tell you what the patient needs. This was also demonstrated in survey by Rezi which stated that the likelihood of overall satisfaction was found to be significantly and independently increased by the physician's ability to give explanations and to show empathy for the patient's conditions⁸ It is also very important to communicate it back to the patient that the problem has been understood and using his critical thinking skills find a solution that meets his patient's needs.

Treating a patient as a whole and not merely the disease, giving them options and alternatives and making them a part of their treatment planning, makes them feel they have control over the situation and are not merely guinea pigs in our hands goes a long way in enhancing their experience regarding dental visits. According to Harris Interactive health-care poll, 85% of those polled said treating a patient with dignity and respect is an extremely important quality in a doctor, and 85% cited listening carefully and being easy to talk to as important qualities.⁹

There was a marked increase in the level of dissatisfaction of patients when it came to managing discomforts during treatments and while following up with patients especially in the event of complications, dentists need to be humane and compassionate, positively reassuring the patient, being calm while working and providing symptomatic care whenever in necessary. A sincere apology in an event of an error would go a long way in strengthening relations, reinforcing displaced trust and avoiding medico-legal complications.

A pleasant dental experience is a team approach. Training the receptionist to greet the patients, asking him, how was his appointment while concluding his visit, making follow-up calls if discomfort is anticipated, properly conversing over the telephone and avoiding any miscommunications, help build relations with the whole team and make them feel more comfortable.

An average of 20% patients has marked the option of beyond expectation in questions related to soft skills of a

dentist and the same is reflected on the number of patients marking excellent. This clearly reflects that better the soft skills, happier the patients. Holt and McHugh found the most important factor influencing dentist/practice loyalty to be “care and attention” rated as very important by 90% of respondents.⁴ Corah *et al.*, pointed out those evaluations of technical competence (measured by asking patients to respond to statements such as: “The dentist was thorough in doing the procedure” and “I was satisfied with what the dentist did”) are most likely based on interpersonal factors such as “communication” and “caring” and “information-giving.”¹⁰

CONCLUSION

Within the limitations of the present study, we conclude that soft skills form an integral part of a dentist’s personality and needs to be mastered not only as a person but as a team (i.e., with associates and staff) for a successful practice with happy patients.

Patients perceive service quality by comparing their expectations to actual experience. It is very necessary to understand the patient psychology and accordingly formulate a treatment that meets their requirements. Putting it simply if the patient perceives care at a certain level but expected something more different, and then they will be dissatisfied. Both perception and expectation are states of mind and we as dentists need to understand this interrelation to keep our patients happy.

By making our patients fully informed partners in the care we provide, we ensure that the gesture is returned by being loyal and continuing care with us. Work satisfaction, renewed motivation and increased productivity can be achieved by using effective communication skills. While doing so also make sure you as a professional convey to

the patient what you feel is the best plan for them and also any compromises if expected.

We recommend monitoring social media as negative feedback is more frequently and freely written publicly in these websites than is communicated to the dentist in person.

We recommend that a workshop on developing soft skills and communication skills should be a part of the undergraduate curriculum and also promote the same as continuing dental education/continuing medical education events.

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How to cite this article: Rambhia M, Shah K, Bhate P, Kalra D, Rajeev H. Evaluation of Patient Satisfaction Based On Communication Skills of Dentists in Mumbai City: A Cross-Sectional Questionnaire Based Survey. *Int J Sci Stud* 2016;3(11):48-52.

Source of Support: Nil, **Conflict of Interest:** None declared.

Abdominal Surgical Site Infection Occurrence and Risk Factors in Krishna Institute of Medical Science, Karad

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Abstract

Introduction: Surgical site infections (SSI) tend to be the most common problem following an operation and the third most frequently reported nosocomial infections.

Objective: The current study was undertaken to identify the occurrence of SSI and the risk factors associated with it, and the common organism isolated and its antibiotic sensitivity and resistance.

Materials and Methods: This proposed study was carried out as a prospective, randomized clinical trial in 100 patients. Infected samples from patients were collected by following all aseptic precautions and are processed without delay by the standard microbiological techniques.

Results and Conclusions: 14% was the total infection rate. The SSI rate was the highest in dirty surgeries (40%). Male patients were affected more (18.2%) than the female patients (5.9%). The SSI rate increased with increasing age and it also increased significantly with the increasing duration of pre-operative hospitalization. The SSI rate was higher in emergency surgeries as compared to the elective. With increase in the time of surgery, the risk of infection increased. The most commonly isolated organism from SSIs was *Pseudomonas* (42.85%), followed by *Klebsiella* sp. (28.5%) and other bacteria. Among the organisms that were isolated, the most of them were multidrug resistant.

Key words: Abdominal surgical site infections, Risk factors for surgical site infections, Antibiotic sensitivity and resistance, Nosocomial infection

INTRODUCTION

Our skin is filled with landmines, little bacterial bombs just lying in wait for the right moment to explode into action. As long as we are healthy it is thwarted; a person who is ill, however, may a compromised immune system incapable of raising a defense. A surgical incision is all that bacteria needs for the battle to begin. Surgical infections are the result of

any surgical procedure. These infections are associated with greater morbidity, mortality, and healthcare cost.¹

Surgical site infections (SSI) can double the length of time a patient stays in hospital and thereby increase the costs of health care. The healthcare costs are due to re-operation, extra nursing care and interventions, and drug treatment. The factors which influence SSI are characteristics of the patient, operation, personnel, and hospital.²

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Month of Submission : 12-2015
 Month of Peer Review : 01-2016
 Month of Acceptance : 01-2016
 Month of Publishing : 02-2016

METHODOLOGY

Source of Data

The material for the present study is obtained from patient's undergone abdominal surgery in Department of General Surgery, Krishna Institute of Medical Science, Karad, from

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1st November 2013 to 1st November 2015. The surgical site was considered as infected according to the definition by nosocomial infection surveillance. The wounds are classified according to the wound contamination class system. 100 patients who fulfilled the inclusion criteria were included in the study.

Inclusion Criteria

1. Only those who have undergone abdominal surgeries in Krishna Institute of Medical Science Hospital, Karad were included.

Exclusion Criteria

1. Patient with previous abdominal surgery
2. Wound site previously infected
3. Stitch abscess cases.

Method of Collection of Data

A detailed history of the patients about the presentation of the wound, type of surgery, emergency or elective, pre-operative preparation, and post-operative management was done until the patient is discharged from the hospital, and then followed up the patient on outpatient department basis for any signs of wound infection.

In history, presenting complaints, duration, associated diseases, and coexistent infections at a remote body site, personal history including diet, smoking, and history of alcohol consumption were noted. Pre-operative findings that include bathing and skin preparation, pre-operative abdominal skin culture, nasal swab for culture for commensals, and pre-operative antibiotics use. Operative findings include type of incision, wound contamination, drain used and its type, and duration of the operation.

Post-operative findings include the day of wound infection, the day of 1st dressing, and frequency of change of dressing. A condition of the wound on the day of diagnosis of wound infection is noted which included fever, erythema, discharge, type, and color shown Figures 1 and 2, and the exudates were collected from the depth of the wound using a sterile cotton swab and was sent to the microbiology department for culture and sensitivity.

RESULTS

This study included 100 patients who underwent abdominal surgery, out of which 14 were infected. So, the occurrence is 14%. The incidence of infection among males is 18.2%, whereas the incidence of infection among females is 5.9%. SSI is more commonly found in the age group 0 above 61-year-old patients with an incidence of 28.6%. Mean age being 58.29 years with standard deviation of ± 11.15 . The incidence of infection among emergency surgery is 26.3% and among elective is 6.5%.



Figure 1: Infected post-operative wound with pus discharge

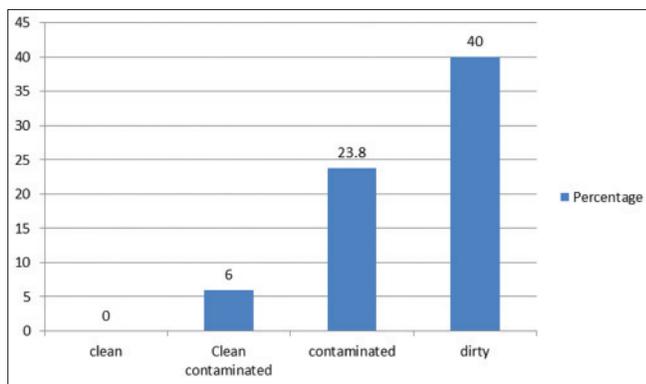


Figure 2: Wound dehiscence

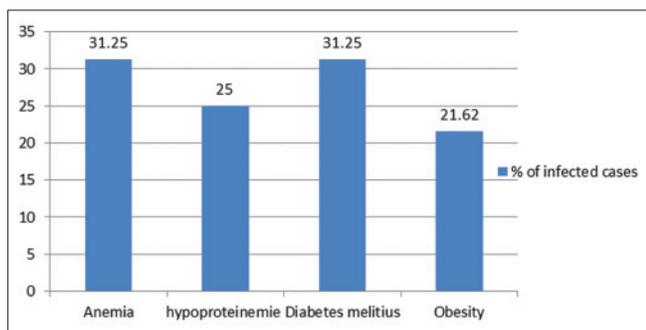
Out of 100 cases, 14 were clean cases with no infection, 50 were clean contaminated with 6% incidence of infection, 21 were contaminated that had 23.8% SSI, and 15 were dirty cases, wherein the infection rate was 40% as shown in Graph 1. Most of the patients had body mass index (BMI) of 20.1-25, followed by 25-30. The incidence of infection was more in an extreme of the BMI that is 31.25% in >30 BMI group and 7.69% in <20 BMI group. The infection rate in patients with anemia is 31.25%, hypoproteinemia is 25% and in patients with diabetes mellitus is 31.25%, shown Graph 2. The most common risk factor for infection in elective cases is obesity and in emergency cases is the dirty type of SSI.

Acute/chronic appendicitis and duodenal perforation were the most common operations performed. SSI was more among patients with acute necrotizing pancreatitis, duodenal perforation, carcinoma caecum, and chronic cholecystitis. The incidence of infection in the cases with a duration of surgery <1.5 h is 5.1% and with 1.5-4 h is 26.8%. The incidence of infection increased with the duration of the procedure.

In most cases, wound infection was seen on the 5th post-operative day. Out of 14 infected cases, 6 cases had



Graph 1: Percentage of incidence in relation to type of surgical site infections

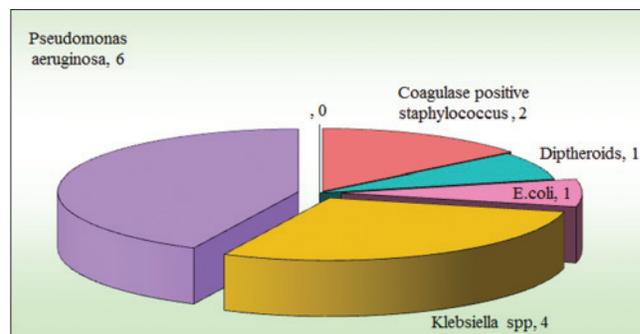


Graph 2: Percentage of incidence in relation to risk factors

Pseudomonas infection, 4 had *Klebsiella*, 2 had coagulase positive staphylococci, 1 had *Escherichia coli*, and 1 had diphtheroid infection as shown in Pie Chart 1. *Pseudomonas* was the most common organism isolated. The most of the organisms were sensitive to cefoperazone/sulbactam (64.2%) and cefepime (57.1%) and were resistant to tigecycline (57.1%) antibiotic followed by piperacillin/tazobactam, colistin, and amikacin.

DISCUSSION

100 cases are included in this study; the SSI incidence was 14%, which is well above the 14-16% reported in other studies.³ The Indian hospitals have much higher rate of infection than other countries such as USA (2.8%) and European countries (2-5%).⁴ The higher infection rate in Indian hospitals may be due to the poor set up of our hospitals and also due to the lack of attention toward the basic infection control measures. The infection rate is the highest (28.6%) in patients above 60 years. More the age, more are the chances for certain chronic conditions, malnutrition and decrease in immunological efficiency, leading to more SSI.⁵ SSI is not related to sex,⁶ in agreement with previous findings. The literature shows that SSI increases with obesity. In this study, it is found that both



Pie Chart 1: Number of organisms isolated from wound swab culture

low (15.4%) and high (25%). BMI are associated with increased incidence of infection, due to decrease in blood circulation in fat tissues.⁷ Malnutrition is another factor predisposing to SSI.⁶

The findings of this study also proved the risk of SSI to be less in elective surgeries (6.5%) than the emergency (26.3%) surgeries like acute abdomen.

Acute/chronic appendicitis and duodenal perforation were the most common procedures performed. SSI was more among acute necrotizing pancreatitis, duodenal perforation, hepatic abscess, carcinoma stomach, sigmoid volvulus, carcinoma caecum, and chronic cholecystitis. The findings supported the literature by showing that administration of prophylactic antibiotic ½ h before the operation would bring about the best results and the lowest SSI.⁸ The studies show that with the duration of above 1.5 h, the risk of SSI increases.⁵ In this study, 59 cases with the duration of surgery, <1.5 h had an incidence of infection of 5.1%, 41 of cases with the duration of surgery of about 1.5-4 h had an infection rate of 26.8%. The incidence of SSI was more in longer duration procedures. The time of shaving when it approaches the operation and if done by Clippers, reduces the SSI risk.^{9,10}

The source of SSI is the patient's endogenous microorganisms.^{11,12} The rates of SSIs between the clean and the clean contaminated wounds differed due to endogenous contamination and between the clean contaminated and the dirty wounds, it is the effect of exogenous contamination. The endogenous flora is responsible for infection in most cases. The opening of the gastrointestinal tract increases the likelihood of Gram-negative bacilli that was our finding in this study. This group of organisms tends to be endemic in the hospital environment due to easy transfer from object to object; they also tend to be resistant to antiseptics and are difficult to eradicate in the long term. This group of organisms is

increasingly playing a greater role in the many hospitals acquired infections.

The conditions responsible for SSI other than included in this study are - personal hygiene, immunological disorders, smoking, techniques of surgery, duration of surgical scrub, pre-operative skin preparation, failure to obliterate dead space, and inadequate sterilization of instruments.

CONCLUSION

The SSI rate was higher in the middle-age group, emergency surgeries as compared to the elective. Anemia, diabetes mellitus, hypoproteinemia, and obesity are associated with SSI. With increase in the time of surgery, the risk of infection increased. The most commonly isolated organism from SSI was *Pseudomonas* (42.85%). Among the organisms that were isolated, the most of them were multidrug resistant.

ACKNOWLEDGMENT

We are thankful to M. C. Deshingkar, Rupali Salunkhe, Satish Damame, Vikas Nikam for there technical support.

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How to cite this article: Janugade HB, Nagur BK, Sajjan KR, Biradar SB, Savsaviya JK, Reddy M. Abdominal Surgical Site Infection Occurrence and Risk Factors in Krishna Institute of Medical Science, Karad. *Int J Sci Stud* 2016;3(11):53-56.

Source of Support: Nil, **Conflict of Interest:** None declared.

Role of Ultrasonography in Molar Pregnancy Coexisting with Viable Fetus: A Prospective Study

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Abstract

Introduction: Mole with coexisting viable fetus (MCF) is a rare condition, and the diagnosis is important because of the risk of developing severe complications in pregnancy and beyond.

Aim: The aim of this study was to report the sonographic features of molar pregnancy with coexisting viable fetus in singleton and twins.

Materials and Methods: A prospective and randomized study of 12, 350 patients those who were referred for a routine antenatal ultrasound scan in the Department of Radiology, MGM Hospital, Warangal was conducted. The duration of study was 2 years (November 2013–October 2015).

Results: In the present study, 40 patients were diagnosed with a gestational trophoblastic disease on ultrasound. In that, 8 patients were suspected as MCF. Four cases, on follow-up, confirmed the initial diagnosis of molar pregnancy with coexisting viable fetus.

Conclusion: Ultrasonography is useful in diagnosis and follow-up of molar pregnancy with a viable fetus and in detecting further complications. As a continuation of pregnancy with molar changes and the coexisting normal viable fetus is an acceptable option, close surveillance is necessary to detect early signs of complications in such cases.

Key words: Fetus, Molar pregnancy, Ultrasonography

INTRODUCTION

Molar pregnancy with viable fetus has been divided into three types. The first type is a twin pregnancy with one normal fetus having normal placenta and another complete mole (CHMCF). The second type is a twin pregnancy with a normal fetus, placenta, and another partial mole. The third and most uncommon occurrence is singleton normal fetus with the partial molar placenta (PMCF), where the fetus should have a normal karyotype to survive. The cases with molar pregnancies concurrent with normal intrauterine pregnancies (MCF) have been reported as 2.5-5% of molar pregnancies^{1,2} or 1 in 20,000-1,00,000

pregnancies.³ The clinical entity has aptly been described as sad fetus syndrome⁴ and should be reviewed time to time.^{5,6} (Twin MCF resulting in a viable live born infant mostly having (a) less discrepantly grown uterine size, (b) lower frequency of preeclampsia, (c) significantly lower serum beta-human chorionic gonadotropin (hCG) values, (d) diagnosed later in gestation - All indicating growth of molar changes are slow or even molar degeneration and subsequently a more benign clinical course. Most of the CHMCF will be terminated prematurely either because of persisting hemorrhage or severe preeclampsia. Nearly, 40% of the patients with gestational trophoblastic disease (GTD) with a viable fetus who opted for continuation of their pregnancies have Lived babies, delivered beyond 32 weeks gestation. Twin pregnancies including a mole and a healthy fetus Give rise to complex clinical considerations, especially in a strongly desired pregnancy. Sebire *et al.*, reported the largest series so far comprising 77 CHMCF, with approximately 27% of the pregnancies achieving live birth and 19% developed persistent GTD (pGTD), without significant differences between those who choose

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Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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to electively terminate pregnancy and those who did not. Recently, Massardier *et al.*,⁷ published a series of 14 cases with similar percentages of live birth and a 50% pGTD. Single case reports were also published⁸⁻¹⁰ which shows the importance of the role of ultrasound in diagnosing the disease. Pregnancies complicated by CHMCF may result in a viable live-born infant in approximately 40% of the cases. Continuation of such Pregnancies may be an option but, close surveillance is needed to detect complications, most of these pregnancies were electively terminated due to this potential risk. The results of these studies emphasize the value of ultrasound as a screening technique.

MATERIALS AND METHODS

Between November 2013 and October 2015, 12350 patients were referred for routine antenatal scans were included in this study. Ethics Committee Approval was taken to conduct the study. Written informed consent was obtained from patient who participated in this study. 40 patients were diagnosed as molar pregnancies, out of which 8 cases were suspected with molar pregnancy concurrent with live fetus. A chart to document complete mole with a viable fetus and partial mole with viable fetus was performed. All the scans are done on Esoate my Lab 40, Voluson E8 BT 10 Version, and Voluson 730 Pro Machines. Beta-hCG levels were determined by AxSYM total hCG assay. Standard normal ranges were provided by the manufacturer.

RESULTS

In this descriptive study between November 2013 and October 2015, 12350 pregnant women who referred for antenatal scan were included, and 40 cases of hydatidiform mole were diagnosed (0.3% or 3/1000 pregnancy). In that, 8 patients were suspected as molar pregnancy with coexisting viable fetus. Four of them in early gestation suspected as MCF (Figure 1), with advanced gestation three of them showed regression of the suspected molar tissue. One patient aborted spontaneously, and histopathology showed no evidence of molar changes. Four cases, on follow-up, confirmed the initial diagnosis of molar pregnancy with coexisting viable fetus. so It is conventional to wait until the diagnosis becomes clear on ultrasound to avoid the risk of evacuating a healthy pregnancy. The typical ultrasonographic findings of a molar pregnancy consist of a complex cystic pattern with a “snowstorm” appearance, but it should be differentiated from a missed abortion with its degenerated gestational sac, especially during the early pregnancy, or even a partially necrotic leiomyoma which can produce a similar

appearance.¹¹ Twin complete MCF is 2/40 (5%). In 2 cases, ages of the patients were 20-25 years. No H/o infertility/previous molar pregnancy/malnutrition/smoking. Blood group was o+ in both the cases. Partial mole with live fetus is diagnosed in 2 cases out of 40 cases (5%). Ages of the patients were 20-21 years. No h/o infertility/previous molar pregnancy/malnutrition/smoking. Blood group B+ in 1 case, O+ in another one.

Two patients of PMCF (Figure 2) both cases are gravida 2, para 1. The first patient unbooked came with spotting at 33 weeks for ultrasonography which showed single live fetus corresponding to 33 weeks with well-defined multicystic snowstorm like appearing mass approximately measuring 10 cm × 8 cm in the posterior upper uterine cavity and is connected to normal placenta. No evidence of anomalies detected. Oligohydramnios noted. Beta-hCG levels are >10,000 Miu/ml. Follow-up scan done at 35-36 weeks showed severe oligohydramnios and increased the size of lesion noted. Lower segment caesarean section performed at 35-36 weeks, delivered a male baby of 2 kg. Newborn did not show any abnormalities. The second patient came for a routine antenatal scan which revealed singleton normal live fetus

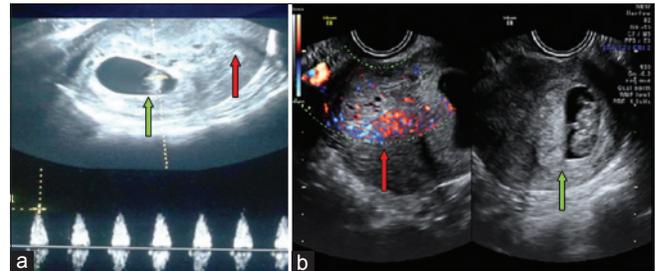


Figure 1: (a and b) Normal gestational sac with live fetus. Adjacent to sac heterogeneous lesion suspected as molar tissue. Spontaneously regressed with advanced gestational age. Green arrow indicates normal placenta; red arrow represents suspected molar tissue

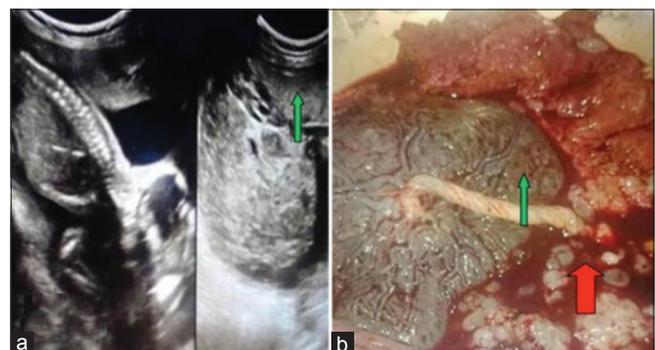


Figure 2: (a) Snowstorm like mass connecting to normal placenta and live 35 to 36 weeks fetus, (b) Macroscopic image of placenta shows molar tissue and normal placenta. Green arrow indicates normal placenta; Red arrow represents molar tissue

of 20 weeks gestation with heterogeneous echogenic mass showing a cluster of cystic spaces of size 15 cm × 7 cm, connected with the small normal placenta. The liquor was less. Serum beta-hCG levels are 44,000 mIU/ml. The patient was advised for amniocentesis and counseling was done. The patient opted termination of pregnancy. Histopathology confirmed the molar changes. Microscopic examination of the placenta in both cases revealed normal villi co-existing with villi showing hydropic changes, cistern formation, and diffuse circumferential trophoblastic hyperplasia consistent with partial molar changes. Comparing our cases to literature reported cases in Table 1.

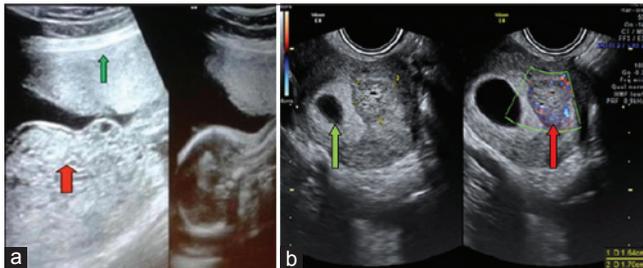


Figure 3: (a) Multi cystic Snowstorm like mass noted at upper posterior uterine cavity with out any connection to normal placenta. Normal placenta noted at upper anterior segment and coexisting live fetus, (b) dichorionic - diamniotic twin with normal gestational sac with adjacent molar tissue in early pregnancy. Arrow indicates normal placenta; red arrow represents molar tissue.

CHMCF (Figure 3) both cases are prime. First patient came for nuchal translucency scan which revealed single live fetus of 11 weeks with the normal placenta and an additional intrauterine echogenic mass with features of hydatidiform mole. We counseled the patient about the continuation of pregnancy and its Outcome need for amniocentesis, possible complications, and postnatal management. With close monitoring patient continued the pregnancy. At 17-18 weeks, patient developed hypertension ultrasound scan revealed increased lesion size and theca lutein cysts. Doppler study showed raised RI values, and persistent early diastolic notch in the uterine artery, and we referred the patient to higher center for further management. Later she developed severe hypertension and pregnancy was terminated at 20-22 weeks of gestation at higher center. The second patient of CHMCF came with spotting for evaluation. Serum beta-hCG levels are 86,878 mIU/ml scan revealed dichorionic diamniotic twins with co-existing complete molar pregnancy in sac B and live fetus of 7 weeks gestational age (GA) in sac A, ended up in medical termination of pregnancy due to vaginal bleeding. Histopathology confirmed the diagnosis. Comparing our cases to literature reported cases given in Table 2.

In contrary to the existing literature; we observed that in all the above cases, the patients age was around 20-25 years with no history of previous molar pregnancies or infertility

Table 1: Clinical variables in 7 patients with a partial hydatidiform mole and a coexisting live term singleton fetus with diploid karyotype

Authors	Maternal age	Gravida/para	Presenting symptoms	Gestational age at diagnosis/delivery	Ultrasound features	Outcome	Persistence of disease and treatment
Jones and Lauersen ¹⁹	Not specified	Not specified	Not specified	40/40	Focal HM with normal karyotyping	Normal fetus 46 XX	Not specified
Wunderlich ²⁸	Not specified	Not specified	Vaginal bleeding	40/40	Focal HM with normal karyotyping	Normal fetus	Not specified
Hartfield ²⁹	Not specified	1/0	Vaginal bleeding	38/38	Focal HM with normal karyotyping	Normal fetus XY	No
Pool <i>et al.</i> ³⁰	20	1/0	Detected after delivery	38/38	Molar degeneration represented 25% of placenta. No chromosomal analysis	3450 g healthy male baby	No
Parveen <i>et al.</i> ³¹	NS	NS	Vaginal bleeding	38/38	Large placenta with focal molar changes. 46 XX	2100 healthy female baby	No
Dhingra <i>et al.</i> ³²	28	1/0	Vaginal bleeding	38/38	Large placenta, focal molar changes, 46, XX	2100 g, healthy female	No
Our presented cases (2)	21 and 20 years	2/1 2/1	Vaginal bleeding Routine ultrasound	33 and 35/36 20 weeks	Large multicystic Snowstorm like appearing mass (of placenta) connecting to normal placenta Echogenic mass with cystic spaces connecting to small normal placenta Both cases presented with oligohydramnios. No chromosomal analysis	2 kg healthy male baby Aborted	No

NS: Not specified, GA: Gestational age, HM: Hydatidiform mole age (weeks), G/P: Gravidity/parity

treatment. This indicates the change in the presentation pattern of the GTD with viable fetus.

DISCUSSION

Cytogenetically, partial moles usually have triploid karyotype with the extra haploid set of chromosomes of androgenic derivation may be due to dispermic fertilization or with an unreduced diploid sperm. Most of them will have 46 XX and less number with 46 XY karyotype. Whereas complete moles have a diploid karyotype that is entirely of paternal origin. Complete mole consists of multiple vesicles without any e/o fetal parts. Cystic changes are less in partial mole compared to the complete mole. In partial mole usually fetus and large placenta noted, and the fetus usually dies within few weeks of conception (Figure 4). Complete and partial moles have distinct fetal and maternal complications. In partial mole with coexistent live fetus, the fetus is almost always triploid, and the indication for a termination of pregnancy is evident. In contrast, the fetus may be normal in CHMCF and continuation of pregnancy is frequently associated with severe maternal and fetal complications. Differences between the partial and complete molar pregnancy is described in Table 3. There have been so

far, about 200 cases of twin pregnancy with CHMCF fully documented in literature, while only 56 cases resulted in a live birth.¹² Ultrasonography has made it possible to diagnose hydatidiform mole and co-existent fetus in the first trimester.¹³ Prenatal testing of fetal karyotype is essential in deciding continuation and prognosis of the pregnancy. A triploid karyotype indicates a triploid fetus which is severely malformed and, in such cases, termination of pregnancy is recommended. A diploid fetal karyotype (46 chromosomes, 46 XX or 46 XY, 23 maternal and 23 paternal) indicates a viable fetus with a normal placenta co-existing alongside a twin molar placenta. In such a case, the pregnancy can be allowed to continue since it has a considerable chance to result in a normal live baby. Nevertheless, parents who choose to continue a twin pregnancy with complete hydatidiform mole should agree to take the risk of possible maternal complications associated with molar pregnancy such as early-onset pre-eclampsia, hyperemesis gravidarum, hyperthyroidism, vaginal bleeding, anemia, development of theca lutein ovarian cysts, respiratory distress because of trophoblastic embolization to the lungs, and persistent trophoblastic disease (PTD). Parents must be counseled that maternal complications may lead to fetal intrauterine growth retardation, fetal distress, and premature delivery.¹⁴⁻¹⁶ A “wait-and-see” approach should be considered rather than immediate termination of pregnancy because the risk does not increase with advancing GA. Diagnosis should also include molar placental karyotype. Although, not available for our patients, as in most documented case. Marcorelles *et al.*,¹⁷ had suggested that in the case of a normal fetal karyotype, it is justifiable to await developments in the absence of maternal complications.

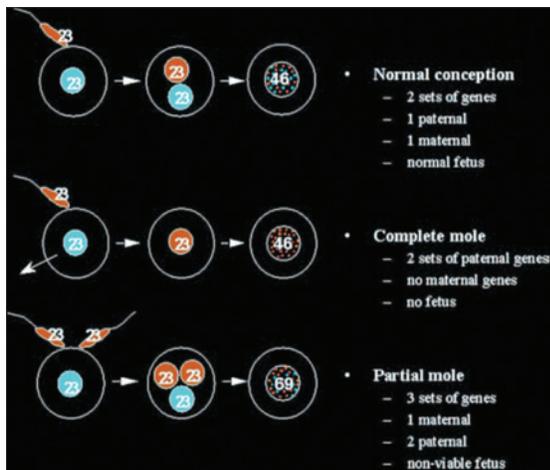


Figure 4: Genetic events occurring in normal conceptions and complete and partial molar pregnancies

In cases of singleton normal fetus with the partial molar placenta, fetal survival depends upon several factors.

1. Normal karyotype of the fetus¹⁸
2. Smaller molar placenta compared to normal placenta¹⁸⁻²⁰
3. The onset of molar degeneration and its speed of degeneration
4. Absence of anemia in the fetus²¹
5. Absence of maternal complications such as pre-eclampsia.²²

Table 2: Clinical variables in CHMCF

References	n	Intended previable TOP	TOP due to SA, Maternal complications or IUFD	Live neonate (%)	Pre-eclampsia	Persistent GTT (%)	Matastatic GTT
Bristow <i>et al.</i> ⁵	26	19	NA	7 (27)	7 (27)	15 (57)	5/22 (lung, vagina)
Fishman <i>et al.</i> ³³	7	5	NA	2 (28)	NA	4 (57)	0
Matsui <i>et al.</i> ³	18	5	10	3 (17)	5 (28)	9 (50)	6 (lung)
Sebire ¹⁶	77	24	32	20 (26)	NA	15 (93)	NA
Total	128	53		32 (25)		43 (34)	
Our presented cases	2	1	1	0	1	0	0

TOP: Termination of pregnancy, IUFD: Intra uterine fetal death, GTT: Gestational trophoblastic tumor, NA: Not available

Table 3: Difference between complete mole and partial mole

Feature	Partial mole	Complete mole
Karyotype	Most commonly 69, XXX or XXY	Most commonly 46 XX, XY
Pathology		
Fetus	Often present	Absent
Amnion, fetal RBC	Usually present	Absent
Villous oedema	Variable, focal	Diffuse
Trophoblastic proliferation	Focal, slight-moderate	Diffuse, slight-severe
Clinical presentation		
Diagnosis	Missed abortion	Molar gestation
Uterine size	Smaller for dates	50% large for dates
Theca lutein cyst	Rare	25-30%
Medical complications	Rare	10-25%
Post molar GTN	2.5-7.5%	6.8-20%

GTN: Gestational trophoblastic neoplasia, RBC: Red blood cells

Szulman and Surti²³ reported 8 cases of partial mole coexisting with live fetus with normal karyotype after 15 weeks of gestation, but only 2 of the neonates survived. Agarwal *et al.*,²⁴ from AIIMS, New Delhi reported partial molar pregnancy with a diploid live fetus which was terminated at 28 weeks with good neonatal outcome. In a large study by Vaisbuch *et al.*,²⁵ they reported 130 cases of twins with CHMCF pregnancy of which 41% were terminated because of the positive probability of serious maternal complications. The recent study by Niemann²⁶ in 2007 revealed that the risk of PTD after a diploid mole with a viable fetus is similar to that after a singleton molar pregnancy and risk does not change with GA. Elective early termination of such pregnancy because of the risk of PTD alone should not be recommended.¹³ Another study in 2009 which evaluated the registered data of patients from 1999 to 2006 showed the 50% (7 cases in 14) rate of gestational trophoblastic neoplasia (GTN) after CHMCF. A high level of beta-hCG at the time of admission may be an indication of poor prognosis of the disease. Partial and complete molar pregnancies have obvious fetal and maternal risks.²⁷ Thus such pregnant women should be followed more carefully in specialized centers.

CONCLUSION

Ultrasonography plays a key role in diagnosing GTD with coexisting live fetus, guiding disease management, and early detection of its complications. Although detection rate of GTD in the second trimester by ultrasound is 100% whereas it is less in early trimester so, it needs correlation with repeat scans, beta-hCG levels, and histopathological findings. However, beta-hCG is a useful biochemical marker; it is not diagnostic when considered in isolation. We strongly suggest that with a normal karyotype and no gross abnormalities on sonography, pregnancy may be

continued as long as maternal complications are absent or, if present, controllable. As a continuation of pregnancy in MCF is an acceptable option, close surveillance is necessary to detect early signs of complications in such cases. An early diagnosis of CMF by high-resolution ultrasound is important for clinical management and helps the patient in making a decision whether to terminate the pregnancy or continue with close fetomaternal monitoring.

ACKNOWLEDGEMENT

The authors are thankful to Dr. K. Radhika, Dr. T. Kalpana Devi, Dr. Birbadhra Rao, Dr. Nadheem Ahamad and Dr. Bhageeradhi for their contribution.

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How to cite this article: Routhu M, Chouhan S. Role of Ultrasonography in Molar Pregnancy Coexisting with Viable Fetus: A Prospective Study. *Int J Sci Stud* 2016;3(11):57-62.

Source of Support: Nil, **Conflict of Interest:** None declared.

Evaluation of Cervical Lesions: A Prospective Study

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Abstract

Introduction: Cancer cervix has a long pre-invasive stage, giving an opportunity for its early detection and treatment. The main objective of present study was the earliest detection of cancer cervix by simple and low-cost screening programs in the low setting, in countries like India. Papanicolaou smear remains easiest, simple, quick, and oldest method of screening premalignant lesions of the cervix.

Aims and Objectives: To study the clinicopathological profile in various high-risk group patients, to differentiate between benign and malignant cervical lesions and to study the prevalence of cervical dysplasia in relation to various high-risk factors.

Materials and Methods: The present study became a hospital-based short-term prospective study and was conducted from November 2006 to October 2007 in the Department of Obstetrics and Gynecology, People's College of Medical Sciences and Research Center and People's Hospital, Bhopal, Madhya Pradesh, India. These cases have been closely studied by taking history; physical examination and cervical smear examination.

Result: Out of 500 high-risk cases, normal smear cases were found in 1.6%, inflammatory smear cases in 80%, low-grade squamous intraepithelial lesions (LSIL) were in 14.4%, while high-grade squamous intraepithelial lesions (HSIL) were found in 2.8%, dysplasia (LSIL + HSIL) in 17.2%, and malignancy were found in 1.2% of cases. The higher number of dysplasia cases were seen in rural population (82.55%) as compared to urban population (17.44%). Maximum number of dysplasia was seen in the age group of 30-39 years (34.88%) and invasive carcinomas among the age group of 40-49 years (50%). Prevalence of dysplasia was high (79.34%) in women of high parity. Most frequent complaints of the patients in relation to dysplasia were leucorrhoea (97.67%), pain in lower abdomen (54.65%), and backache (39.53%).

Conclusion: The cytological method of diagnosis is a convenient, valuable, technically sound, and feasible method for detection of unsuspected carcinoma of the genital tract and precancerous lesions at the time when they are not evident clinically.

Key words: Carcinoma, Cervix, Dysplasia, Pap smear, Precancerous

INTRODUCTION

Carcinoma cervix worldwide accounts for 15% of all cancers diagnosed in women.¹ It is estimated that cervical cancer is one of leading cancers in women in about 5.0 lakhs new cases every year of which 80% occur in developing countries like India.² In India, it is estimated that the number of new cases are over 140,000.³ Cancer

cervix occupies the top rank or second among cancers in women in developing countries.

So that, there is an urgent need for initiation of community screening and educational programs within the source for the control and prevention of cervical cancer in India.⁴

Papanicolaou (Pap) smears are used to screen for cervical cancer, here the "screening for cancer" means looking for cancer before a person has symptoms. There are no organized screening programs in any province or region of India. Screening of asymptomatic women is practically absent, even among otherwise well-organized health care programs of the industrial and military sectors.⁵ Resource constraint has been a major hurdle in organizing screening programs. It has been estimated that in India, even with

Access this article online



www.ijss-sn.com

Month of Submission : 12-2015

Month of Peer Review : 01-2016

Month of Acceptance : 01-2016

Month of Publishing : 02-2016

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a major effort to expand cytology services, it will not be possible to screen even one-fourth of the population once in a lifetime in the near future.⁶

Conventional cytology is offered sporadically to women in selected urban areas attending health services for other reasons, but not as routine screening of asymptomatic women. According to the WHO Health Survey in 2002, 2.6% of 4586 women aged 18-69 years ever had a Pap smear.⁷

In India, the operating factors are low standards of cleanliness, coitus or marriage at an early age, the frequency of sexual intercourse, promiscuity of both partners, men in jobs which require frequent travel and those whose first wife died of cancer cervix constitute a group termed as high-risk males. High parity, sexual transmitted diseases, HIV infection, herpes simplex virus II, family history of cancer, drug abuse and alcohol, make the women at risk for cancer cervix.

Although cervical cancer remains a serious problem in developing countries, its incidence and mortality rates have decreased significantly in developed countries due to effective screening programs.

Hence, the main objective of this study is the early detection of cancer cervix by simple and low-cost screening programs in low-resource settings, in countries like India because cancer cervix has a long pre-invasive stage, giving an opportunity for its early detection and treatment. Pap smear remains easiest, simple, quick, and oldest method of screening premalignant lesions of the cervix.

MATERIALS AND METHODS

The present study became a hospital-based short-term prospective study and was conducted from November 2006 to October 2007 in the Department of Obstetrics and Gynecology, People's College of Medical Sciences and Research Center and People's Hospital, Bhopal, Madhya Pradesh, India. The target population in which the present study was carried out comprised of 500 women of different age, parity, religion, educational, and socioeconomic status, who have been attending the outpatient department (OPD) of above department.

Inclusion Criteria

Women with complaints or history suggestive of: Leucorrhoea, lower genital tract infections, post coital bleeding, irregular menstruation, and post-menopausal bleeding.

Exclusion Criteria

Post-operative cases of hysterectomy, Advance cases of cervical cancer.

Data Collection Methodology

Selection of study participants

All patients, those were attending the OPDs of Department of Obstetrics and Gynecology People's College of Medical Sciences and Research Center and People's Hospital, Bhopal, Madhya Pradesh, India.

Collection of sample and preparation of smear

Detail patient's history, physical examination, and per speculum examination was done, the vaginal discharges were noted, and the condition of cervix and vagina was observed. Subsequently, cervical smear was taken; this was followed by per vaginal examination in which the uterus and the adnexa were examined thoroughly.

Two cervical smears were prepared from every case. Slides were fixed in 95% alcohol and stained by Pap method. All slides were thoroughly studied in the Department of Pathology, Peoples Medical College and Research Centre, Bhopal.

Method of taking vaginal smear

For the collection of vaginal secretions, various workers have devised different technique and used different instruments. In the present study, cervical scraped method was performed.

Statistical Analysis

The data have been collected on excel sheet and results were analyzed by applying Chi-square and fisher exact test (*P*) accordingly. The results obtained were depicted in the form of tables and graphs that are self-explanatory.

RESULTS

Out of 500 high-risk cases, normal smear cases were found in 1.6% ($n = 8$), inflammatory smear cases in 80% ($n = 400$), low-grade squamous intraepithelial lesions (LSIL) were in 14.4% ($n = 72$), while high-grade squamous intraepithelial lesions (HSIL) were found in 2.8% ($n = 14$), dysplasia (LSIL + HSIL) in 17.2% ($n = 86$), and malignancy were found in 1.2% ($n = 6$) of cases (Table 1).

Table 1: Distribution of cases depending on cytology report

Cytology report	Number of cases	Percentage
Normal smear	8	1.6
Inflammatory smear	400	80
LSIL	72	14.4
HSIL	14	2.8
Malignancy	6	1.2
Total	500	100

LSIL: Low-grade squamous intraepithelial lesions, HSIL: High-grade squamous intraepithelial lesions

The higher number of dysplasia cases were seen in rural population (82.55%) as compared to urban population (17.44%) (Table 2).

Maximum number of dysplasia was seen in the age group of 30-39 years (34.88%) and invasive carcinomas among the age group of 40-49 years (50%) (Table 3).

In the present study, early childbirth below 18 years of age shows a strong correlation of disease with dysplasia. Out of 332 numbers of cases which belong to this group, dysplasia was found in 53 (61.63%). Out of 6 patients who had malignancy 4 (66.66%) were <18 years of age at the time of their first childbirth (Table 4).

Prevalence of dysplasia was high (79.34%) in women of high parity (Table 5).

Out of 500 cases illiterate patients were 286 (57.2%) and literate 214 (42.8%). The maximum number of dysplasia was among the illiterate population, i.e., 54 (62.79%).

Out of 500 cases, the history of addiction of tobacco intake was found in 135 (27%) cases from which 31 (36.04%) cases turned out to be positive for dysplasia (Table 6).

Out of total 500 cases, only 15 (3%) cases have a history of genital carcinomas in their family, and only 2 (2.32%) had dysplasia.

Most frequent complaints of the patients in relation to dysplasia were leucorrhoea (97.67%), pain in lower abdomen (54.65%), and backache (39.53%). Among post-menopausal women, dysplasia was detected in (10%) and invasive carcinoma in (50%) of cases (Table 7).

High number of dysplasia and cervical cancer were seen in association with unhealthy cervix which bleeds on touch (34.88%) and erosion (27.91%) (Table 8).

In the present study, out of 500 cases 55 (11%) used Barrier methods, 61(12.2%) used oral contraceptive pills and 233 (46.6%) had tubectomy done, and 151 (30.2%) cases did not use any method of contraception (Table 9).

Among the Barrier contraceptive users, dysplasia was found in 7 (8.14%), and malignancy was not reported in any of the

patients. This clearly shows a protective effect of Barrier methods from cervical carcinoma. Among the non-users, dysplasia was found in 36 (41.86%) and malignancy 3 (50%) cases. This is because of the poor motivation of family planning methods among the low socioeconomic group.

There is a strong correlation between non-contraceptive users and pre-invasive and invasive cancer which is statistically significant.

Out of 500 cases, Hindus comprised of 451 (90.2%), and Muslims comprised of 48 (9.6%). The cases of dysplasia in Hindus were 72 (83.72%) while in Muslims 14 (16.28%). This was apparently due to a higher percentage of Hindus in the population which resides in the nearby locality (Table 10).

DISCUSSION

Gupta *et al.*⁸ in their study observed that the epithelial abnormalities constituted (3.23%) of all cases. LSIL formed the largest number (1.36%), while HSIL formed (0.91%). 11 cases of squamous cell carcinoma (SCC) were detected. In the present study, the incidence of dysplasia was (14.4%), and malignant lesions were in (1.2%).

Patel *et al.*⁹ in their study showed that there were 94.5% benign and inflammatory and (5.5%) were a premalignant and malignant lesion, out of which premalignant lesions (83.6%) were atypical cells of undetermined significance (ASCUS) and atypical glandular cells of undetermined significance (AGUS). ASCUS progresses to LSIL, HSIL, and SCC. AGUS progresses to adenocarcinoma.

In the present study, the maximum age of dysplasia has been found in the age group of 30-39 years (34.88%) and for invasive carcinoma 40-49 years (50%) and above. This fits with an average duration of 10-12 years for a pre-invasive lesion to become invasive. A recent study by Gupta *et al.* also found the maximum numbers of cases (40.37%) were among the age group of 30-39 years.

The present study demonstrates that cervical dysplasia was higher in rural population (82.55%) as compared to the urban population (17.44%). This may be explained by the better accessibility of health services and hence

Table 2: Distribution of cases according to residential status

Residential status	Normal smear	Inflammatory smear	LSIL	HSIL	Total (LSIL+HSIL)		Malignancy	Total	
					No.	%		No.	%
Rural	8	304	58	13	71	82.55	5	388	77.6
Urban	0	96	14	1	15	17.44	1	112	22.4
Total	8	400	72	14	86	100	6	500	100

LSIL: Low-grade squamous intraepithelial lesions, HSIL: High-grade squamous intraepithelial lesions

early detection of disease. There is a lack of personal hygiene in rural setup further contributing to infection and dysplastic changes in them. Mhaske *et al.*¹⁰ considering the high prevalence of cervical cancer and various risk factors among rural women, community-based screening camps should be arranged so as to reduce the morbidity among rural women. As the significant association between age at marriage below 17 years, age at first childbirth <20 years, high parity and act regarding age at marriage should be strictly implemented in rural areas.

Table 3: Distribution of cases according to age

Age (in years)	Number of cases		
	Benign	Malignant	Total
10-29	104	16	120
30-39	171	31	202
40-49	93	32	125
>50	40	13	53
Total	408	92	500
Chi-square test=8.95		P=0.030	
Statistically significant			

Table 4: Distribution of cases according to first childbirth

First childbirth (in years)	Number of cases		
	Benign	Malignant	Total
<18	258	74	332
>18	150	18	168
Total	408	92	500
Chi-square test=9.954		P=0.002	
Fisher exact test (P)=0.001			
Statistically significant			

Table 5: Distribution of cases depending on the parity

Parity	Number of cases		
	Benign	Malignant	Total
<3	139	19	158
>3	269	73	342
Total	408	92	500
Chi-square test=6.252		P=0.012	
Fisher exact test (P)=0.013			
Statistically significant			

Table 6: Distribution of cases according to tobacco intake

Tobacco intake	Normal smear	Inflammatory smear	LSIL	HSIL	Total (LSIL+HSIL)	Malignancy	Total
					n (%)		n (%)
Yes	3	100	20	11	31 (36.04)	1	135 (27)
No	5	300	50	3	53 (61.62)	5	365 (73)
Total	8	400	72	14	86 (100)	6	500 (100)
Chi-square test=3.465					P=0.063		
Statistically not significant							

LSIL: Low-grade squamous intraepithelial lesions, HSIL: High-grade squamous intraepithelial lesions

In our study, dysplasia was found in (54.63%) among women who had their marriage between 14 and 16 years of age. When studied according to the age at first childbirth, the majority of cases of dysplasia (61.63%) were found in women who had the birth of their first child below 18 years of age. Dutta *et al.*¹¹ in their study found that estimated relative risk for developing cancer cervix among women getting married before 17 years of age was found to be 7.9 as compared to women who were married after the age of 17 years.

Mohanty *et al.*¹² in their study observed that there was a decline of cancer cervix as the age of 1st marriage/1st pregnancy advanced to 20-24 years. Early age at marriage indicates an early exposure sexual activities and early pregnancy which are well-known etiological factors for carcinoma cervix.

In our study, the majority of women with dysplasia and malignancy were with parity >3 children (79.34%). According to Tapasvi *et al.*¹³ among the 100 cases, 51 women had a history of 3 or 4 paras and only 7 women were nulliparous. It was observed that higher he parity, greater the frequency of occurrence of carcinoma of the cervix and associated premalignant conditions. 1 (7.6%), 6 (46.15%), and 6 (46.15%) patients had dysplastic changes among the 1-2 para, 3-4 para, and 5 and above paras, respectively. Similarly, 6 (20.7%), 15 (51.72%), and 8 (27.6%) women had cervical intraepithelial neoplasia (CIN)/cervical carcinoma *in situ* (CIS) changes on cytology among the 1-2 para, 3-4 para, and 5 and above paras, respectively. None of the nulliparous women had either of dysplasia, atypical transformation zone (TZ), CIN/CIS, or invasive carcinoma.

In present study, 11% of patients were using Barrier contraception while (46%) were sterilized. Tapasvi *et al.* also observed that 4/10 women who practiced Barrier contraception using condoms had CIN on histopathology. Out of 13 cases that had dysplasia on cytology 11 (84.6%) had a history of bilateral tubectomy. 17/52 women who had a history of bilateral tubectomy had CIN on histopathology. This higher incidence of cervical cancer in patients with high possibility of unprotective intercourse

Table 7: Distribution of cases according to presenting complaints

Complaints	Normal smear	Inflammatory smear	LSIL	HSIL	Total (LSIL+HSIL)	Malignancy	Total
					n (%)		n (%)
White discharge	8	362	70	14	84 (97.67)	5	459 (91.8)
Pain in lower abdomen	5	262	38	9	47 (54.65)	0	314 (62.8)
Backache	1	102	30	4	34 (39.53)	0	137 (27.4)
Irregular menses	2	34	8	4	12 (13.95)	1	48 (9.6)
Urinary complaints	0	4	2	0	2 (2.32)	0	6 (1.2)
Post-menopausal complaints	0	27	0	2	2 (2.32)	0	29 (5.8)
Blood mixed discharge	0	5	0	0	0 (0)	0	5 (1)
Itching in private parts	0	5	0	0	0 (0)	0	5 (1)
For checkup (asymptomatic)	0	0	0	0	0 (0)	0	0 (0)
Others	0	0	0	0	0 (0)	0	0 (0)

Chi-square test=5.2

P=0.023

Fisher exact test (P)=0.019

Statistically significant

LSIL: Low-grade squamous intraepithelial lesions, HSIL: High-grade squamous intraepithelial lesions

Table 8: Distribution of cases according to per speculum examination of cervix

Per speculum examination of cervix	Normal smear	Inflammatory smear	LSIL	HSIL	Total (LSIL+HSIL)	Malignancy	Total
					n (%)		n (%)
Normal	0	4	2	0	2 (2.32)	0	6 (1.2)
Congested	3	19	6	1	7 (8.14)	1	30 (6)
Bleeds on touch	0	23	19	11	30 (34.88)	3	56 (11.2)
Erosion	5	208	23	1	24 (27.91)	1	238 (47.6)
Hypertrophy	0	101	20	0	20 (23.25)	0	121 (24.2)
Growth/ulcer	0	12	0	0	0 (0)	0	12 (2.4)
Nabothian cyst	0	33	2	1	3 (3.48)	1	37 (7.4)
Total	8	400	72	14	86 (100)	6	500 (100)

LSIL: Low-grade squamous intraepithelial lesions, HSIL: High-grade squamous intraepithelial lesions

Table 9: Distribution of cases according to contraceptive uses

Contraceptive method	Normal smear	Inflammatory smear	LSIL	HSIL	Total (LSIL+HSIL)	Malignancy	Total
					n (%)		n (%)
Barrier	0	48	7	0	7 (8.14)	0	55 (11)
OCP	4	51	5	0	5 (5.81)	1	61 (12.2)
Sterilization	3	190	33	5	38 (44.17)	2	233 (46.6)
Nil	1	111	27	9	36 (41.86)	3	151 (30.2)
Total	8	400	72	14	86 (100)	6	500 (100)

LSIL: Low-grade squamous intraepithelial lesions, HSIL: High-grade squamous intraepithelial lesions, OCP: Oral contraceptive pills

Table 10: Distribution of cases according to religions

Religion	Normal smear	Inflammatory smear	LSIL	HSIL	Total (LSIL+HSIL)	Malignancy	Total
					n (%)		n (%)
Hindu	7	366	59	13	72 (83.72)	6	451 (90.2)
Muslim	1	33	13	1	14 (16.28)	0	48 (9.6)
Christian	0	1	0	0	0 (0)	0	1 (0.2)
Sikh	0	0	0	0	0 (0)	0	0 (0)
Total	8	400	72	14	86 (100)	6	500 (100)

LSIL: Low-grade squamous intraepithelial lesions, HSIL: High-grade squamous intraepithelial lesions

is in concordance with other studies conducted in various parts of the world.¹⁴

In the present study, tobacco addiction was present in (27%) of cases out of which 36.04% cases were have

dysplasia. Brinton *et al.*¹⁵ stated that smoking increased risk for SCC and the risk increased with duration and intensity of smoking. A study by Gupta *et al.* also found that the prevalence of dysplasia was more in smokers (17.24%) as compared to nonsmokers (2.61%).

In our study, a higher incidence of dysplasia (87.72%) was found in Hindu community as compared to Muslim (16.28%). This can be explained by the fact that Hindus comprised of major number in the study were belonging to low socioeconomic status, and their partners were uncircumcised.

Tapasvi *et al.*, among 100 women studied, 67 women practiced Hinduism, from which 19 (28.35%) women had atypical TZ and 31 women were Muslims from which 07 (22.6%) of women had Atypical TZ.

In our study, dysplasia cases were (60.47%), and malignancy (50%) was among income group 500-2000 which is a low-income group, and it clearly shows an association of low socioeconomic status and high prevalence of dysplasia and invasive cancer. Similarly, in a study by Tapasvi *et al.*, with regards to socioeconomic status, 37 women were found as unskilled workers (Status V) and formed the largest occupational/socioeconomic group, whereas only 3 women were spouses of highly qualified professionals such as professors, doctors, and lawyers. Wives of semi-skilled workers formed the second largest group of workers with 28 women forming this occupational/socioeconomic group. 9 (24.32%) women belonging to Status V socioeconomic status showed atypical TZ and 7 (18.91%) cases showed dysplastic cells by cytology.

In our study, patients with dysplasia presented most commonly with leukorrhea (97.53%) followed by pain in lower abdomen (54.65%) and backache (39.53%). Hence, patients with these complaints fall in a high-risk category for carcinoma cervix and dysplasia and must be screened by cervical cytology.

High incidence of inflammatory smear has been seen in association with erosions in (52%) and hypertrophied cervix in (25.25%) of cases. Unhealthy cervix which bleeds on touch very frequently showed severe dysplastic changes (34.88%) and invasive carcinoma (50%).

Abd *et al.*¹⁶ observed that the overall predictive value of cytology was 87% while the predictive value for high-grade lesions was 80%.

Lulla *et al.*¹⁷ considered age at marriage, years of married life, parity, genital infection, use of the intrauterine contraceptive device, etc., to be significant risk factors.

The sensitivity of cytology in detecting dysplastic changes is undoubtedly high since the cervical scrape method from the TZ has been used, but true false negative and false positive results exist. False negative results might also be due to unsatisfactory smears. It was not feasible to make an

evaluation of false negative results, as patients with negative smear did not report for follow-up studies.

Misra *et al.*¹⁸ concluded that women of high age with high parity are at very high-risk of developing carcinoma cervix, and this may be due to the cumulative effect of both these risk factors. Hence, women of this category need special attention for mandatory cytological screening.

CONCLUSION

It can be concluded from this study that prevalence of cervical dysplasia and the invasive lesion is quite remarkable. The cytological method of diagnosis is convenient, valuable, technically sound, and feasible method for detection of unsuspected carcinoma of the genital tract and precancerous lesions at the time when they are not evident clinically.

It is important to identify the high-risk population and suggest social measures to motivate and educate women for a positive attitude toward cancer consciousness and to make screening program useful for prevention of premalignant and malignant diseases of the cervix.

ACKNOWLEDGMENT

We acknowledge to Dr. B. Bhardwaj, Professor and Head Department of Obstetrics and Gynecology, People's College of Medical Sciences and Hospital, Bhopal, Madhya Pradesh, India; for their encouragement, advice, and providing support to us for the study.

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How to cite this article: Jain R, Walker R, Jain L, Jatav JK. Evaluation of Cervical Lesions: A Prospective Study. Int J Sci Stud 2016;3(11):63-69.

Source of Support: Nil, **Conflict of Interest:** None declared.

Assessment of Matrix Metalloproteinase-1 and its Tissue Inhibitor of Metalloproteinase-1 in Pre-eclampsia

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Abstract

Introduction: Pre-eclampsia is a systemic inflammatory condition associated with maternal endothelial dysfunction. Matrix metalloproteinase (MMP) results in a poor trophoblastic invasion of the maternal spiral arteries, poor fetoplacental perfusion, and release of factors which affect the vascular tone and remodeling.

Objectives: To compare the serum values of MMP-1, tissue inhibitor of metalloproteinase (TIMP)-1, and their ratio in the second and third trimester of normal and pre-eclamptic pregnancy.

Materials and Methods: 30 females progressing to normal pregnancy were compared with 16 females who developed pre-eclampsia. MMP-1 and TIMP-1 concentrations were measured in serum samples (II and III trimester) of the females by enzyme linked immuno-sorbent assay.

Results: There was no significant difference in the levels of MMP-1, TIMP-1, and ratio of MMP-1 and TIMP-1 in pre-eclamptic and normal pregnancy females.

Conclusion: There is a lack of alteration in the levels of MMP-1, TIMP-1, and their ratio during the progression of pre-eclampsia when compared with normal pregnancy. Further studies with a larger sample size are required to validate this data.

Key words: Pre-eclampsia, Matrix metalloproteinase-1, Tissue inhibitor of metalloproteinase-1

INTRODUCTION

Pre-eclampsia is a systemic inflammatory condition characterized by high blood pressure and excess protein in the urine and is a leading cause of maternal and neonatal problems. The mechanisms that contribute to the disturbed endothelial homeostasis in the patho-physiology of pre-eclampsia remain unclear.¹ The main pathogenic feature of pre-eclampsia is maternal endothelial dysfunction that results from impaired angiogenesis and reduced endothelial repair capacity. It is proposed that the trophoblastic invasion into the spiral arteries insufficiently impacts the

process of vascular remodeling resulting in the hypertensive disease of pregnancy.

Reactive oxygen species and tumor necrosis factor- α have been implicated in the pathogenesis of pre-eclampsia.² They tend to induce vascular expression of extracellular matrix proteins, particularly matrix metalloproteinases (MMPs).³ Beyond their matrix remodeling properties, MMPs are involved in short-term biological processes, including regulation of vascular reactivity and leukocyte activation.⁴ Recently, the role of MMPs in the pathogenesis of pre-eclampsia has aroused interest. MMPs are zinc- and calcium-dependent enzymes playing an important role in physiological as well as pathological mechanisms.⁵ MMPs are implicated in the pathogenesis of angiogenesis and vascular remodeling by degrading extracellular matrix proteins associated with pre-eclampsia.⁶ Evidence also suggest that decreased activity of MMPs results in poor trophoblastic invasion of the maternal spiral arteries, poor fetoplacental perfusion, and release of certain factors

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www.ijss-sn.com

Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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which affect the vascular tone and remodeling.⁷ Specific endogenous inhibitors that bind MMPs are tissue inhibitors of metalloproteinases (TIMPs), and their expression is regulated during the development and tissue remodeling. The zymolytes of MMP-1 are collagen and metagelatin, which play an important role in the trophoblastic invasion⁸ and are important factors in the regulation of trophoblastic invasion. MMPs and TIMPs together form a balance to maintain normal pregnancy and placental development.

Studies have indicated variations^{9,10} in the levels of MMP-1 and TIMP-1 in the maternal umbilical cord serum, trophoblasts, and decidua in pre-eclampsia. Little is known regarding the serum levels of MMP-1 and TIMP-1 with the progression of pregnancy leading to pre-eclampsia, and it remains uncertain whether enhanced levels are present before the clinical signs of pre-eclampsia develop. With this in mind, the present study was carried out to assess the serum levels of MMP-1 and TIMP-1 trimester-wise in normal pregnancy and pre-eclampsia.

MATERIALS AND METHODS

Study Population

A prospective study approved by the Institutions Ethics Committee (NKPSIMS/7/2010 dated 20/8/2010) was carried out at NKP salve Institute of Medical Sciences, Nagpur, India. 30 primigravidas with uncomplicated normal pregnancies in the first trimester who were followed until the last trimester (control) and 16 primigravidas who developed pre-eclampsia (study group) in the third trimester were selected by random sampling.

Inclusion Criteria

All subjects within the age group of 18-35 years were selected for the study. Pre-eclampsia was defined as persisting elevated diastolic blood pressure (90 mmHg), proteinuria (>300 mg in a 24 urine sample), and the presence of edema. Subjects willing to participate were included in the study. The females with normal pregnancy were included as the control group.

Exclusion Criteria

Subjects with non-confirmed pre-eclampsia, essential hypertension, malaria, hemolytic anemia, and any other infections such as urinary tract infection or upper respiratory tract infection.

Collection of Sample

2 ml blood sample was collected from the antecubital vein under strict aseptic precautions (between 24-26 weeks and 36-38 weeks of pregnancy). The blood was allowed to clot for 30 min at room temperature and centrifuged at

3000 rpm for 15 min. The serum was then pipetted and placed in sterilized vials free of endotoxins at -20°C until analysis.

Biochemical Analysis

Human MMP-1 and TIMP-1 enzyme linked immunosorbent assay (ELISA) was measured by Ray Bio (Ray Biotech, Inc., USA). This kit is an in vitro ELISA that quantitatively measures human MMP-1 and TIMP-1 in serum, plasma, cell culture supernatants, and urine. This assay uses human-specific MMP-1 and TIMP-1 antibodies coated on a 96-well plate. Standards and samples were pipetted into the wells, and the MMP-1 and TIMP-1 bound to the wells through the immobilized antibody. The wells were washed, and biotinylated antihuman MMP-1 and TIMP-1 antibodies were added. After washing to remove unbound biotinylated antibody, we pipette HPR-conjugated streptavidin into the wells. The wells were washed, and subsequently, a tetra methylbenzidine substrate solution was added to the wells. Color developed in proportion to the amount of MMP-1 and TIMP-1 bound to the well. The stop solution changed the color from blue to yellow, and the color intensity was measured at 450 nm. MMP-1 and TIMP-1 concentration were determined using a standard curve.

Statistical Analysis

Statistical analysis was performed using EPI info software. *P* value was calculated. A value of $P < 0.001$ was considered to be significant.

RESULTS

As depicted in Table 1 and Figure 1, we observed that there was no statistically significant difference in the levels of MMP-1, TIMP-1, and MMP-1/TIMP-1 in the second and third trimester of females with normal pregnancy or those who developed pre-eclampsia.

DISCUSSION

Pre-eclampsia, characterized by hypertension, proteinuria accounts for considerable mortality and morbidity. In a normal pregnancy, the luminal diameter of the spiral

Table 1: Comparison of MMP-1 and TIMP-1 levels among the study groups

Groups (ng/ml)	Normal pregnancy		Pre-eclampsia	
	II trimester	III trimester	II trimester	III trimester
MMP-1	4.26±2.48	4.99±2.75	4.38±1.15	4.83±2.84
TIMP-1	34.98±8.66	32.97±7.08	36.69±9.007	36.69±8.97

MMP-1: Matrix metalloproteinase-1, TIMP-1: Tissue inhibitor of metalloproteinase-1

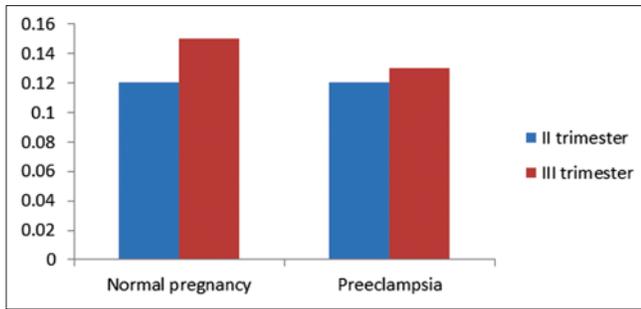


Figure 1: Comparison of matrix metalloproteinase-1/tissue inhibitor of metalloproteinase-1 ratio among the study groups

arteries is increased, and the vascular smooth muscle is replaced by trophoblastic cells. This process is deficient in pre-eclampsia. Though numerous pathophysiologies have been proposed for the development of pre-eclampsia, a poorly perfused fetoplacental unit is considered to be the major cause. One of the emerging pathway involved is the MMPs. MMPs are known to play an important role in endothelial invasion, angiogenesis, and in tumor progression.¹¹ MMP-1 or interstitial collagenase is a proteolytic enzyme produced in tissues under conditions of inflammation which break down collagen. TIMPs are known to regulate this proteolytic activity of MMPs.

Our study demonstrates that there is no significant difference in the serum values of MMP-1, TIMP-1, or their ratio in pre-eclamptic females when compared with that of normal pregnancy. Moreover, according to our findings, there is no statistical difference in the MMP-1 and TIMP-1 values in females as the pregnancy proceeds from second to the third trimester. This may be attributed to the small sample size of the study.

Galewska *et al.*¹² have suggested a decrease in the content of MMPs in the umbilical cord artery in pre-eclamptic females. Deng *et al.*⁹ and Jurajda *et al.*¹³ have demonstrated that the expression levels of MMP-1 in the umbilical cord blood, placenta, and deciduas of patients with hypertension disorders in pregnancy were significantly lower than compared with normal pregnancy. The invasion ability of the trophoblasts was lower in hypertensive disorders and TIMPs bind to MMPs in 1:1 stoichiometry, and hence decrease in the levels of MMP-1 and TIMPs.

The Virginia Commonwealth University School of Medicine Researchers recently has suggested that there is a significant increase in the levels of MMP-1 in the blood vessels of women with pre-eclampsia. Pre-eclampsia is said to be associated with an imbalance in collagen-regulating genes that favor collagen breakdown. Leakage of protein out of the blood vessels into the surrounding tissue (edema) and through the blood vessels of the kidney and into the

urine (proteinuria) may be due to the increase in the MMP-1 levels, which compromises the integrity of the mother's blood vessels. MMP-1 also causes blood vessel contraction by the activation of a receptor known as protease-activated receptor-1 which is also found in high concentrations in pre-eclampsia.

Merchant and Davidge¹⁴ have suggested that MMP enhanced the myogenic tone and endothelium-dependent relaxation in vessels suggesting a greater role of MMPs in mediating vasodilation. This may be due to the depolarization of the vascular smooth muscle cell and an increase in intracellular calcium.¹⁵

CONCLUSION

Variation in research data is available regarding the role of MMPs and TIMPs in pre-eclampsia. Our study is not able to demonstrate the effectiveness of the measurement of these blood parameters specially MMP-1 and TIMP-1 in pre-eclampsia. Further studies with a larger sample size may be taken into consideration to validate the results and to assess the usefulness of MMPs as a predictive marker of pre-eclampsia.

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How to cite this article: Gupta M, Chari S. Assessment of Matrix Metalloproteinase-1 and its Tissue Inhibitor of Metalloproteinase-1 in Pre-eclampsia. *Int J Sci Stud* 2016;3(11):70-73.

Source of Support: Nil, **Conflict of Interest:** None declared.

Comparison of Menopausal Symptoms and Quality of Life after Natural and Surgical Menopause

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Abstract

Background: Estrogen deficiency, whether arising from surgical or natural menopause, can have both medical and psychological adverse consequences for a woman's health and well-being, that is, her health-related quality of life (QOL).

Aim and Objective: This study was undertaken to determine the menopause-related symptoms and its impact QOL of women at surgical menopause with that of women at natural menopause.

Materials and Methods: A cross-sectional study was carried among 192 women at surgical and 200 women at natural menopause, attending the Outpatient Department in the SMGS hospital, and a house to house survey infield practice area of Government Medical College, Jammu by interviews with the help of a pretested semi-structured standard questionnaire. For assessment of the menopausal symptoms menopause rating scale (MRS) and for QOL World Health Organization (WHO) QOL-BREF questionnaire was used.

Main Outcome Measures: Total MRS along with the subscale scores and the total WHOQOL-BREF along with the individual domain scores were compared between the two groups.

Results: There was a significant difference between the MRS total scores of the women at surgical (16.47 ± 7.74) and natural (12.82 ± 5.60) menopause group. The somatic, psychological and urogenital symptoms were high in women at surgical menopause than at natural menopause. The mean transformed scores (0-100) of physical health, psychological, social relationships, and environmental domains was more in natural than the surgical menopause group.

Conclusion: The high individual and subscale scores of MRS were observed in both natural and the surgical menopause group. The severity of symptoms was found more distressing for surgical menopause group. The QOL in women at natural menopause where the symptoms experienced were less severe is average and better than the QOL in women at surgical menopause having severe menopause symptoms.

Key words: Menopause, Natural menopause, Post menopause, Quality of life, Surgical menopause

INTRODUCTION

Menopause is the permanent cessation of menstruation resulting from reduced ovarian hormone secretion that occurs either naturally or is induced by surgery, chemotherapy, or radiation. Natural menopause can be

recognized after 12 months of amenorrhea that is not associated with a pathologic cause.¹ Surgical menopause is the cessation of menses resulting from surgical removal of the uterus, leaving one or both ovaries, or the removal of both ovaries.² Estrogen deficiency, whether arising from surgical or natural menopause, can have both medical and psychological adverse consequences for a woman's health and well-being, that is, her health-related quality of life (HRQOL).³ HRQOL evaluates the patient's satisfaction with a level of function. It represents the functional effects of illness and its treatment on a woman, as she perceived herself.⁴ Of late, the concept of "QOL" has gained much popularity, with increasing number of clinicians incorporating HRQOL scales into both routine

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Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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practice and research.³ The QOL is defined by the World Health Organization (WHO) as “individuals’ perception of their position in life in the context of the culture and value systems in which they live, and about their goals, expectations, standards, and concerns.” QOL is a broad concept which incorporates in a complex way the person’s physical health, psychological state, the level of independence, social relationships, personal beliefs, and relationships to the physical environment.⁵

Various studies existing have indicated that menopause has been negatively related to QOL.⁶⁻⁹ This realization has led the researchers to consider incorporation of QOL in clinical practice, but most studies on QOL of postmenopausal women are from developed countries. Very scarce information exists about QOL of postmenopausal women in developing countries like India with hardly any study comparing the surgical with the natural menopause.

Hence, this study was undertaken to determine the menopause-related symptoms and its impact on QOL in postmenopausal women with natural and surgical menopause.

MATERIAL AND METHODS

A cross-sectional study had been conducted in 2013-2014 in the SMGS Hospital, Government Medical College Jammu and in the field practice area Ranbir Singh Pura. The study population was all patients with either natural or surgical menopause. The following women had been excluded in the study:

1. Who had already taken some form of estrogenic preparations in the preceding months
2. Who had severe medical disorders, such as renal, liver or cardiac disease, uncontrolled diabetes, or hypertension
3. Who were taking psychotropic medications
4. Who had undergone radical surgeries for malignancy
5. And who had a history of psychiatric disorders.

The group of women at surgical menopause comprised of all those who came to the Outpatient Department twice a week for gynecological follow-up during the specified period while a house to house survey had been conducted in the rural field practice area in a village; which was selected randomly to select the women at natural menopause. All women were interviewed by us with the help of a pretested semi-structured standard questionnaire.

Information regarding socio-demographic profile and reproductive parameters (such as parity, the age of menarche, regularity of menses, the age of menopause

(natural or surgical), and years since last menstruation were recorded by us.

For assessment of the menopausal symptoms menopause rating scale (MRS),¹⁰ was used. MRS is an 11-item questionnaire comprising three independent dimensions: Psychological, somatic, and urogenital subscale. Each of the 11 symptoms in MRS can get 0 (no complaints) or up to 4 scoring points (severe symptoms) depending on the severity of the complaints perceived by the women while completing the scale. By adding up the scores of each item of the respective dimensions, the composite scores for each of the subscales is calculated. The composite score (total score) is the sum of the dimension scores, and it is proportional to the severity of subjectively perceived symptoms.¹¹

WHOQOL-BREF questionnaire in English version¹² translated to local language was used for the assessment of HRQOL. The scores had been calculated according to the standard methods, and the raw scores were converted to transformation scores. The first transformation converts scores to the range of 4-20 and the second transformation converts domain scores to 0 to 100 scales. Higher scores reflect better QOL. The WHOQOL-BREF contains 26 items which are categorized under four main domains, i.e., physical, psychological, social, and environmental.

For the measurement of each item a separate 5 point scale ranging from never (4) to always (0 points) was used. Total score of each domain was 108. The higher score indicated a good QOL and the lower score indicated a poor QOL with high effect of menopausal symptoms on QOL. Those who obtained 0-33.3% scores were considered poor QOL, scores from 33.3 to 66.7% were taken as average QOL, and more than 66.7% scores were considered to have good QOL.

Statistical analysis

The data analysis was performed by computer software MS Excel and SPSS Version 21.0 (SPSS IBM Chicago Inc.) for windows. The quantitative variables are presented as the mean and the standard deviation. Menopausal symptoms are presented as percentages. Statistical differences between the groups are evaluated using Student “*t*” test. A $P < 0.05$ had been considered statistically significant. All *P* values reported are two-tailed.

RESULTS

As is evident from Table 1 both the groups were almost similar in characteristics on age, marital status, parity and age of menopause but there was a little difference in the

Table 1: Distribution of women at natural and surgical menopause according to age, marital status, parity, age at menopause and years since last menstrual period

Characteristic	Menopausal women		Statistical inference
	Natural (n=200)	Surgical (n=192)	
Age (in years)			
Mean±SD	53.2±6.20	54.4±6.65	t=-1.78 P=0.10 (NS)
Marital status			
Married	180 (90.00)	171 (89.06)	Chi-squared ₁ =0.09 P=0.76 NS
Widowed	20 (10.00)	21 (10.94)	
Parity status			
P1 and P2	44	27	Chi-squared ₂ =4.84 P=0.08 NS
P3-P5	139	142	
P6 and above	17	23	
Age of menopause (years)			
Mean±SD	45.8±3.84	45.0±4.14	t=-1.83 P=0.06 (NS)
Years since last menstrual period (years)			
Mean±SD	5.36±0.37	6.75±0.48	t=-3.06 P=0.02 (Significant)

NS: Not significant, SD: Standard deviation

years since last menstrual period though the difference was statistically significant but not much clinically.

As shown in Table 2. There was a significant difference between the MRS total scores of the natural (12.82 ± 5.60) and surgical (16.47 ± 7.74) group. The somatic, psychological and urogenital symptoms were more in surgical menopausal women than in natural menopausal women. However for urogenital subscale, the results were not statistically significant.

As evident from the Table 3 the mean raw scores of physical health, psychological, social relationships and environmental domains is more in natural than the surgical menopause group, and the result is statically highly significant. The mean transformed scores (0-100) including the physical health, psychological, social relationships, and the environmental domains are more in the natural menopause group than the surgical menopause group.

DISCUSSION

The aim of this study was to compare the effect of menopause on the QOL in two groups of women undergoing natural and surgical menopause. For the surgical menopause, hysterectomy itself may affect the QOL. To reduce this potential confounding effect in this study, the sample had been restricted to women who had undergone the surgery for benign gynecological conditions. Studies have shown that in the majority of women suffering

Table 2: Comparison of women at surgical and natural menopause according to menopause rating scale

Menopause rating scale	Menopausal women n (%)		Statistical inference
	Natural (n=200)	Surgical (n=192)	
Psychological subscale	4.66±2.89	6.37±4.02	t=4.846 P≤0.001 (HS)
Somatic subscale	4.78±2.56	6.23±3.53	t=4.678 P≤0.001 (HS)
Urogenital subscale	3.37±2.40	3.86±2.70	t=-1.915 P=0.056 (NS)
Total score	12.82±5.60	16.47±7.74	t=-5.378 P=<0.001 (HS)

NS: Not significant, HS: Highly significant

Table 3: Comparison of menopausal women from surgical and rural areas according to WHOQOL-BREF raw score

WHOQOL-BREF raw score	Menopausal women n (%)		Statistical inference
	Natural (n=200)	Surgical (n=192)	
Domain 1: Physical health	27.39±5.23	25.07±3.90	t=4.98 P≤0.001 (HS)
Domain 2: Psychological	22.01±3.58	20.49±3.80	t=4.070 P=<0.001 (HS)
Domain 3: Social relationships	9.64±2.81	8.56±2.69	t=3.87 P≤0.001 (HS)
Domain 4: Environment	31.09±6.35	27.67±5.29	t=5.77; P≤0.001 (HS)

HS: Highly significant, WHOQOL: World Health Organization quality of life

from benign gynecological conditions, QOL is improved within a month after hysterectomy; furthermore, such surgery does not appear to produce any psychological disturbance in otherwise psychologically healthy women.¹³ No doubt, years of painful periods or severe pelvic pain, for example, may motivate a woman to undergo surgery, and in such cases, an improvement in mood and a drop in the incidence of psychiatric morbidities can be due to the relief of these distressing gynecological symptoms. Nonetheless, an association between psychological and gynecological problems has been recognized for a long time.

The symptoms of estrogen deficiency reduce a woman's QOL.^{14,15} Surgical menopause causes a sudden drop in estrogen levels. In contrast, a woman at natural menopause passes through a phase of fluctuating hormone levels, and although a majority of these women report bothersome symptoms when questioned, only a few of these relate to the hormonal changes of the menopausal transition.

The present study revealed that proportions of menopausal symptoms were significantly high in both in the natural and surgically menopausal women. The findings of the present study showed that the women with the surgical menopause suffered from severe different menopausal symptoms such

as: Hot flushes, musculoskeletal and sweating symptoms as well as Depressive Mood, Anxiety, and Sleep problems as compared to women with natural menopause. It has also been depicted that the surgical menopause, as compared with natural menopause, was associated with more severe psychological and somatic symptoms which are in concordance with the studies made by Benschushan *et al.*,¹⁶ and Bhattacharya and Jha.¹⁷

It is worth mentioning that the urogenital symptoms including sexual problems, bladder problems, and dryness of vagina were less frequent in both the groups; the individual and overall scores of MRS were also low for urogenital domain especially more so in women with surgical menopause but the difference was not found to be statistically significant in concordance with Bhattacharya and Jha,¹⁷ but their result was statistically significant.

In this study, we have found the WHOQOL-BREF scores for all domain lower for women with surgical menopause, i.e., the women at surgical menopause showed a considerably worse QOL in the physical health, psychological, social relationships, and the environmental domains of the WHOQOL-BREF questionnaire when compared to their natural menopause counterparts and the results were significant statically.

Our study shows that an acute drop in estrogen levels in women, i.e., the women with surgical menopause have more severe menopausal symptoms and have a significantly worse effect on QOL than a slow drop. However, further studies are required to clarify the role of hormones in producing the menopausal symptoms and their effect on QOL.

CONCLUSION

The QOL was found to be significantly worse in surgical menopause group. Ratings on all three of the MRS subscales was higher, and all four WHO-QOL subscales were significantly lower (reflecting worse symptoms) in the group experiencing the acute drop in estrogen level induced by surgical menopause than the one with slow drop, i.e., the natural group. Therefore, we agree with the current recommendation that healthy premenopausal ovaries should be retained by surgeons, if there is no family history

of ovarian cancer or when the woman is not suffering from an estrogen-dependent disease such as endometriosis. The short- and potentially long-term consequences of the routine practice of oophorectomy at hysterectomy should be considered. Hormone replacement therapy needs to be recommended as and when required. However, HRT alone cannot help unless accompanied by regular exercise, proper diet, social interaction, mental occupation, and medical therapy whenever indicated.

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How to cite this article: Mahajan N, Kumar D, Fareed P. Comparison of Menopausal Symptoms and Quality of Life after Natural and Surgical Menopause. *Int J Sci Stud* 2016;3(11):74-77.

Source of Support: Nil, **Conflict of Interest:** None declared.

Clinico-etiological Profile and Predictors of Outcome in Acute Encephalitis Syndrome in Adult

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Abstract

Introduction: Acute encephalitis syndrome (AES) is a group of diseases having clinically similar neurologic manifestation caused by viruses, bacteria, fungi, parasites, spirochetes, or chemical/toxins, etc.

Aims: Present study has tried to establish etiology, clinical presentation, prognostic factors, and outcome in adult AES patients.

Materials and Methods: A prospective study was done on 200 patients of AES admitted to Nehru Chikitsalaya of B.R.D Medical College, Gorakhpur from July 2013 to June 2014. Clinical history, general examination, detailed central nervous system (CNS) examination, cardiovascular system examination, respiratory system examination, and blood investigations were performed for all the patients. An outcome was measured on the basis of modified Rankin scale.

Results: Out of 200 patients 96 (48%) were male, and 104 (52%) were female. About half of the patients 98 (49%) were from the age between 15 and 30 years. A total 172 (86%) patients were admitted to the hospital between August and October. The most common presenting symptoms were fever and altered sensorium. CNS examination of AES cases revealed that at the time of admission Glasgow coma scale (GCS) was ≤ 7 in 31 (15.5%) of cases and GCS > 7 in 169 (84.5%) cases. Hepatomegaly was the most common finding on abdominal examination. In the majority of the cases, hemoglobin was between 9 and 12 g/dl. Outcome observations revealed that complete recovery was seen in 136 cases (68%).

Conclusion: Disease has a higher incidence in the younger population. Japanese encephalitis was most common in 40 (20%) patients followed by enterovirus encephalitis. Most of the patients recovered as an outcome.

Key words: Etiology, Acute encephalitis syndrome, Japanese encephalitis, Uttar Pradesh

INTRODUCTION

Encephalitis is an acute inflammatory process that affects brain parenchyma, presents as a diffuse and/or a focal neuropsychological dysfunction and is almost always accompanied by inflammation of adjacent meninges. Children, elderly, and immunocompromised persons are most commonly affected.¹

The incidence of viral encephalitis is 3.5-7.4/100,000 persons per year.² Herpes simplex encephalitis is the

most common cause of sporadic encephalitis in western countries; the overall incidence is 0.2/100,000 (neonatal Herpes simplex virus (HSV) infection occurs in 2-3 per 10,000 live births). Arboviruses are the most common cause of episodic encephalitis with reported incidence similar to that of HSV Japanese encephalitis (JE), occurring in Japan, southeast Asia, China, and India, are the most common viral encephalitis outside the United States, affecting around 50,000 people per year acute encephalitis syndrome (AES) is reported mainly from Assam, Bihar, Karnataka, Uttar Pradesh, and Tamil Nadu which contributes approximately 80% of cases. North-eastern Uttar Pradesh has been experiencing regular epidemics of encephalitis since 1978.² The case fatality and morbidity are very high. The state of Uttar Pradesh has experienced periodic AES outbreaks since 1978, but following a major outbreak in 2006, the annual caseload has exceeded 3,000 patients, three times the level prior to that year.³ The state has accounted for almost half (over 20,000) of cases and 3,560 deaths since

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Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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2008.⁴ Only 8.1% of the cases have been confirmed for JE, and the state has annually hosted a variety of investigative teams.⁵ It has been suggested that shallow wells pumping up contaminated drinking water are a major problem. However, making any conclusions about what is causing AES outbreaks in Uttar Pradesh is hampered by poor patient record systems.⁶

JE is considered as a main viral etiology of patients with AES. Infection with JE virus may cause febrile illness, meningitis, myelitis, or encephalitis and is clinically indistinguishable from other causes of an AES.⁷ Children and young adults are usually the most frequently affected groups.¹

This study is conducted to identify the etiological pattern of AES and to study clinical differences among the adult patients admitted in the Department of Medicine, B.R.D. Medical College. To establish prognostic factors and outcomes in a patient of AES is also the secondary endpoint of this study.

MATERIALS AND METHODS

A prospective study was done on 200 patients of AES admitted to Nehru Chikitsalaya of B.R.D Medical College, Gorakhpur from July 2013 to June 2014.

Patients of any age, at any time of year with an acute onset of fever and a change in mental status (including symptoms such as confusion, disorientation, coma, or inability to talk) and/or new onset seizures (excluding simple febrile seizures), increase in irritability, somnolence, or abnormal behavior greater than that seen with usual febrile illness were included in the study.

Clinical history including duration of fever, headache, vomiting, altered sensorium, seizures, paralysis, cough, breathlessness, chest and abdominal pain, diarrhea, swelling of body, and gastrointestinal bleeding was recorded for all patients.

The general examination including pulse, blood pressure, respiratory rate, temperature, pallor, icterus, cyanosis, clubbing, edema, lymphadenopathy, and state of hydration was also done on all patients.

A detailed central nervous system (CNS) examination was carried out with special emphasis on the state of higher centers, level of consciousness, signs of meningeal irritation, involvement of cranial nerves, sensory, motor examinations, superficial and deep tendon reflexes, cerebellar signs, involuntary movements, gait of the patients, and fundus examination.

In cardiovascular system examination, tachycardia, peripheral circulatory failure, gallop rhythm, features of congestive heart failure, heart murmurs, and heart sounds (muffled or loud) were done. Abdominal examination including hepatomegaly, splenomegaly, hepatosplenomegaly, and ascites was performed. In respiratory system examination including types of breath sounds, adventitious breath sounds (crepts/rhonchi), and respiratory failure was also recorded for all patients.

Blood investigations including hemoglobin, total leucocyte count (TLC), differential leucocyte count, platelet count, general blood picture, random blood sugar, renal function tests, liver function tests, serum electrolytes, and rapid diagnostic test for malaria parasite were done by standard methodology. Blood culture was also done in selected cases.

Other examination including urine, cerebrospinal fluid (CSF), chest X-ray (posterior-anterior view), electrocardiogram, immunoglobulin (IgM) enzyme-linked immunosorbent assay for JE virus and enterovirus (EV) in serum and CSF, IgM, and NS1 antigen for dengue virus, computed tomography scan and magnetic resonance imaging brain, real time-polymerase chain reaction (PCR) assay for quantitation of the viral RNA from the specimens were also done.

The outcome was measured on the basis of modified Rankin scale. The scale runs from 0 to 6, running from perfect health without symptoms to death. Rankin scale is as follows:

0 - No symptoms, 1 - No significant disability, able to carry out all usual activities, despite some symptoms, 2 - Mild disability, able to look after own affairs without assistance, but unable to carry out all previous activities, 3 - Moderate disability, requires some help, but able to walk unassisted, 4 - Moderately severe disability, unable to attend to own bodily needs without assistance, and unable to walk unassisted, 5 - Severe disability, requires constant nursing care and attention, bedridden, incontinent, and 6 - Dead.

In statistical analysis, multiple logistic regressions were applied to know about prognostic factors of the outcome.

RESULTS

Out of 200 patients, 96 (48%) were male, and 104 (52%) were female. About half of the patients 98 (49%) were from the age between 15 and 30 years. Only 24 (12%) patients had age more than 60 years.

Month wise distribution of patients admitted to hospital showed that a total 172 (86%) patients were admitted to the hospital between August and October.

Duration of stay in the hospital showed that 184 (92%) patients had to stay in the hospital for <10 days. Only 2 (1%) patients had a hospital stay of >15 days.

Area wise distribution of AES cases revealed that 171 (85.5%) patients were from Uttar Pradesh area from districts of Gorakhpur and Basti division, 22 (11%) were from Bihar, and 1 (0.5%) was from Nepal. Only 6(3%) belonged to other districts of Mau, Ballia, and Balrampur.

The most common presenting symptoms were fever and altered sensorium, which was present in all cases (100%) followed by vomiting in 137 (68.5%), headache 131 (65.5%), and seizures in 104 (52%).

Pyrexia was the predominant feature in 164 cases (82%) followed by tachycardia in 154 (77%) and pallor in 49 (24.5%). Icterus was present in 23 (12.5%) and shock in 20 (10%).

CNS examination of AES cases revealed that at the time of admission Glasgow Coma Scale (GCS) was ≤ 7 in 31 (15.5%) of cases and GCS >7 in 169 (84.5%) cases, signs of meningeal irritation was present in 119 (59.5%) patients and cranial nerve palsy present in 3 (1.5%) patients, dilated sluggish reacting pupil was seen in 10 (5%) patients. The tone was normal in 116 (58%) patients, increased in 48 (24%) patients, and decreased in 36 (18%) patients. The deep tendon reflex exam was increased in 33 patients (16.5%) and decreased in 46 (23%) patients. Plantar was extensor in 100 cases (50%) and mute in 26 (13%). Papilledema was present in 15 (7.5%). Extrapyrimal and cerebellar signs were found in only 5 (2.5%) and 6 (3%) cases, respectively while hemiparesis in only 5 (2.5%) cases.

Findings of other systemic examination of AES cases showed that hepatomegaly was the most common finding on abdominal examination found in 6 (3%) cases followed by splenomegaly in 5 (2.5%) and ascites in 2 (1%). Adventitious sounds (crepts/rhonchi) were present in 29 cases (14.5%), ventilator support was required in 10 (5%), and bronchial breath sounds in 3 (1.5%). Raised jugular venous pressure (JVP) was the most common cardiac abnormality found in 3 cases (1.5%) followed by muffled heart sounds and gallop rhythm in 2 (1%). In JE positive group, none had a cardiac abnormality.

Hematological and biochemical investigations showed that in the majority of the cases hemoglobin was between 9 and 12 g/dl 102 (51%) cases followed by >12 in 52 (26%). Leukocytosis was found in 98 cases (49%). Serum glutamic pyruvic transaminase was raised in 142 cases (71%). Serum creatinine was raised in 46 cases (23%).

Evaluation of CSF found that CSF protein level was between 40 and 100 mg/dl present in 95 cases (47.5%) and more than 100 in only 68 (34%). Sugar was decreased in only 25 cases (12.5%) and normal in rest of them. Gram-positive cocci were not seen in any of the samples. Protein <40 and sugar >40 was present in 19 (9.5%) patients which suggested of viral encephalitis. CSF protein was between 40 and 100 mg% and sugar >40 mg% found in 42% of the patients which suggested that patient may be partially treated acute bacterial meningitis or tubercular or viral meningitis. Protein >40 and sugar <40 was present in 11% of cases which suggested acute bacterial meningitis.

In JE patients, most common CSF finding was protein between 40 and 100 mg% and sugar >40 24 (60%). Only in 11 (27.5%) patients, CSF protein was >100 and sugar in normal range. In EV positive patients, most common CSF finding was CSF protein >100 and sugar >40 in 9 (64.3%) patients only in 3 (21.4%) patients, CSF protein was 40-100 and sugar >40 mg%.

Virological analysis of CSF and serum showed that out of total cases (200) studied, 40 cases (20%) were found to be JE positive. IgM for JE positivity was found in CSF was (9%) and serum (15%). 14 (7%) cases were found to be EV positive. 2 patient (1%) had HSV positive in CSF by PCR and 2 patient (1) were Dengue positive.

In 59% of cases, etiology could not be known. Out of all known etiologies (41%) AES, JE was most common seen in (20%) followed by EV encephalitis 14 (7%) and rest 14% were of tuberculosis meningitis, acute bacterial meningitis, cerebral malaria, HSV encephalitis, or dengue virus encephalitis.

Outcome observations revealed that complete recovery was seen in 136 cases (68%). 34 (17%) cases of AES expired while 15% were discharged with sequelae. Out of 34 patients, who expired etiology of AES was uncertain in 20 cases (58.8 %) and 6 (17.6%) patients were JE positive, while rest 3 (8.8%) patients each had acute bacterial meningitis and cerebral malaria only 1 (2.9%) EV positive patients expired out of 14 patients.

Out of 200 patients, 26 (13%) had aspiration pneumonitis followed by shock 20 (10%), ventilatory support was required in 10 (5%) cases while sequelae was seen in 7 (3.5%) and psychosis in 3 (1.5%) cases (Tables 1 and 2).

DISCUSSION

North-eastern Uttar Pradesh has drawn national and international attention due to continuing epidemics of AES

Table 1: CNS examination findings of JE and non-JE cases*

CNS examination findings	Number of cases	JE positive (n=40)	Non-JE viral (n=18)	Non-JE unknown and other (n=142)
GCS				
<7	31 (15.5)	3 (7.5)	2	26
7-12	169 (84.5)	37 (92.5)	16	116
>12	0	0	0	0
Signs of meningeal irritation (NR/KS/both)	119 (59.5)	28 (70)	8	83
Cranial nerve palsies	3 (1.5)	0	0	3
Pupil				
NS/NR	150 (75)	32 (80)	16	102
SS/SR	40 (20)	6 (15)	1	37
Dilated/SR	10 (5)	2 (5)	1	7
Fundus (papilledema)	15 (7.5)	2 (5)	1	12
Cranium and spine deformity	0 (0)	0	0	0
Tone				
Normal	116 (58)	19 (47.5)	15	82
Increased	48 (24)	18 (45)	1	29
Decreased	36 (18)	3 (7.5)	2	31
Hemiparesis	5 (2.5)	1 (2.5)	0	4
DTR				
Normal	121 (60.5)	22 (55)	14	85
Increased	33 (16.5)	14 (35)	2	17
Decreased	46 (23)	4 (10)	2	40
Plantar				
Extensor	100 (50)	16 (40)	10	74
Flexor	50 (25)	13 (32.5)	4	37
Mute	26 (13)	4 (10)	3	19
Withdrawal	24 (12)	7 (17.5)	1	16
Cerebellar signs	6 (3)	2 (2.5)	1	3
Extrapyramidal signs	5 (2.5)	4 (10)	0	1

*Data is expressed as no of patients (%). JE: Japanese encephalitis, DTR: Deep tendon reflex exam, GCS: Glasgow coma scale, CNS: Central nervous system

Table 2: Relation of blood and CSF parameters with outcome

Outcome	TLC/mm ³	Platelet lac/mm ³	Serum creatinine mg%	SGPT IU/DL	CSF protine in mg%	CSF sugar in mg%	CSF TLC
mRS 0	11199	1.6	1.2	73	109	65	124
mRS 1	12500	1.6	1.1	138	102	62	84
mRS 2	11500	1.75	0.8	40	68	30	159
mRS 3	9200	1.7	0.92	67	57	63	68
mRS 4	11400	1.5	0.89	113	156	51	126
mRS 5	8333	1.3	1.1	47	180	52	66
mRS 6	14800	1.3	1.5	90	137	64	122
LAMA	13100	2.1	1.2	71	193	53	290
REFER	7271	1.28	1.9	66	120	65	147
Total (average)	11797	1.5	1.3	79	116	64	206

*Data are expressed as average. TLC: Total leucocyte count, SGPT: Serum glutamic pyruvic transaminase, CSF: Cerebrospinal fluid

and its changing pattern. Moreover, it has a wide socio-political implication. Mostly, AES affects children though significant numbers of adults are also affected. Several epidemics of AES has occurred since 1978,²

which has drawn massive public and political attention, Despite all the efforts, the epidemics are regularly occurring causing heavy mortality and morbidity.

Demography

A total of 200 consecutively admitted cases of AES in the Department of Medicine, BRD Medical College Gorakhpur were included in this study. Mean age of

patients was 37 years (range 16-80 years). Age of 45% of cases was <30 years of age suggesting that the disease mostly affected the younger population. Younger patients were more affected most probably because of lack of cumulative immunity due to natural infection.⁸ In our study, 48% patients were male, and 52% patients were female. Male: female ratio was 1:1.08.

Although the cases were seen throughout the year, the incidence peaked in the month of October (34.5%). The peak incidence of the disease was from August to October, i.e., post monsoon period suggesting the seasonal occurrence of the disease. It is well-known fact that the

incidence of arboviral and EV infections increases in this period.

The average duration of hospital stay was 5.7 days. In 62.5% of cases, the duration of hospital stay was ≤ 5 days and in 29.5% of cases, it was between 6 and 10 days. Duration of stay was more than 15 days in only 1%. The majority of patients were from Uttar Pradesh. Gorakhpur division accounted for 68.5% cases followed by Basti division (17%) and adjoining regions of Bihar and Nepal. Only 6 (3%) patients belonged to other districts/regions of Uttar Pradesh like Mau, Ballia, and Balrampur.

Clinical Features

The most common presenting symptoms were fever and altered sensorium which was present in all cases (100%) cases, followed by in vomiting 68.5% and headache in 65.5%. Abdominal pain was present in 7.5% patients, loose stools in 4.5%, breathlessness in 4%, and swelling over the body in only 3%. Abdominal pain, loose stools, and swelling over body are more common in EV infection. The cause of swelling over the body may be due to myocarditis producing congestive heart failure or due to multiorgan involvement by the virus. Pyrexia (temperature >100 F) was the predominant feature in 82%, followed tachycardia in 77% patients and pallor in 24.5%. Icterus and edema were present in 11.5% and 3% of cases, respectively. Both these signs is usually seen in EV encephalitis and cerebral malaria.⁹ At the time of admission, GCS was ≤ 7 in 31 (15.5%) of cases in which 3 patients had JE encephalitis while 28 patients had non-JE encephalitis. Signs of meningeal irritation were present in 119 (59.5%) patients. Response were present in 30 (28%) and 42 (39.3%) subjects, respectively. In our study, papilledema was seen in 15 (7.5%) cases only. The extrapyramidal sign was present in 5 (2.5%) patients out of which 4 patients had JE while cerebellar signs were found in only 6 (3%) cases. Hemiparesis was found in only 5 (2.5%) cases out of which only 1 patient had JE. Focal neurological deficits at presentation were present in only 10 (9.3%) cases.

Hepatomegaly was the most common finding on abdominal examination found in 6 cases (3%) followed by splenomegaly in 5 (2.5%) and ascites in 2 (1%). None of the patients in JE positive group had positive abdominal examination finding. Adventitious sounds (crepts/rhonchi) were present in 29 cases (14.5%) followed by the requirement of ventilator support in 10 (5%) and bronchial breath sounds in 3 (1.5%). The patients with adventitious sounds may be due to a higher incidence of complication like aspiration pneumonitis.

Raised JVP was the most common cardiac abnormality found in 3 cases (1.5%), followed by muffled heart sounds

and gallop rhythm in 2 each (1%). In JE positive group, none of the patients had positive cardiac examination finding.

All these findings may be due to EV infection causing myocarditis. Out of all, the EVs, Coxsackie B virus is most commonly implicated in heart infection.¹⁰

Etiology

JE accounted for 40 (20%), EV encephalitis 14 (7%), tubercular meningitis 11 (5.5%), septic meningitis 7 (3.5%), cerebral malaria 6 (3%), HSV encephalitis 2 (1%), and dengue encephalitis in 2 (1%) patients of AES. In 118 (59%) cases, cause of AES could not be ascertained. Clearly, in more than half of the cases, the etiology could not be known. This calls for separate epidemiological and microbiological studies to find out the exact etiological agent for the unknown agent's causing AES and thus planning the preventive measures.

The cause of viral encephalitis was established as JE in 19 (17.7%) patients and herpetic encephalitis in 4 (3.7%) patients. Pyogenic meningitis was the second most common diagnosis responsible for 45 (42%) cases. Cerebral malaria was documented in 8 (7.5%) children and tubercular meningitis in 4 (3.7%) children presenting as acute febrile encephalopathy. Typhoid fever was a cause of encephalopathy in one subject. In our study, the predominance of viral etiology over bacterial meningitis may be due to more prevalence of vector borne and water borne diseases in our study population.

Outcome

The outcome was measured on the basis of modified ranking scale (mRS) poor outcome were taken as mRS 4, mRS 5, and mRS 6. A good outcome is taken as mRS 0-mRS 3. Most of the patients 136 (68%) belongs to mRS 0 which was fully recovered, 41 patients had poor outcome (mRS 4, mRS 5, and mRS 6) out of which 34 (17%) patient has been expired (mRS 6) and 7 (3.5%) patient had morbidity (mRS 4 and mRS 5).

In our study, case fatality rate was 17%. Etiology wise mortality showed that out of 34 patient who expired, 20 (58.8%) patients were of unknown etiology, 6 (17.6%) patients had JE, 1 (2.9%) patient in each were suffering from EV encephalitis, and tubercular meningitis while 3 (8.8%) patient each belonged to septic meningitis and cerebral malaria group. It suggested that mortality is more in septic meningitis, cerebral malaria, and patients in which etiology is uncertain. The average duration of stay was more in mRS 4 and mRS 5 group. It may be due to because these patients had severe morbidity. Out of 31 patients who had low GCS (<7), 28 (90.3%) belonged to mRS 6 group. It was observed that low GCS associated with poor outcome.

TLC was markedly raised (average - 14800 cells/mm³) in mRS 6 group which suggests that high TLC may be correlated with poor outcome. Other blood and CSF parameter did not show many differences in between expired patients and survivors.

In the univariate analysis, we assessed all potential variables including clinical features, demographic parameters, blood and CSF examination, etiologies of AES, and complications for their association with poor outcome.

On univariate correlation, the presence of seizure, low GCS, high TLC, aspiration pneumonia, and requirement of ventilator support, and low platelet count was statistically significantly associated with poor outcome in AES Patients. In multivariate analysis, we assessed parameter which found to be significant on univariate analysis with poor outcome.

On multivariate analysis, low GCS, high TLC, aspiration pneumonitis, and respiratory failure had statistically significant correlation with poor outcome, but seizure and low platelet count which had significant correlation on univariate analysis found no significant on multivariate analysis.

CONCLUSION

The patients of almost all the age groups suffered from disease. Mean age was 37.7 years. Almost half of the patients (49%) were between 15 and 30 years of age, suggesting the disease has a higher incidence in the younger population. A maximum number of patients came during the month of August-October, suggesting the seasonal occurrence of the disease. The most common presenting symptoms of AES patients were fever and altered sensorium followed by vomiting, headache, and seizures. The most common finding of a general examination of AES patients was pyrexia followed by tachycardia and pallor. Most of the patients presented with signs of meningeal irritation and raised intracranial tension. In 118 (59%) patients, etiology of AES could not be ascertained. Out of known agents, JE was most common in 40 (20%) patients followed by EV encephalitis in 14 (7%) patients than tubercular meningitis, septic meningitis, cerebral malaria, HSV encephalitis, and dengue virus encephalitis. On univariate correlation, the presence of seizure, low GCS, high TLC, aspiration pneumonia, requirement of ventilator support and low

platelet count was statistically significantly associated with poor outcome in AES Patients.

On multivariate analysis, low GCS, high TLC, aspiration pneumonitis, and respiratory failure had statistically significant correlation with poor outcome. In spite of best of our effort and limited resources, etiologies of more than 50% AES cases could not be ascertained. Further research and analysis are required to analyze AES cases due to unknown agents. Out of known etiologies of AES, JE (vector borne), EV encephalitis (water borne), and cerebral malaria (vector borne) are preventable. So, the burden of the disease could possibly be reduced by educating people and preventive measures.

Aspiration pneumonitis (13%) was the most common complication in AES patients followed by respiratory failure (5%). As these complications may be prevented so early hospitalization, proper positioning, and general care of patients could possibly help in reducing morbidity and mortality. New strategies for pathogen identification and continued analysis of exposures and clinical features could help us improve our ability to diagnose, treat, and prevent AES.

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How to cite this article: Shahi RK, Nigam P. Clinico-etiological Profile and Predictors of Outcome in Acute Encephalitis Syndrome in Adult. *Int J Sci Stud* 2016;3(11):78-83.

Source of Support: Nil, **Conflict of Interest:** None declared.

Comparative Study of Knowledge, Attitude and Practices toward Contraception among Tribal and Non-Tribal Wives of Eligible Couples in a Rural Area of Assam

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Abstract

Background: If all unplanned pregnancies could be eliminated, it is estimated that there would be 22 million fewer abortions each year, and the associated complications would be lessened.

Aims and Objectives: (1) Compare knowledge, attitude, and practices toward contraceptives among wives of tribal and non-tribal eligible couples of Rani Community Development Block, Kamrup, Assam, (2) to study various factors influencing contraceptive practices.

Materials and Methods: It is a community based cross-sectional study done from August 2014 to July 2015. Wives of currently married couples in the reproductive age group of 15-45 years were interviewed. A total of 150 tribal eligible couples and 150 non-tribal eligible couples were taken for the study.

Results: Knowledge about contraceptive methods is almost universal about 90.6% of tribal wives, and 92.33% of non-tribal wives knew about contraceptive. Association of age, education status, occupation, and socioeconomic status was found to be statistically significant with contraceptive usage.

Conclusion: Besides having a good knowledge about contraception the practice is still lagging, and only 36% among tribal and 46% among non-tribal are using modern methods of contraception which is very low. Regarding modern contraceptive prevalence rate, although there was some improvement compared to the past national averages; however, the current figure for prevalence rate is still low when compared to the national target.

Key words: Attitude, Contraception, Knowledge, Practices, Tribal and non-tribal

INTRODUCTION

Contraception is defined as intentional prevention of conception or impregnation by interfering with the normal process of ovulation, fertilization and implantation through the use of various devices, agents, drugs, sexual practices, or surgical procedures.

Acceptance of contraception by a couple is governed by various socio-cultural factors, such as religion and education of husband and wife. Use of various contraceptive methods varies within different societies, caste, religion, and regions. This variation which is at an individual, family and community level influenced by various factors such as socioeconomic status, literacy, religious acceptance is always a matter of concern among the researchers trying to unearth the real hindrance of various family welfare program.¹

According to the National Family Health Survey (2005-2006) Schedule Tribes in India have very high total fertility rate (3.12) than other social groups and

Access this article online



www.ijss-sn.com

Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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National Health Policy of India prioritizes Schedule Tribe population as special needs group for extending the health care services.² Besides having all the resources, there are still some hindrance which is acting as barrier for contraceptive usage.³ Keeping these in background the objective of my study is to:

1. Compare knowledge, attitude, and practices toward contraceptives among tribal and non-tribal wives of eligible couples of Rani Community Development (CD) Block, Kamrup, Assam
2. To study various factors influencing contraceptive practices.

MATERIALS AND METHODS

Rani CD Block comes under Kamrup district of Assam situated having geo points 25.80° North 91.27° East. The total area of Kamrup District is 3105 km² with a total population of 1,517,542. Rani comes under the filed practice area of Department of Community Medicine, Gauhati Medical College. This is a community based cross-sectional study done from August 2014 to July 2015. Wives of currently married couples in the reproductive age group of 15-45 years were the respondents.

Inclusion Criteria

1. Wives of eligible couples where wife is in the age group of 15-45 years
2. Residing in the Rani area at least for a period of 1-year.

Exclusion Criteria

1. Wives of eligible couples not giving consent for the study
2. Divorced, separated, and widowed couples are excluded from the study.

According to Annual Health Survey 2010-2011, contraceptive prevalence including both traditional and modern method among the eligible couples of Kamrup district of Assam is 78.8%.³ For comparative analysis and in the absence of the availability of similar studies, the sample size was calculated assuming the difference in percentages of contraceptive practices among tribal and non-tribal eligible couples as 15%. Using the formula for comparison of two proportions, and taking prevalence of contraceptive use among non-tribal as 78.8% (p_1), with a difference of 15% on either side, for 95% confidence interval and 80% power, the sample size calculated was 142 in each group, rounding the figure to 150, i.e., there will be 150 tribal eligible couples and 150 non-tribal eligible couples making a total sample size of 300 eligible couples.

$$n = (Z_{\alpha/2} + Z_{\beta})^2 * (p_1(1-p_1) + p_2(1-p_2)) / (p_1 - p_2)^2$$

There are 54 villages under the Rani CD block according to census 2011. On the basis of the proportion of the tribal population, the villages are divided into two group tribal and non-tribal, 23 tribal villages and 28 non-tribal villages. Using random number table, 10 villages from each group are selected, and from each village, 15 wives of eligible couples are selected. Thus, making a total sample size of 300 eligible couple 150 tribal and 150 non-tribal eligible couples. Data were collected by house to house visit using a pre-tested pre-designed schedule containing both open and closed ended question. Data were compiled in Excel sheets and analysis was done using Graphpad's Instat taking a $P < 0.05$ statistically significant. Ethical permission was taken from Institutional Ethics Committee.

RESULTS

A total of 150 tribal and 150 non-tribal wives of eligible couples were selected. The maximum number of tribal wives (28%) and non-tribal wives (30%) were in the age group of 26-30 years. While among the tribal wives the least number of wives were seen in the age group of 41-45 years (9.33%) and among non-tribal it was the 15-20 years age group (7.33%) (Table 1). Among tribal couples about 78% were Hindu are 22% are Christian. There were no

Table 1: Distribution of socio demographic profile of tribal and non-tribal wives of eligible couples

Characteristics	Tribal (%) n=150	Non-tribal (%) n=150
Age (wives) in years		
15-20	15 (10)	11 (7.3)
21-25	27 (18)	31 (20.6)
26-30	42 (28)	45 (30)
31-35	30 (20)	27 (18)
36-40	22 (14.6)	18 (12)
41-45	14 (9.33)	18 (12)
Education level		
Illiterate	30 (20)	26 (17.3)
Primary school	25 (17.3)	16 (10.6)
Middle school	21 (14)	20 (13.3)
High school	33 (22)	31 (20.6)
Matriculate	24 (16)	30 (20)
Higher secondary	11 (7.3)	17 (11.3)
Graduate and above	6 (4)	10 (6.6)
Occupation		
Home makers	59 (39.3)	52 (34.6)
Daily wage earners	42 (28)	37 (24.6)
Business	39 (26)	47 (31.3)
Service	10 (6.6)	14 (9.3)
Socioeconomic status (B.G. Prasad)		
Class I	8 (5.3)	10 (6.6)
Class II	22 (14.6)	18 (12)
Class III	25 (16.6)	32 (21.3)
Class IV	40 (26.6)	37 (24.6)
Class V	55 (36.6)	53 (35.3)

Figures in parenthesis represent column-wise percentage

tribal couples of Islam religion. However, among the non-tribal couples about 36% were Muslim and only 3.4% were Christian. About 20% of the tribal wives were illiterate which is higher than the non-tribal wives (17.33%). In both tribal and non-tribal groups, the maximum number of wives had studied up to high school.

About 39.33% of tribal wives and 34.67% of non-tribal wives were housewives. Only 6.67% of tribal and 9.33% of non-tribal were doing service either under Government or Private sector. Most the housewives were also seasonal cultivators who help their husbands at the time of sowing and harvesting. In this study, maximum number of couples including tribal and non-tribal belong to Class V socioeconomic class, 36.6% and 35.33% among tribal and non-tribal eligible couples, respectively (Table 1). Among tribal 42.6% couples were below poverty line and among non-tribal 38.6% were below poverty line. The proportion of BPL couples among tribal is higher than the non-tribal which emphasized that they are an underdeveloped community. Among the tribal couples about 54% were living in joint families while among non-tribal it is 61.4%. Among the tribal wives majority (50%) were Parity 2 and among non-tribal 40% are Parity 2. There were only 5% tribal wives with Parity 0.

The difference of knowledge about various contraceptive methods among tribal and non-tribal wives was found to be statistically insignificant with $P = 0.3859$ (Table 2). Knowledge about a natural method like withdrawal is highest among both tribal and non-tribal wives, but knowledge about lactational amenorrhea and calendar method is low. Above 90% of the wives knew about any one of the contraceptive methods, besides this only 5.33% of tribal wives and 6.67% of non-tribal wives knew about implant contraceptives. Among the modern contraceptive methods, oral contraceptive pills (OCP) is the most popular method both in tribal and non-tribal wives, Cu-T (IUCD) is second most popular (73.33%)

among tribal and tubectomy (80.67%) among non-tribal wives. Among tribal wives positive attitude toward contraception was found in 69.3% and 72% among non-tribal wives, on statistical analysis this difference among tribal and non-tribal was found to be insignificant ($P = 0.8984$) (Table 2).

Among the eligible couples 28% tribal couples and 34% of non-tribal couples were using one or more methods of contraception currently. This difference of usage rate among tribal and non-tribal is found to be statistically significant with a $P = 0.0238$ on Chi-square analysis (Table 2).

The most common source of information is health workers (Doctors, Nurses, ASHA, and MPW) among the tribal (51%) but among the non-tribal wives, the most common source (52%) was Mass Media (including Newspaper, Radio, TV). Among the tribal users, 40.5% were using natural methods of contraception out of which the most practiced one is withdrawal method (25.8%) and among the modern methods the most preferred one is the OCP, about 27.9% of the total users. Not a single couple had undergone vasectomy or used injectable contraceptives. OCP were the most preferred (31.8%) among the non-tribal also, and there were no users of injectable contraceptives and implants, but there is a single non-tribal husband who had undergone vasectomy.

It was seen that the maximum usage rate is in the age group of 26-30 years which is 88.09% and next to it is in the age group of 31-35 years (73.33%), the lowest usage rate is in the age group of 36-40 years (27.27%) and on doing Chi-square test this association is found to be significant with a $P < 0.0001$. Similarly, among the non-tribal wives the maximum usage rate (88.89%) is in the age group of 26-30 years and 31-35 years, lowest usage is in the age group of 41-45 years; on Chi-square analysis, this relation is found to be significant with a $P < 0.004$ (Table 3).

Table 2: Knowledge and attitude and practices about contraception among wives of tribal and non-tribal eligible couples

Parameters	Tribal wives (%)	%	Non-tribal wives (%)	%	Total	P value
Contraceptive knowledge						
Present	136 (90.6)	49.1	141 (94)	50.9	277 (92.33)	0.3859*
Absent	14 (9.4)	60.9	9 (6)	39.1	23 (7.67)	
Total	150 (100)	50	150 (100)	50	300 (100)	
Attitude						$P=0.8984 \chi^2=0.01630$
Positive	106 (69.3)	49.5	108 (72)	50.5	214	
Negative	44 (31.7)	51.1	42 (28)	48.9	86	
Total	150 (100)	50	150 (100)	50	300	
Contraceptive Users	93 (62)	45.1	113 (75.4)	54.9	206 (68.7)	$P=0.0238 \chi^2=5.108$
Non-users	57 (38)	60.6	37 (24.6)	39.4	94 (31.3)	
Total	150 (100)	50	150 (100)	50	300 (100)	

*Fisher's exact test figures in parenthesis represent column-wise percentage

On Chi-square analysis, the association between education level and contraceptive use is also found to be significant in both tribal and non-tribal wives with a $P = 0.002$ and <0.001 respectively (Table 4).

Of total 24 wives doing service either on Government or Private sector 19 were using contraception, among them 8 were tribals and 11 non-tribals. The association of contraceptive usage and occupation was found to be significant in both tribal and non-tribal wives (Table 5).

Among tribal users about 33% were from Class V socioeconomic status. The association was also significant between socioeconomic status (B. G. Prasad) and contraceptive use in both tribal and non-tribal wives (Table 6).

DISCUSSION

This study was conducted to compare the KAP toward contraception among wives of tribal and non-tribal. Similar to this study Pegu *et al.*, in their KAP study among the Khasi's found that the maximum number of wives were in the age group of 20-30 years (48%).⁴ Bora and Kumar among the Garhwals, found that the literacy rate of wives is 63% only and the maximum number of wives (28.7%) studied up to primary level,⁵ literacy rate in both the studies was lower than the present study.

Kaur *et al.*, in their study found that awareness was about 55.7% about various contraceptive methods out of which condom and OCP were the most commonly known. Similarly, in this study, the most known was OCP among

Table 3: Association of age (in years) with contraceptive usage among wives of tribal and non-tribal eligible couples

Age	Tribal (n=150) (%)		P value	Non-tribal (n=150) (%)		P value
	Users	Non-users		Users	Non-users	
15-20	9 (9.67)	6 (10.5)	$\chi^2=29.3, P<0.0001$	7 (6.19)	4 (10.81)	$\chi^2=22.8, P<0.004$
21-25	13 (13.97)	14 (24.56)		24 (21.2)	7 (18.9)	
26-30	37 (39.8)	5 (8.77)		40 (35.3)	5 (13.56)	
31-35	22 (23.66)	8 (14.04)		24 (21.2)	3 (8.11)	
36-40	6 (6.45)	16 (28.09)		11 (9.75)	7 (18.9)	
41-45	6 (6.45)	8 (14.04)		7 (6.19)	11 (29.73)	
Total	93 (100)	57 (100)	Total	113 (100)	37 (100)	

Table 4: Association of education status and contraceptive usage among wives of tribal and non-tribal eligible couples

Education level	Tribal (n=150) (%)		P value	Non-tribal (n=150) (%)		P value	
	Users	Non-users		Users	Non-users		
Illiterate	15 (16.13)	15 (26.31)	$\chi^2=24.078, P=0.002, df=5$	16 (14.1)	10 (27.02)	$\chi^2=29.70, P<0.001, df=5$	
Primary school	8 (8.60)	17 (31.57)		4 (3.53)	12 (32.43)		
Middle school	10 (10.75)	11 (19.29)		17 (15)	3 (8.10)		
High school	26 (27.96)	7 (12.28)		26 (23)	5 (13.51)		
Matriculate	21 (22.58)	3 (5.26)		27 (23.8)	3 (8.10)		
HS	8 (8.60)	3 (5.26)		14 (12.3)	3 (8.10)		
Graduate and above	5 (5.38)	1 (1.75)		9 (7.96)	1 (2.7)		
Total	93 (100)	57 (100)		Total	113 (100)		37 (100)

Table 5: Association of occupation and contraceptive usage among wives of tribal and non-tribal eligible couples

Occupation	Tribal (n=150) (%)		P value	Non-tribal (n=150) (%)		P value	
	Users	Non-users		Users	Non-users		
Home maker	27 (29.03)	32 (56.14)	$\chi^2=11.32, P=0.0101, df=3$	32 (34.5)	20 (54.1)	$\chi^2=10.38, P=0.015, df=3$	
Daily wage earners	31 (33.33)	11 (19.29)		28 (24.7)	9 (24.32)		
Business	27 (29.03)	12 (21.05)		42 (30.9)	5 (13.5)		
Service	8 (8.61)	2 (3.5)		11 (9.73)	3 (8.10)		
Total	93 (100)	57 (100)		Total	113 (100)		37 (100)

Table 6: Association of socioeconomic status (B.G. Prasad classification) and contraceptive usage among wives of tribal and non-tribal eligible couples

Socioeconomic status	Tribal (n=150) (%)		P value	Non-tribal (n=150)		P value
	Users	Non-users		Users	Non-users	
Class I	6 (6.45)	2 (3.5)	$\chi^2=8.461, P=0.0036, df=1$	8 (7.1)	2 (5.4)	$\chi^2=7.550, P=0.0060, df=1$
Class II	20 (21.51)	2 (3.5)		15 (13.3)	3 (8.1)	
Class III	18 (19.35)	7 (12.2)		30 (26.5)	2 (5.4)	
Class IV	18 (19.35)	22 (38.59)		28 (24.7)	9 (24.4)	
Class V	31 (33.33)	24 (42.10)		32 (28.3)	21 (56.8)	
Total	93 (100)	57 (100)	Total	113 (100)	37 (100)	

tribal and tubectomy among non-tribal wives.⁶ Srivastava *et al.*, found that the female sterilization was the most popular method (82.2%) and emergency contraceptive pill was the least popular one.⁷

According to Annual Health Survey of Assam among the currently married women who are in the reproductive age group 67.7% are using contraceptive methods of which 38.4% are using modern methods and 28.2% are using traditional or natural methods. In Kamrup (rural) district, a total of 78.8% is using contraception out of which 46% are using modern and 32.9% are using traditional methods these findings go parallel to our study. Pegu *et al.*, found that among Khasi women only 38% were using contraceptives method, this low percentage of users may be due to non-inclusion of traditional or natural methods in the study. Rao and Babu also found that the users among the Rocha Kaya tribe were only 41.3%.⁸ Kaur *et al.*, found that 40.1% of women were using contraception at the time of the survey. Similarly Mishra *et al.*, in the study among tribes of Bankura, West Bengal found that only 40.07% were using contraception at the time of the survey which is very low in comparison to our study.⁹

Similar to our study Mishra *et al.*, study in Bankura (West Bengal) among the tribal also found that highest usage rate was in the age group of 30-35 years, and the association with age was significant with a $P < 0.001$. Rao and Babu in the study among Racha Koyas of Andhra Pradesh found that among literate 41% of women are using contraceptive and 40.6% among illiterate which shows an insignificant association between education and contraceptive use. However, on the contrary, Mishra *et al.*, in the study among the tribes of Bankura, West Bengal found a significant association between education and contraceptive use. This study also shows a significant association between education status and contraceptives uses. Mishra *et al.*, like our study found a significant association of contraceptive use and socioeconomic status. Among upper class, the use of contraception is more in comparison with the lower class.

CONCLUSION

Knowledge about contraceptive methods is almost universal about 90.6% of tribal wives and 92.33% of non-tribal wives knew about contraceptive. The most known method of contraception among both tribal and non-tribal is Natural methods. The least known is implant contraceptive both in tribal and non-tribal wives. Though the knowledge about various contraceptive methods are universal except for some methods such as injectable and implant contraceptives. The attitude toward contraception is also positive among most of the non-tribal eligible couples (82%) and some of the tribal couples (68%). Besides having a good knowledge about contraception, the practice is still lagging, and only 36% among tribal and 46% among non-tribal are using modern methods of contraception which is very low. Regarding modern contraceptive prevalence rate, although there was some improvement compared to the past national averages, however, the current figure for prevalence rate is still low when compared to the national target. Use of vasectomy is also poor as only one couple out of 300 eligible couples opted for a vasectomy. Giving counseling for contraceptive use to both husband and wife together can play an important role to adopt family planning methods. Creating more awareness about vasectomy will help to create a positive attitude among the husbands for a vasectomy.

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How to cite this article: Bharali MD, Baruah R, Ojah J. Comparative Study of Knowledge, Attitude and Practices toward Contraception among Tribal and Non-Tribal Wives of Eligible Couples in a Rural Area of Assam. *Int J Sci Stud* 2016;3(11):84-89.

Source of Support: Nil, **Conflict of Interest:** None declared.

Comparison of Z-Plasty and Limberg Flap Techniques in Management of Sacrococcygeal Pilonidal Sinus

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Abstract

Introduction: Pilonidal sinus is a fairly common problem encountered in general surgical practice. Though there are many surgical techniques for its management, controversy still continues regarding best surgical technique to treat with respect to postoperative complications, patient compliance, and minimizing recurrence.

Aims and Objectives: The aim of this study was to compare the two techniques of Limberg flap method and Z-plasty in the management of pilonidal sinus in terms of duration of surgery, postoperative pain, duration of hospital stay, drain removal time, postoperative complications, and recurrence rate.

Materials and Methods: A prospective comparative study was conducted in the Department of General Surgery, Victoria Hospital. A total of 50 cases were included, of which 31 underwent Limberg flap procedure and 19 underwent Z-plasty.

Results: The mean age of sacrococcygeal pilonidal sinus presentation was 29 years with male preponderance presenting with pain and seropurulent discharge as most common complaints. The parameters regarding the duration of surgery, the mean duration of hospital stay, postoperative complications were comparable between 2 groups. Postoperative pain was significantly less in Limberg method. The drain could be removed earlier in the Limberg flap procedure than in the Z-plasty technique, the difference being statistically significant.

Conclusion: In this study, Limberg flap methods had a shorter duration of operation, lesser postoperative pain, and earlier drain removal time when compared to Z-plasty. Hence, Limberg flap may be a better alternative to Z-plasty in the management of sacrococcygeal pilonidal sinus.

Key words: Limberg flap, Pilonidal sinus, Prospective comparative study, Z-plasty

INTRODUCTION

The term pilonidal is derived from the Latin word pilus meaning hair and nidus meaning nest. It is a characteristic epithelial tract (the sinus) located in the natal cleft, generally containing hair.¹ It is a common disorder affecting young adults, in the age group 15-30 years. Sex hormones affecting pilosebaceous glands and body hair growth have been

implicated for this age prevalence. The incidence of the disease varies from 10 to 26 per 100,000 population.^{2,3}

Karyadaki's theory is the most popular theory accepted to explain the pathogenesis of the disease. He proposed that pilonidal sinus results from the interplay of three main factors resulting in the insertion of hair into the natal cleft which are: The presence of loose hairs (the invader), some force facilitating hair insertion into the skin, and the vulnerability of the skin, such as intergluteal sulcus depth.⁴ A deep natal cleft favors sweating, hair penetration, and bacterial contamination. Buttock movements while walking further cause hair to penetrate the skin, thus, initiating a foreign body reaction and inflammation. This gradually leads to pilonidal abscess and/or sinus formation.^{5,6}

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Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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Controversy exists regarding the ideal treatment. All the surgical methods described include complete excision of the sinus but differ in the management of the wound after excision.⁷ Excision and packing, excision and primary closure, marsupialization, and flap techniques are some of the surgical procedures that have been developed for the treatment of pilonidal sinus.⁸ An ideal operation is one that is cost effective, ensures speedy return to work, is simple to perform, not requiring a prolonged hospital stay, inflicts minimal pain, and has a low disease recurrence rate.^{9,10}

MATERIALS AND METHODS

This is a prospective comparative study which was conducted in the Surgery Department of Victoria Hospital. A total of 50 cases were included in this study. Patients were divided into two groups randomly. Group A included 31 patients who underwent Limberg flap procedure. Group B included 19 patients who underwent the Z-plasty procedure. Informed consent was obtained from all the patients. Statistical analysis was done using the Chi-square test. $P < 0.05$ was considered significant.

Inclusion Criteria

1. Pilonidal sinus in the natal cleft of the sacrococcygeal area
2. Patients aged between 16 and 60 years.

Exclusion Criteria

1. Pilonidal abscess
2. Patients having systemic conditions which affect postoperative wound healing like diabetes mellitus, Human immunodeficiency virus positive patients, on cancer chemotherapeutic drugs, immunosuppressant therapy
3. Recurrent pilonidal sinus.

Methods

All patients in both treatment groups were given subarachnoid blockade and placed in the prone position with buttocks taped apart.

A rhomboid was marked around the lesion with a marking pen, and one of the angles was extended and dropped as with a conventional Limberg's flap. The lesion and all the sinus tracts were excised in entirety in all cases. The fasciocutaneous flap was raised and rotated. Skin closure was achieved after hemostasis with ethilon 3-0 sutures. For the Z-plasty, a vertical ellipse was initially marked with a marking pen with the sinus tract as its center and thus forming the vertical limb of the Z-plasty. Two horizontal limbs were then drawn depending on the length of the vertical limb. The lesion with all the sinus tracts was excised

into and after raising flaps, the Z-plasty was completed to cover the defect. The skin was closed using ethilon 3-0 sutures.

In both methods, suction drain was placed and removed when drain output was <10 cc over 24 h.

Two methods were compared with respect to the duration of surgery, postoperative pain and complications, average time of drain removal, mean duration of hospital stay and recurrence.

RESULTS

A total of 50 patients, of mean age 29 (range: 19-41) were included in the study, of which 6 (12%) were females, and 42 (88%) were males. The most common clinical presentations were pain (86%), seropurulent discharge (78%), and swelling (16%).

Of the 50, 31 (62%) patients underwent Limberg flap procedure while the rest nineteen (38%) underwent Z-plasty. The former operation lasted for 45 min on an average (range: 40-50 min) while the latter for 52 min on average (range: 35-60 min). The difference between the two was not statistically significant ($P = 0.783$) (Figure 1).

The patients of each group were asked to rate their pain on a visual analog scale on postoperative day 1, 2, and 3. Average of 3 values was taken into consideration. Among the former group, the average pain score was 3.65 (range: 3-5) and among the latter, 4.05 (range: 3-5). The difference between the two were statistically significant ($P = 0.049$) (Figure 2).

The mean duration of hospital stay was 4 days for both the procedures, the range being 3-5 days for the former group and 3-7 days for the latter group, the difference not being statistically significant ($P = 0.064$). The drain was

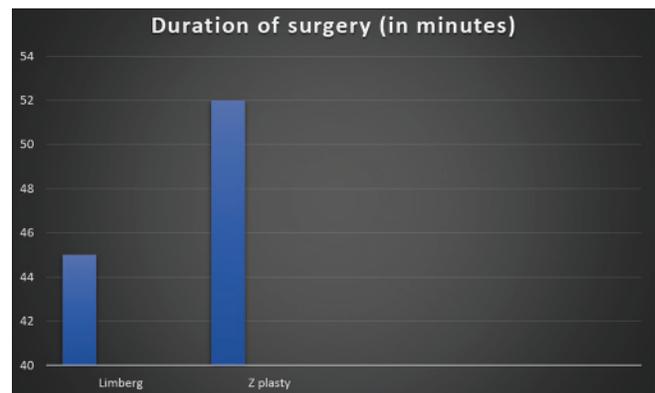


Figure 1: Graph comparing duration of surgery between Limberg and Z-plasty in minutes

removed after an average of 3 days in the former group (range: 2-4 days) and 4 days (range: 2-5 days) in the latter. The difference between the two procedures was found to be statistically significant ($P = 0.042$) (Figure 3). The sutures were removed after an average of 10 days.

Wound infection was noted in 2 patients (6.25%) of those who underwent Limberg procedure and in 2 patients (11.11%) of those who underwent Z-plasty. One incident of flap necrosis was noted in a patient

who underwent Limberg procedure (3.13%). Seroma formation was noted in 4 patients in the former group (12.5%) and in 3 patients in the latter group (16.67%). A single incidence of wound dehiscence was noted in the latter group (5.55%). No significant difference was noted in both groups with regard to complications ($P = 0.69$ for wound dehiscence, $P = 0.526$ for flap necrosis, $P = 0.398$ for seroma formation). Table 1 showing comparison between Limberg method and Z-plasty with respect to various parameters.



Figure 2: Graph depicting postoperative pain score

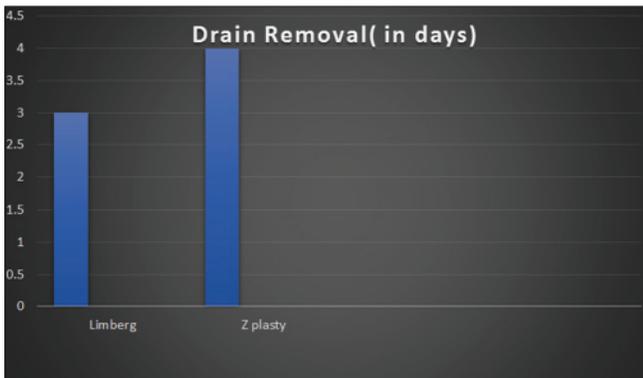


Figure 3: Graph comparing drain removal time between two methods

Table 1: Comparing different parameters between Limberg and Z-plasty

Parameter	Limberg method (n=31)	Z-plasty (n=19)	P value
Duration of operation	45 min	52 min	0.783
Postoperative pain score	3.65	4.05	0.049
Mean duration of hospital stay	4 days (range: 3-5 days)	4 days (range: 3-7 days)	0.064
Drain removal	3 days (range: 2-4 days)	4 days (range: 2-5 days)	0.042
Postoperative complications			
Wound infection	2	2	0.69
Flap necrosis	1	0	0.526
Seroma	4	3	0.398

DISCUSSION

Many surgical treatment methods have been described in literature but the controversy remains regarding the ideal treatment method, which has not yet been established for pilonidal disease. Complete excision of the sinus is widely practiced, but controversy remains about what to do with the wound after excision. Limberg flap method and Z-plasty are the two common methods followed in surgical practice. This study was conducted to compare the two methods in various aspects so as to arrive at the conclusion which method is better.

In this study, most of the patients were male in their 3rd decade of life. Most of the patients presented with pain and seropurulent discharge as common complaints. In a study conducted by Khan, most patients were also in the 3rd decade with male preponderance which is comparable with our study.¹¹

In the present study, duration of surgery was comparatively short for Limberg method. The mean postoperative pain score on day 1, 2, and 3 was significantly less in Limberg flap method when compared to Z-plasty. The drain was removed earlier in patients who underwent Limberg procedure, and it was statistically significant when compared to Z-plasty.

Duration of hospital stay was decided when the patient could walk freely without any significant pain and mean average duration of hospital stay was 4 days for both groups. In a study conducted by Akin *et al.*,¹² mean duration of stay was 3.2 days for Limberg method which is comparable with our study.

Main complications in the present study were wound infection, seroma, flap necrosis, and wound dehiscence. Moreover, recurrence was defined as persistent purulent or bloody discharge from in and around operated site. Wound infection was managed conservatively with antibiotics and regular wound dressings, seroma by aspiration, and antibiotics. Wound dehiscence was managed by antibiotics, regular debridement and delayed primary suturing.

According to study conducted by Priyadarshini *et al.*,¹³ on Z-plasty postoperative complications were present in 36% and recurrence in 5% of subjects. In the present study, 14% patients had postoperative complications and zero recurrence. In a study conducted by Akin *et al.*, on Limberg flap postoperative complications were present in 16% and recurrence in 3% of patients. In the present study, it was 12% and 0%, respectively. There was no statistical difference with respect to postoperative complications and recurrence between Limberg and Z-plasty in our study.

CONCLUSION

Postoperative pain was significantly more in the patients who underwent Z-plasty than in the patients who underwent Limberg flap procedure. The drain could be removed earlier in the Limberg flap procedure than in the Z-plasty technique, the difference being statistically significant. The duration of operation was insignificantly more in the Z-plasty procedure than in the Limberg flap procedure. No significant difference was noted in both groups with regard to postoperative complications and mean duration of hospital stay. Thus, Limberg flap may be a better alternative to Z-plasty in the management of pilonidal sinus as it has a shorter duration of operation, lesser postoperative pain, and earlier drain removal time.

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How to cite this article: Manjunath BD, Kumar AP, Nischal N, Ramachandra R. Comparison of Z-Plasty and Limberg Flap Techniques in Management of Sacrococcygeal Pilonidal Sinus. *Int J Sci Stud* 2016;3(11):90-93.

Source of Support: Nil, **Conflict of Interest:** None declared.

Rapid Laboratory Techniques in Diagnosis of Malaria in a Tertiary Care Hospital, Chennai

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Abstract

Introduction: The resurgence of malaria has renewed interest in developing not only preventive measures, but also rapid diagnostic techniques. Several methods have been developed to supplement and replace the conventional microscopic method.

Purpose: To study the efficacy and accuracy of rapid laboratory techniques in the diagnosis of malaria.

Methods: A cross-sectional study of 230 samples of which 190 from clinical malaria cases, 20 samples each from disease and healthy population. 190 samples from clinical malaria cases were tested by peripheral blood smear (PBS) and quantitative buffy coat (QBC). Among 190 samples, 61 were selected by the simple random method and tested by recent diagnostic tests such as immunochromatography, dot-enzyme immunoassay (ELISA) for *Plasmodium falciparum* and polymerase chain reaction (PCR).

Results: All the 190 clinical malaria cases were tested by Jaswant Singh Battacharya stained PBS and QBC. They have shown 29.4% and 57.3% positivity, respectively, for malarial parasite. Out of 61 randomly selected samples, 32 (52.4%) cases (*Plasmodium vivax* 29, *P. falciparum* 3) were positive immunochromatography, whereas 31 (*P. vivax* 28, *P. falciparum* 3) 50.8% cases were positive by PCR assay. Through, dot-ELISA, only three samples were detected of *P. falciparum*. Those samples were also detected by immunochromatography and PCR. None of the control samples were positive for malarial parasite. Through the analysis of all samples, it was observed that predominant species are causing malarial infection to be *P. vivax*.

Conclusion: PBS is a simple and inexpensive test for detection of the malarial parasite, while QBC assay was found to be more sensitive. The recent techniques of immunochromatography, DOT-enzyme immunoassay for *P. falciparum* and PCR are found to be more sensitive, specific, and accurate enough to identify the *Plasmodium* species.

Key words: Gold standard, Immunochromatography, Malaria, Microscopy, Polymerase chain reaction, Rapid techniques

INTRODUCTION

Malaria presents a diagnostic challenge to the medical community worldwide and has always been a major public health concern, probably representing the most important parasitic disease in human.¹ Human malaria is basically a febrile illness caused by species belonging to the genus *Plasmodium* and is transmitted by the bite of infected

female *Anopheles* mosquitoes, which breeds in fresh water.² The species that infect humans are *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium ovale*, *Plasmodium malariae*, and *Plasmodium knowlesi*. A heavy burden on tropical communities poses a threat to non-endemic countries and a danger to travelers.³ Malaria remains uncontrolled to date due to various reasons viz. Emergence of drug resistant parasite, pesticide resistant mosquito vector, and non-availability of suitable and effective malarial vaccine.⁴ Malaria rapid diagnostic devices (MRDD) have been developed with the hope that they would offer accurate, reliable, rapid, cheap, and easily available alternative to traditional methods of diagnosis.⁵ Assay for rapid diagnosis has the potential to enhance diagnostic capabilities in those instances in which skilled microscopy is not readily available.⁶ Conventional peripheral blood smear (PBS)

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Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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examination for a demonstration of malarial parasite remains the “gold standard” for diagnosis of malaria.⁷ The quantitative buffy coat (QBC), Dot-enzyme immunoassay (ELISA) for *P. falciparum*, immunochromatographic test (ICT), and polymerase chain reaction (PCR) have been evaluated here, particularly to overcome the disadvantages of conventional PBS study. Rapid, accurate diagnosis is fundamental to effective management and control of malaria. Modern methods of malaria diagnosis include fluorescent microscopy, flow cytometry, automated blood cell analysis, serology-antibody detection, molecular methods and laser desorption mass spectrometry, immunochromatographic assays detect malarial antigen Histidine-Rich Protein 2 (HRP-2) and enzymes parasite lactate dehydrogenase (pLDH), aldolase, and PCR. All these new technologies are compared with the accepted “gold standard” method.⁶ The present study highlighted the efficacy and accuracy of recent techniques to diagnose malaria, also to meet the need for a reliable diagnostic adjunct to microscopy in diagnosing malaria with a low level of parasitemia.

MATERIALS AND METHODS

The study design was a cross-sectional study.

The study group includes:

1. 190 patients with clinically diagnosed as malaria
2. Patients diagnosed as enteric fever, 20 in number - disease control
3. Apparently healthy individuals, 20 in number - healthy control.

A total of 230 blood samples was collected, of these 190 samples were from clinically diagnosed as malaria patients with symptoms of fever and chills irrespective of age and sex. 20 blood samples each were from patients diagnosed with enteric fever (disease control) and from healthy individuals (healthy control). The criteria for the selection of healthy control were the history of absence of fever for a period of one month prior to the study. Patients already on antimalarial drugs were excluded from the study. 190 samples of clinically diagnosed as malaria and control group were tested by PBS and QBC. 61 random samples were tested by recent methods such as ICT for antigen detection (HRP-2 and pLDH), Dot-ELISA for *P. falciparum* and PCR assay.

The data obtained were analyzed using SPSS statistical software. The proportions were calculated and the diagnostic performance was determined by calculating the test sensitivity, specificity and predictive values. Statistical significance was stated at the 5% level and 95% confidence

interval. Ethical clearance for the study was obtained from the Institutional Ethical Committee. Under strict aseptic precautions, thick and thin PBS were obtained by finger prick, and 3-5 ml of blood samples was collected in a pre-sterilized aliquot with anticoagulant (EDTA) by venipuncture before administration of anti-malarial drug. Samples were transported to the laboratory immediately. Smears were stained by Jaswant Singh Battacharya (JSB) technique. QBC. Assay was also carried out simultaneously. The remaining portion of the samples was aliquoted and stored at -20° for subsequent Dot-ELISA, ICT, and PCR assay.

PBS

Thick and thin PBS were prepared on a clean grease-free glass slide and examined under oil immersion.

QBC Assay

QBC was done using QBC malaria test kits provided by BD (Becton Dickinson) diagnostics. The QBC capillary tube was filled with about 50-60 μ l of blood soon after the collection, centrifuged, and examined using paralens in the region between the red blood cell and granulocytes where parasites are most abundant.

ICT (Detection of HRP-2 and Pan Malarial Antigen [PMA])

The samples were tested for Pf HRP-2 and PMA of other species of malaria, according to manufacturer's instruction using the NOW ICT test kit.

Dot-ELISA for *P. falciparum*

Pf HRP-protein against *P. falciparum* was detected by Dot-ELISA.

PCR

PCR was performed as per the method of Mullis and Falona (1987) and Saiki *et al.* using Qiagen Taq PCR core kit.

All the parameters of the tests were assessed with microscopic detection as the gold standard and recorded (Table 1).

RESULTS

“Of the 190 samples from patients with clinical malaria, 55 were positive for *P. vivax* and 1 was positive for *P. falciparum*

Table 1: Primers specific for *P. falciparum* and *P. vivax*

Primer	Primer sequence	Product size
Pf 1	5' AGA AAT AGA GTA AAA AAC AAT TTA 3'	918 bp
Pf 2	5' GTA ACT ATT CTA GGG GAA CTA 3'	
Pv 1	5' CCG AAT TCA GTC CCA CGT 3'	523 bp
Pv 2	5' GCT TCG GCT TGG AAG TCC 3'	

P. falciparum: Plasmodium falciparum, *P. vivax*: Plasmodium vivax

by thin PBS. In thick smear, 56 cases (29.4%) were positive for malarial parasite and its 95% confidence interval was 23-36%. Disease and healthy control ($n = 40$) were negative for malarial parasite by JSB staining method. Among the total of 190 clinically suspected cases, QBC assay detected the presence of the malarial parasite in 109 (57.3%) cases and its 95% confidence intervals is 50-64%. The control group was found to be QBC negative.

Table 2 shows the sensitivity of 100%, specificity of 69.5%, positive predictive value (PPV) of 51.3%, and negative predictive value (NPV) of 100% of QBC assay. By comparing the QBC assay and smear method, QBC assay shows higher positivity. Of the 61 cases, 32 (52.4%) were positive for malarial parasite (P.v. 29, P.f. 3) by ICT method and its 95% confidence interval was 40% to 65%. The control group was found to be negative by this technique.

Among the total 61 cases, only 3 cases were positive by Dot-ELISA for *P. falciparum* (DRDE). The control group was negative by this technique. Dot-ELISA for *P. vivax* was not done. Hence, this method was not included in the comparative study with PBS. 31 (51.8%) out of 61 cases were positive for malarial parasite (*P. vivax* 28, *P. falciparum* 3) by PCR technique and its 95% confidential interval was 38-63%. Control group was negative by PCR method. The sensitivity, specificity, PPV, and NPV of PCR assay were calculated against the gold standard of PBS (Tables 3-5).

Out of 190 cases tested with different techniques in detecting malarial parasite, the predominant species identified was *P. vivax* (Table 6).

Table 2: Comparison between JSB stained PBS and QBC

QBC assay	JSB stained PBS		Total
	Positive	Negative	
Positive	56	53	109
Negative	0	121	121
Total	56	174	230

McNemar test $P < 0.0001$, Kappa agreement value 0.526. JSB: Jaswant Singh Battacharya, QBC: Quantitative buffy coat, PBS: Peripheral blood smear

Table 3: Comparison between JSB stained PBS and ICT

ICT	JSB Stained PBS		Total
	Positive	Negative	
Positive	20	12	32
Negative	1	68	69
Total	21	80	101

McNemar test $P = 0.003$, Kappa agreement value 0.672, sensitivity 95.2%, specificity 85%, PPV 62.5%, and NPV 98.5%. ICT: Immunochromatographic test, JSB: Jaswant Singh Battacharya, PBS: Peripheral blood smear, PPV: Positive predictive value, NPV: Negative predictive value

DISCUSSION

The resurgence of malaria has renewed interest in developing not only preventive measures, but also rapid diagnostic techniques. Several methods have been developed to supplement and replace the conventional microscopic method. The most promising new malaria diagnostics are the QBC. Assay, Assay for detection of antigen HRP-2 and PMA by ICT, only HRP-2 by Dot-ELISA for *P. falciparum* (DRDE) and detection of specific nucleic acid sequences (P.f. 918 bp, P.v., 523 bp) by PCR. In this study, 190 clinically diagnosed as malaria patients were tested by PBS and QBC assay for presence of *P. vivax* and *P. falciparum* in blood. Out of 190 samples, 61 were selected by the simple random method and tested with recent techniques such as ICT, Dot-ELISA for *P. falciparum* and PCR. The control group was also tested with PBS, QBC, ICT, and Dot-ELISA for *P. falciparum* and PCR assay. The results obtained were as follows. Romanowsky stains (Giemsa's, Leishman's, Fields', and JSB) still appear superior in species identification. In the present study, malarial parasite was detected in 56 cases (P.v. 55, P.f. 1) by PBS

Table 4: Comparison between PCR technique and JSB stained PBS

PCR	JSB stained PBS		Total
	Positive	Negative	
Positive	19	12	31
Negative	2	68	70
Total	21	80	101

McNemar test $P = 0.013$, Kappa agreement value 0.584, sensitivity 90.5%, specificity 85%, PPV 61.3%, NPV 97.1%. JSB: Jaswant Singh Battacharya, PBS: Peripheral blood smear, PPV: Positive predictive value, NPV: Negative predictive value, PCR: Polymerase chain reaction

Table 5: Evaluation of recent techniques in diagnosis of malaria

Test	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
QBC	100	65.5	51.3	100
ICT	95.2	85	62.5	98.5
PCR	90.5	85	61.3	97.1

PPV: Positive predictive value, NPV: Negative predictive value, PCR: Polymerase chain reaction, ICT: Immunochromatographic test, QBC: Quantitative buffy coat

Table 6: Positivity of malarial parasite by various techniques

Test	Number of sample	Positive (%)	<i>P. vivax</i>	<i>P. falciparum</i>
PBS	190	29.4	55	1
QBC	190	57.3	-	-
ICT	61	52.4	29	3
PCR	61	50.8	28	3
Dot-ELISA for P.f.	61	-	-	3

PCR: Polymerase chain reaction, ICT: Immunochromatographic test, QBC: Quantitative buffy coat, PBS: Peripheral blood smear, *P. falciparum*: *Plasmodium falciparum*, *P. vivax*: *Plasmodium vivax*, ELISA: Enzyme immunoassay

(29.4%). Various studies from different areas have reported different positivity rate among the studied population 3.07%, 10.5%, 20%, 31%, and 42.1%, respectively.⁸⁻¹² This could be due to multiple factors including training and skills, maintenance, slide preparation techniques, workload, condition of microscope, and quality of essential laboratory supplies. This variability combined with the risk of untreated malaria in the face of safe, inexpensive therapy in the past led clinicians to treat febrile patients without regard to the laboratory results.¹³⁻¹⁵ In our study, two blood samples which were detected positive for *P. falciparum* through ICT, Dot-ELISA and PCR assay, were found to be negative in the blood smear examination. This may be explained through the fact that *P. falciparum* can sometimes sequester and may not be present in circulating blood. Stained PBS examination is simple and inexpensive. Parasite stages and species could be identified accurately. The main disadvantages are it takes more time and requires skilled personnel. It may also give poor results with low parasitemia.^{5,16} Still the staining procedures are used for screening purpose. QBC method is based on fluorescent staining of the blood cells and parasites. In the present study, QBC assay detected 57.3% cases out of 190 clinically suspected cases, showed 100% sensitivity, 65.5% specificity, PPV 51.3%, and NPV 100%. Moreover, detected more number of positive cases, i.e., 109 (57.3%) than peripheral smear 56 (29.4%) which is consistent with Singh *et al.*,¹⁷ Pinto *et al.*,⁹ and Krishna *et al.*⁸ Compared to peripheral smear, QBC was found to be 100% sensitive as it was able to detect additional 53 cases which were negative on peripheral smear. All the blood samples which were negative by QBC were also negative by peripheral smear. This is in agreement with Bhandari *et al.*¹⁸ who had 100% sensitivity with QBC. QBC is of great importance in peripheral smear negative cases and should be preferably used as a final diagnostic test and not as a screening test or first line investigation considering its high cost and tend to report false positives.¹⁸ Compared to Leishman stained thick and thin film, sensitivity of QBC assay varies from 97% to 100%. The QBC assay would be ideal to supplement the stained blood film in both clinical and epidemiological studies. The limiting factors for QBC assay are the cost of the microscope, special accessories, and need for adequate training and expertise.⁷ The QBC tubes do not remain readable for more than a few days and hence are not suitable for record purposes.⁸ The important factor of false positive impression of malarial parasite in QBC system should be considered here. In our study, 8 cases of QBC positive were found negative by PBS, ICT, and PCR. This could be Howell – Jolly bodies, artifacts such as cell debris and bacterial contamination may possibly give false positive results.^{8,19} One of the serological method, ICT based on the use of HRP-2 antigen to detect *P. falciparum* infection and a PMA to detect *P. vivax* and infection with other

species of malaria. In the present study, we evaluated the performance of ICT Malaria P.f/P.v, P.m and P.o., and Dot-ELISA for *P. falciparum* (DRDE) based on HRP-2 antigen. Only 32 cases (P.v. 29, P.f. 3) were positive by Now ICT method (52.4%) out of 61 cases; showed the sensitivity of 95.2% and specificity of 85% with positive and negative predictive values of 62.5% and 98.5%, respectively. This is in accordance with findings of Tjitra *et al.* by ICT malaria.²⁰ Antigen detection test was superior to peripheral smear in our study, especially for malignant tertian malaria as it could detect 2 Pf cases which were negative by peripheral smear. This could be due to the persistence of HRP-2 following clearance of *P. falciparum* or due to sequestration *P. falciparum*. The study by Forney *et al.*¹² also reported a sensitivity of 87% and specificity of 87% for *P. vivax* and sensitivity of 100% and specificity of 93% for *P. falciparum* by the parasight F+V assay. The sensitivity of the test increases with increase in parasite density and it is in relation to the observations by Iqbal *et al.*¹¹ and Rajendran *et al.*²¹ Only 3 cases of *P. falciparum* were detected by Dot-ELISA (DRDE) which were also detected by ICT and PCR assay. Thereby indicating 100% efficiency in detection of *P. falciparum* cases. We should consider the merits and demerits of ICT compared to the “gold standard.” ICT assay is rapid and no labor-intensive.²² It could be a useful adjunct to blood film microscopy. Moreover, it might permit a reduction in the duration of hospitalization and give an early warning of treatment failure.²³ Furthermore advantage of ICT assay is speciation and can also be used to indicate drug resistant infection.²⁴ The demerits of ICT assay are false positivity due to persistence of HRP-2 and PLDH antigenemia after antimalarial therapy.²⁵ Factors that may contribute to these diverse findings include test kit storage conditions in the field, inadequate adherence to the test protocol, or levels of parasitemia below the detection limit.¹⁰ In our study, one case of *P. vivax* detected by PBS and QBC were not detected by ICT. This may be due to insufficient enzyme production, which occurs during an early malarial infection or the patient’s blood sample contained parasites at a concentration below the detection level.²⁶ There are many published studies showing the improved sensitivity and specificity of PCR-based assays over microscopic and immunochromatographic diagnosis of malaria.²⁷ In the present study, we also demonstrated the performance of PCR assay, which detected malarial parasite in 31 (50%) cases (28 P.v. 3 P.f.) sensitivity of 90.5% and specificity of 85%, PPV of 61.3%, and NPV of 97.5% correlates well the studies of Barman *et al.*, Kathy *et al.*, and Long *et al.*^{19,27,28} In our study 2 cases, of both JSB stained PBS and QBC assay positive, were revealed negative by PCR assay (False negative). The false negative result in PCR could be due to the failure of amplification of target DNA. The failure to amplify the target amplicon could be due to a low copy number of the target sequence to the primer.

False positive results in PCR could also be due to carryover of parasite – DNA during sample processing or lower sensitivity of the designed primer and PCR method itself.¹⁹ Despite the advantages of PCR, it is unlikely to be useful outside of well-equipped laboratories where a reliable source of electricity and expensive equipment are not available. These limitations exclude PCR from consideration as a field – ready, rapid diagnostic test for malaria.²⁹ Unfortunately, conventional PCR assays are technically demanding and time-consuming. Moreover, they are prone to carryover contamination during the manipulation of post-amplification products.³⁰ In the present study, the predominant species identified was *P. vivax*. Our findings are close to Jivabhai *et al.*³¹ who reported *P. vivax* 61.41% and *P. falciparum* 38.56%, but different from Karlekar *et al.*³² who reported *P. vivax* 33.8% and *P. falciparum* 66.6% Idris *et al.*³³ from Pakistan reported prevalence of 72.47% for *P. vivax*, 24.1% *P. falciparum*, and 3.44% mixed species, which is similar to our findings. The difference in prevalence of *P. vivax* and *P. falciparum* in different areas can be due to the presence of endemicity of particular type and higher relapses in vivax type.

CONCLUSION

In the present study, we compared peripheral smear a known “gold standard” with a QBC, antigen detection assay, and PCR assay. The QBC is advantageous where workload is high, but it is costly and gives a false positive report. Antigen detection test is a useful device when microscopy is not available, and immediate clinical diagnosis is required, especially for *P. falciparum* cases which may develop cerebral complications. But it gives false positive results even after treatment. PBS is the simple and inexpensive test for detection of the malarial parasite, and the QBC assay was found to be more sensitive. The recent techniques of ICT, Dot-ELISA for *P. falciparum*, and PCR assay are found to be more sensitive, specific, and accurate enough to identify the *Plasmodium* species. In future, MRDDs will play an increasing role, where reliable microscopy has been frequently poor. The new generation of non-microscopic immune chromatography assay offers a practical chance to move the diagnosis of malaria away from the laboratory and nearer to the patient. New rapid, non-microscopy methods for the diagnosis of malaria that complement or support microscopy of blood films would be of great use in the early diagnosis and treatment of patients with malaria and in epidemiological studies.

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How to cite this article: Santhy B, Ravichandran T, Ramani CP, Sumathy P, Heber A. Rapid Laboratory Techniques in Diagnosis of Malaria in a Tertiary Care Hospital, Chennai. *Int J Sci Stud* 2016;3(11):94-99.

Source of Support: Nil, **Conflict of Interest:** None declared.

Evaluating Facial Esthetics by Relating Upper and Lower Lips with E-plane: A Short Clinical Photographic Study

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Abstract

Background: Replacement of anterior teeth is the challenging job for the dentist since its success depends on many factors mainly on the perception of patients toward beauty. There are many criteria to evaluate facial esthetics - one of them is studied and discussed here.

Aim: The aim of this study is to find co-relation of upper and lower lips position with respect to E-plane in individuals having an esthetic/pleasing smile.

Settings and Design: At the institution approved by the guide and college. Experimental study.

Materials and Methods: Photographs of 100 subjects (50 males and 50 females) were clicked in frontal, oblique, and lateral view. Frontal and oblique views were given to panel members along with a visual analog scale to judge esthetic smile. Lateral views of the selected subjects were then studied in software by marking esthetic (E)-plane and calculating its distance from upper and lower lip.

Statistical Analysis: Statistical analysis was performed using Epi Info Software along with Pittsmann's test and Baretlet's test. Sampling was carried out by simple random technique.

Result: From the values obtained by the study, mean was calculated, and it was found that average distance of upper lip from E-plane was 2.7 mm (~3 mm) and of lower lip was 1.1 mm (~1 mm).

Conclusion: Upper and lower lip have statistically strong correlation with E-plane in the determination of esthetics irrespective of gender.

Key words: Aesthetics, Beauty, E-plane, Pleasing smile

INTRODUCTION

Nature has endowed everyone with dignity and satisfaction of being an individual personality. Human beings are creatures blessed by the God with various gifts such as brain, speech, emotions, feelings, senses, complexions, etc. All these things when blended together give each person a

unique identity and symbolism of that is expressed through the face. The face has been defined as a chart of destiny, an impression of the fullness of life, and mirror of the soul.

Everyone wants to look beautiful, but the definition of beauty differs from person to person. "Everything has beauty, but not everyone sees it!"¹ What looks beautiful to one person (e.g., dentist) may look ugly or unesthetic to other person (e.g., patient or relatives) since everyone has his or her own perception of what exactly the beauty is. Each dentist has his own idea of what constitutes esthetics. The dentist must have some primary intentions of what he wants and plans to do before attempting the procedure; however, he should realize the flexibility of esthetics. "Beauty does really lie in the eye of the beholder."

Access this article online



www.ijss-sn.com

Month of Submission : 12-2015

Month of Peer Review : 01-2016

Month of Acceptance : 01-2016

Month of Publishing : 02-2016

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Esthetic concepts about the face and smile are based on person's opinion rather than sound scientific methods. This might be explained by the difficulty to qualify and quantify beauty. However, the measurement of what is beautiful or the perception of beauty in dentistry is fundamental for providing scientific data that can guide diagnosis and treatment planning. The dentist's esthetic judgment and patient's self-image play an important role in clinical treatment decisions. Patient's anxiety about esthetics is affected not only by his or her own perception but also by the reaction of other people.² It is well explained by the statement, "What others will think has killed more dreams than anything else in the world."

Esthetics is a branch of philosophy dealing with the nature of art, beauty and taste, with the creation and appreciation of beauty.³ It is more scientifically defined as the study of sensory or sensory-emotional values, sometimes called judgments of sentiment and taste.⁴ Beauty is "which gives the highest degree of pleasure to the senses or to the mind and suggests that the object of delight approximates one's conception of an ideal." Viewer interpretations of beauty possess two concepts of value: - Esthetics - Philosophical notion of beauty. Taste - the result of an education process and awareness of elite cultural values learned through exposure to mass culture. Therefore, what is beautiful and attractive for the dentist might not be what the patient understands as a beautiful, attractive, and satisfactory clinical result.

Evaluating the face in smiling profile is an integral part of a complete diagnosis and treatment planning.⁵ However, there are few reports about the effects of labiolingual inclination of the maxillary incisors on smiling profile. Cao *et al.*, studied the effect of maxillary incisor labiolingual inclination and anteroposterior position on smiling profile esthetics and concluded that maxillary incisor labiolingual inclination and anteroposterior position have a key effect on the appearance of smiling profile.⁵ Pinho *et al.*, studied the impact of anterior tooth asymmetries on the perception of smile esthetics and found that laypersons, orthodontists, and prosthodontists have different perceptions of attractiveness.²

What is E (esthetic) Plane?

E-plane is an imaginary line drawn from tip of the nose (pronasale) to the tip of the chin (soft tissue pogonion). It has some correlation with the upper and lower lips pertaining to the esthetics of an individual giving him or her unique identity. The purpose of this study is to find a correlation of upper and lower lips position with respect to E-plane in individuals having esthetic/pleasing smile.

MATERIALS AND METHODS

The study was planned with the following objectives:

- To determine pleasing smile

- To calculate distance of upper lip from E-plane
- To calculate distance of lower lip from E-plane
- To relate above findings with E-plane in esthetic smile to individuals requiring restoration of anterior teeth.

Indian subjects (50 males and 50 females) with a pleasant smile, of age 18-25 years (selected by panel members) were included in this study. Subjects with the history of previous orthodontic treatment or with missing or malformed anterior tooth were excluded from the study. Big question was still persisting, "How to determine pleasing smile?" Pinho *et al.*,² stated that prosthodontists and orthodontists have the highest perception of a smile. Hence, the panel was formed to decide pleasing smile comprising of two prosthodontists and two orthodontists. Out of two specialists in each branch, one was male and one was female; one was of younger age group (25-35 years) and one was of older age group (45-65 years) and one was with less clinical experience (5-10 years) and one with more clinical experience (20-40 years).⁶

Digital single-lens reflex camera (Nikon D90) with fixed focal length of 100 mm macro lens was used to take the photographs with a magnification ratio of 1:8 in three different views, i.e., frontal, lateral and oblique. To standardize the size and resolution, a millimeter ruler was placed away from the field to be evaluated. The camera was maintained at a distance of 1 m from the patient.⁷ Consent was obtained from each subject taking participation in the study. Photographs were then clicked in frontal view while the subjects were smiling normally (Figure 1). Photographs in the lateral view were clicked with lips normally placed in contact along with metal ruler placed over head well away from the area to be studied (Figure 2). To ensure reproducible head position, photographs were taken from the position where the eyebrows first coincide exactly while moving the camera from front to side. To click photographs in an oblique view, a 45° line was measured and drawn on



Figure 1: Frontal view

the floor of the studio and photographs were taken from this line (Figure 3). For better reproducibility of head position, the head was turned away so that the contour of the eye does not overlap the skin contour.

Frontal and oblique view photographs were given to each panel member along with a visual analog scale to assess esthetics smile (Figure 4). Evaluators were advised not to compare the photos, to prevent subjective variation. Photographs claimed to be having pleasing smile by all panel members were selected for the study. Corresponding lateral view of the selected photographs were then studied in the personal computer (Sony Corporation SVE1513CYNB) using a Photoshop software (CS2 version 9.0) by marking E-plane and calculating distance of upper and lower lips from it taking markings on the metal ruler as a reference.

Ethics

Procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the

Helsinki Declaration of 1975, as revised in 2000. A written consent was obtained from each individual participating in the study.

Statistics

Statistical analysis is carried out by Epi Info Software. The correlation between male and female in upper lip is significant ($P = 0.00$) by the Pittsmann’s test while the correlation between male and female in lower lip is also significant ($P = 0.00$) by Baretellet’s test.

RESULTS

As the requirement of the study, mean was calculated in upper and lower lip distance with respect to E-plane. In male subjects, mean distance of upper lip was 2.7 mm and lower lip 1.1 mm. In case of female subjects, mean distance of upper lip 2.9 and lower lip 1 mm. The correlation between male and female in upper lip was significant ($P = 0.00$) while the correlation between male and female in lower lip was also significant ($P = 0.00$). So the average distance of upper lip from E-plane was 2.7 mm (~3 mm) and of lower lip was 1.1 mm (~1 mm) (Graph 1).

DISCUSSION

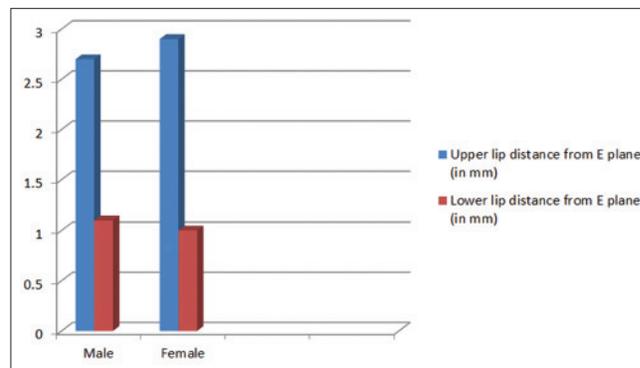
Esthetic appearance has always been a matter of serious concern for most of the patients. As far as anterior teeth restoration is concerned, patients are mainly looking for pleasing or esthetic smile. But the definition of esthetics differs from person to person. It is therefore duty of the



Figure 2: Lateral view



Figure 3: Oblique view



Graph 1: Distance between lip and E plane

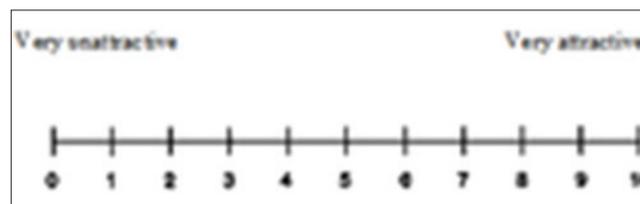


Figure 4: Visual analogue scale (cm)

treating dentist to find the exact need of the patient in terms of beauty and to understand the perspective of the patient what he or she feels is beautiful for him or her since it is the patient who will be living with those teeth and smile provided by the dentist. So, it is the fundamental right of each patient to decide the kind of smile he or she wishes (of course within the scope and limitations).

It has been proved that prosthodontists and orthodontists have the highest perception of smile² but it has to be blended with the expectations and perceptions of the patients for successful treatment outcome.

There are various criteria for selection of shape and size and placement of anterior teeth in order to get esthetic outcome like lip length, gender, type of smile etc. Anteroposterior inclination of anterior teeth also plays very vital role in determining their position which in turn influences position of upper lip.⁵ It should be always kept in mind that teeth has to be placed in neutral zone. Violation of neutral zone will create various problems leading to treatment failure.

Obaidi and Abdul-Qadir⁸ revealed that the upper lip significantly larger behind the esthetic line in female than male at 11, 12 and 14 years age groups.

Statistically, there was no significant difference between distance of upper and lower lips from E-plane in males and females (Graph 1). Though mean was found to be approximately 3 mm for upper lip and 1 mm for lower lip, values were ranging from 1.5 to 4 mm for upper lip and 0 mm to 2 mm for the lower lip. So, further studies with wide sample size are needed to come to any firm decision regarding relation of E-plane with upper and lower lip.

However, this study gives brief idea about relation of upper and lower lip positions with respect to E-plane. Values obtained can be of great clinical importance while replacing upper and lower anterior teeth in dentulous as well as edentulous patients. It is one of the factors to determine the amount of labial inclination of anteriors required for a patient to have pleasing smile.

If patient is having missing upper and lower anterior teeth, then along with lip support, this factor plays a crucial role

in replacing those missing teeth. Furthermore, completely edentulous patients, especially long duration are deprived of normal musculature support. In such patients this factor can be used with great success to get esthetic outcome. To get good clinical results in terms of esthetics, this factor has to be used in conjunction with the other factors which are routinely used on day to day practice.

Many times, patient is having missing upper anterior teeth. In such situation, this factor along with labial fullness and pre-extraction records becomes an integral part if we are desired to get an excellent esthetic outcome.

It is an aid for orthodontists during orthodontic tooth movement although it is not the sole criteria but one of the major criteria to make decisions during anterior rehabilitation procedures.

CONCLUSION

Within the limitations of this study, it has been concluded that upper and lower lip has statistically strong correlation with E-plane in determination of esthetics irrespective of gender. So, along with all other factors, this factor also needs to be taken into consideration while replacing anterior teeth to get a successful outcome.

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How to cite this article: Asawa N, Bulbule N, Kakade D, Shah R. Evaluating Facial Esthetics by Relating Upper and Lower Lips with E-plane: A Short Clinical Photographic Study. *Int J Sci Stud* 2016;3(11):100-103.

Source of Support: Nil, **Conflict of Interest:** None declared.

Refractive Errors of Patients between 20 and 40 Years and its Correlation with Axial Length

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Abstract

Background: Refractive error is a common eye disorder. The result of the refractive error is a blurred vision which is sometimes so severe that it causes permanent visual disability due to amblyopia and complications such as retinal detachment in high myopia. Refractive errors cannot be avoided but identifying such errors is useful in planning appropriate correction early.

Aim: To study refractive errors in patients between 20 and 40 years of age and to correlate them with the axial length of the eyeball. The study also aims to find out the common refractive errors among this age group and to compare them with previous studies.

Materials and Methods: Patients between 20 and 40 years coming to the outpatient department in tertiary care hospital with complaints of defective vision were included in the study. The visual acuity and visual acuity with pinhole were assessed using Snellen's chart. Near visual acuity was also assessed. Retinoscopy and auto refractometry was used to assess the refractive status objectively. Subjective verification of refraction was done. Axial length of eyeballs was measured using A-scan ultrasonogram. Slit lamp and fundus examination was done to rule out other eye pathology.

Results: Refractive errors are more common in females. Myopia was more common than hypermetropia. Prevalence of astigmatism was high. Presbyopia affects adults >35 years. Females had slightly longer axial length than males. Axial length was longer than normal in myopes and shorter in hyperopes.

Conclusion: Refractive errors are commonly present among the economically productive age group. Early detection is needed for the effective correction of such errors to prevent morbidity.

Key words: Astigmatism, Axial length, Hypermetropia, Myopia, Presbyopia, Refractive errors

INTRODUCTION

Refractive error is a very common eye disorder. The result of the refractive error is blurred vision which is sometimes so severe that it causes permanent visual disability due to amblyopia and complications such as retinal detachment in high myopia. The common refractive errors occurring in our population include myopia, hypermetropia, astigmatism, and presbyopia. The number of people globally with refractive errors has been estimated from 800

million to 2.3 billion.¹ Refractive errors cannot be avoided but identifying such errors is useful in planning appropriate correction early. Refractive errors can occur due to various causes like change in axial length of eyeball; change in curvature of cornea and lens; change in refractive index of lens. Hypermetropia can occur congenitally whereas presbyopia is strongly related with age. This study is mainly based on changes in the axial length of the eyeball associated with refractive errors between 20 and 40 years of age. The study also aims to find out the common refractive errors among this age group.

MATERIALS AND METHODS

In this prospective observational study, patients between 20 and 40 years coming to tertiary care hospital with complaints of defective vision were included. Institutional

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Month of Submission : 12-2015
 Month of Peer Review : 01-2016
 Month of Acceptance : 01-2016
 Month of Publishing : 02-2016

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Ethics Committee approval was obtained. 20-40 years was chosen because they are economically productive age group and the study aims to find out the prevalence of refractive error in such population. A total of 37 cases were taken for study after informed consent. The study was done during the period of August and September, 2013.

The visual acuity and visual acuity with pinhole was assessed using Snellen's chart. Near visual acuity was also assessed. Retinoscopy and auto refractometry was used to assess the refractive status objectively. Subjective verification of refraction was also done to arrive at the final distant and near refractive error and the best corrected visual acuity. Axial length of both eye balls was measured using A-scan ultrasonogram. Slit lamp examination and fundus examination was done to rule out other eye pathology. At the end of the study, statistical analysis was done on the number of patients affected by each refractive error and compared with standard results. Axial length between different refractive errors was also compared.

RESULTS

Based on age-wise distribution, most refractive errors occurred in age groups between 20 and 25 years (12 patients) and 31 and 35 years (12 patients). 9 patients were found between 36 and 40 years of age. Only four cases with refractive errors were seen between 26 and 30 years (Table 1).

3 cases of hypermetropia were reported among which 1 male and 2 female patients, these 3 cases had bilateral involvement of the eye (Table 2).

21 patients were diagnosed with Astigmatism, 15 female and 6 male patients, patients, 18 cases had bilateral involvement of the eye (Table 3). Out of these 21 cases, 6 had simple myopic astigmatism, 13 had compound myopic astigmatism, and 2 had mixed astigmatism. No case of simple hypermetropic astigmatism and compound hypermetropic astigmatism. Astigmatism more commonly affected persons between 31 and 35 years of age (8 patients) followed by patients between 20 and 25 years of age (7 patients). Age groups between 26 and 30 years and 36 and 40 years were least affected.

7 cases were diagnosed to have presbyopia. Among these 3 were males and 4 were females (Tables 4 and 5). Between 36 and 40 years 6 cases were reported. One case was found between 31 and 35 years.

Axial lengths of all the patients were recorded. Out of 6 myopes, four had their axial length within normal range and two had it longer than the normal value. 2 hypermetropic

patients had shorter axial length, and one had it within the normal range. Axial length of the astigmatic patients

Table 1: Age-wise distribution of refractive errors in study population

Age (years)	Myopia (%)	Hypermetropia (%)	Astigmatism (%)	Presbyopia (%)
20-25	4 (66.67)	1 (33.33)	7 (33.33)	0 (0)
26-30	1 (16.67)	0 (0)	3 (14.29)	0 (0)
31-35	1 (16.67)	2 (66.67)	8 (38.1)	1 (14.29)
36-40	0 (0)	0 (0)	3 (14.29)	6 (85.71)

Table 2: Gender wise distribution of refractive errors in study population

Refractive error	Male (%)	Female (%)
Myopia	2 (16.67)	4 (16.67)
Hypermetropia	1 (8.33)	2 (8.33)
Astigmatism	6 (50)	15 (62.5)
Presbyopia	3 (25)	4 (16.67)

Table 3: Distribution of eye involvement in refractive errors in study population

Refractive error	Bilateral eye involvement (%)	Unilateral eye involvement (%)
Myopia	5 (83.33)	1 (16.67)
Hypermetropia	3 (100)	0 (0)
Astigmatism	18 (85.71)	3 (14.29)
Presbyopia	7 (100)	0 (0)

Table 4: Age-wise distribution of female patients who had refractive errors

Refractive error	Females-age group (years)			
	20-25	26-30	31-35	36-40
Myopia	2	1	1	0
Hypermetropia	0	0	2	0
Simple myopic astigmatism	0	0	3	1
Simple hypermetropic astigmatism	0	0	0	0
Compound myopic astigmatism	4	1	3	1
Compound hypermetropic astigmatism	0	0	0	0
Mixed astigmatism	0	0	2	0
Presbyopia	0	0	1	3

Table 5: Age-wise distribution of male patients who had refractive errors

Refractive error	Male age group (years)			
	20-25	26-30	31-35	36-40
Myopia	2	0	0	0
Hypermetropia	1	0	0	0
Simple myopic astigmatism	1	1	0	0
Simple hypermetropic astigmatism	0	0	0	0
Compound myopic astigmatism	2	1	0	1
Compound hypermetropic astigmatism	0	0	0	0
Mixed astigmatism	0	0	0	0
Presbyopia	0	0	0	3

Table 6: Distribution of axial length of refractive errors in study population

Refractive error	Number of patients (%)	
	Normal axial length	Abnormal axial length
Myopia	4 (66.67)	2 (33.33)
Hypermetropia	1 (33.33)	2 (66.67)
Myopic astigmatism	11 (52.38)	8 (38.01)
Presbyopia	7 (100)	0 (0)

did not show significant changes, but myopic astigmatic patients showed variations (Table 6).

The analysis was made with the mean values. With reference to age, mean age of occurrence of different refractive errors were found. Out of 24 females, the mean age of affected female was 30.8 years. Of 12 males, the mean age of affected male was 28.25 years. The median age for myopia was 25 years and for hypermetropia was 30 years. Patients with astigmatism and presbyopia had the mean age of 28.95 years and 38.57 years, respectively.

DISCUSSION

In this study, based on age-wise distribution, most refractive errors occurred in age group between 20 and 25 years (33.33%) and 31 and 35 years (33.33%). No standard study results are available to support these results as most of the studies are conducted only in school children and adolescents until 18 years of age. 20-40 years is chosen in this study because they are the economically productive age group. There is a significant female preponderance for refractive errors with male:female ratio of 1:2.^{2,3} 16.67% of the total cases were myopes.

33.33% of myopes were males, and 66.67% were females. Myopia was more common among females. This result was in concordance with the standard study results.¹⁻⁶ 66.67% of the myopes were between 20 and 25 years of age.

Myopia was common among employed (83.33%) than the unemployed (16.67%). This result was found to be in concordance with the study conducted in Bangladesh by Bourne *et al.*⁷ 83.33% of the myopic patients had bilateral eye involvement and 16.67% had unilateral eye involvement.

Hypermetropia was less prevalent in this age group (8.33%). Among them, 33.33% were males and 66.67% were females. Hypermetropia was more common among females. Standard studies have proved that 4-7% of the population between 15 and 20 years are affected by hypermetropia, the trend remains constant through early middle age and increases after 45 years of age.⁸ Studies

have also shown a preponderance of hypermetropia toward females.

58.33% of the total cases were astigmatism. Among them, 28.57% were males and 71.43% were females. The prevalence of astigmatism is high in this study as shown by standard study results^{1-3,9,10} 61.90% of the patients had compound myopic astigmatism, and 28.57% had simple myopic astigmatism. The most vulnerable age groups were between 31 and 35 years (38.1%) and 20 and 25 years (33.33%). Among 21 cases, 85.71% had bilateral eye involvement, and 14.28% had unilateral eye involvement.

Among 37 cases, 19.44% had presbyopia. 42.86% of these were males, and 57.14% were females. All the presbyopic patients were above 35 years of age. Standard studies have proved that presbyopia affects most adults over 35 years of age,^{11,12} International study by Lourdes LI Llorente *et al.*, have shown that presbyopic changes occur early in hyperopes than myopes.¹³ All the cases showed bilateral eye involvement. When myopia and hypermetropia are compared, myopia (16.67%) more commonly affects population between 20 and 40 years than hypermetropia (8.33%). This result coincides with the study conducted in rural South Indian population by Raju *et al.*, which proved that prevalence of myopia was more than that of hypermetropia.⁸

Axial lengths of all the patients were recorded. They were found to vary significantly in myopic and hypermetropic patients. In our study, we found that females had slightly longer axial length than the males. This is in concordance with the study conducted in UK University and Central India.^{14,15} 33.33% of the myopes had longer axial length. 66.67% of hypermetropes had shorter axial length. This fact has been proved by many studies.¹³⁻¹⁶ 38.01% of the myopic astigmatism patients had longer axial length. The axial length did not vary significantly with presbyopic patients proving that it has no relationship with axial length. Presbyopia develops due to loss of power of ciliary muscles and change in curvature of the lens.^{11,13,16} 66.67% of the myopes and 33.33% of the hyperopes had normal axial length. This indicates that refractive error could have resulted from causes other than change in axial length like change in curvature of cornea, lens; change in refractive index of lens.^{5,17-19} Axial length change was an important risk factor for the development of hypermetropia and not so with myopia.

In our study, 66.67% of the myopes and 33.37% of the hyperopes had normal axial length. The refractive error could have occurred due to reasons like change in curvature of the cornea, lens; change in refractive index of lens. Axial length has no correlation with presbyopia, and it remains normal.

With reference to age, the mean age of occurrence of refractive errors among males was 28.25 years (standard deviation: ± 7.81) and among females was 30.8 years (standard deviation: ± 6.30). Mean age for developing myopia was 25 years (standard deviation: ± 5.48) and for hypermetropia was 30 years (standard deviation: ± 6.24). Patients with astigmatism and presbyopia had the mean age of 28.95 years (standard deviation: ± 6.38) and 38.57 years (standard deviation: ± 1.9) respectively. All patients with refractive errors were corrected with appropriate lenses. Most of the patients regained 6/6 vision following correction with lens.

CONCLUSION

Among the refractive errors astigmatism and myopia are common between 20 and 40 years of age with female preponderance. This being the economically productive age group needs special attention for early detection of refractive errors so that they can be effectively corrected to regain normal vision and prevent morbidity. Hence, the need for screening at this age group should be emphasized.

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How to cite this article: Kumaraswamy R, Sivakumar N, Anandan H, Uddin MKR. Refractive Errors of Patients between 20 and 40 Years and its Correlation with Axial Length. *Int J Sci Stud* 2016;3(11):104-107.

Source of Support: Nil. Conflict of Interest: None declared.

Comparative Study of Dermatoglyphic Patterns of Diabetes Mellitus and Diabetic with Hypertension Patients of Hilly Region

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Abstract

Introduction: The study of dermatoglyphics patterns on the digital and palmar region and its association with various diseases, especially having genetic causes, has been reported by various workers in the past. Recently, the number of patients with diabetes and hypertension (HTN) have strikingly increased in the most countries. The prevalence of HTN in patients with Type 2 diabetes is known to be 1.5-3 times higher than in the age-matched non-diabetic population.

Materials and Methods: A total of 100 Type 2 diabetic patients (50 males and 50 females) were compared with 100 diabetics with HTN patients. Dermatoglyphics patterns atd, dat, adt angles, absolute finger ridge count (AFRC), total finger ridge count (TFRC), a-b ridge count, main line index, and pattern index line were studied.

Results: The mean values of TFRC and AFRC were higher in male and lower in female diabetic group than diabetic with HTN group. The mean values of a-b ridge count were lower in male and higher in female in comparison to diabetic with HTN group, and a significant difference was found. The mean values of atd and adt were higher in diabetic group than diabetic with HTN group.

Conclusion: Dermatoglyphics provide a simple, inexpensive, anatomical, and non-invasive means of determining the diseases which have a strong hereditary basis and can be employed as a method of screening for diabetes mellitus of high-risk population on early detection, thus reducing the morbidity and mortality.

Key words: Anatomical, Hypertension, Population, Significant

INTRODUCTION

The term “dermatoglyphics” was coined by Cummins and Mildo in 1926 and was derived from the Greek words “derma” means skin and “glyphics” means carvings.¹ Each dermatoglyphic configuration is unique. They are genetically determined and influenced by physical, topographical and environmental factors. The peculiar patterns of the epidermal ridges serve as a diagnostic

tool in a number of diseases that have a strong hereditary background. Diabetes mellitus (DM) is one such disease with a strong genetic basis and certain dermatoglyphic variations are expected in DM.² DM and hypertension (HTN) are two of the most common diseases in westernized industrialized civilizations and the frequency of both diseases increases with increasing age. The prevalence of HTN in diabetic individuals appears to be approximately two-fold that in the non-diabetic population. It markedly enhances development of macrovascular and microvascular diseases in these individuals. Both DM and HTN are major independent risk factors for accelerated atherosclerosis and ischemic heart disease. The relevance of dermatoglyphics is not to diagnose, but to prevent by predicting a disease, not for defining an existing disease, but to identify people with the genetic predisposition to develop certain diseases.³

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Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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MATERIALS AND METHODS

The present study was performed out in the Department of Anatomy, Sikkim Manipal Institute of Medical Sciences, Gangtok, Sikkim from July 2013 to Jan 2015. Prints of 100 patients (50 males and 50 females) diagnosed with DM and diabetic with HTN were taken; their age group ranges from 21 to 80 years. An equal number of males and females were selected in cases to avoid the bias of sex in the result. All were clinically diagnosed and confirmed by investigations as diabetic and diabetic with HTN patients without any special genetic disease that could affect their dermatoglyphic patterns. The ethical clearance was obtained from the Institutional Ethics Committee prior to this study, and informed consent was informed from the participants.

Materials Required

Black duplicating inks, ink pad, white paper, magnifying hand lens, cotton puffs, scale, pencil pen, protractor - to measure atd angle and needle with a sharp point for ridge counting.

Procedure

Dermatoglyphics prints were taken by the “Ink Method” as described by Cummins⁴ and Cummins and Mildo.⁵ Patients were asked to wash both their hands with soap and water, so as to remove any oil or dirt. The duplicating ink is smeared on both hands uniformly over the palm and digits taking care that hollow of the palm and the flexor creases of the wrist were uniformly inked. The hand of the patient was then placed on the bond paper from proximal to distal end. The palm was gently pressed between intermetacarpal grooves at the root of fingers and on the dorsal side corresponding to thenar and hypothenar regions. The palm was then lifted from the paper in reverse order, from distal to proximal end. The fingers were also printed below the palmar print by rolled fingerprint method. The tips of the fingers were rolled from radial to ulnar side to include all the patterns. The procedure was repeated with the other hand on a separate paper. The prints were then subjected for detail dermatoglyphic analysis with the help of magnifying hand lens, and ridge counting was done with the help of a sharp needle.

RESULTS AND OBSERVATION

The mean values of total finger ridge count (TFRC) and absolute finger ridge count (AFRC) were higher in male diabetic patients and lower in female diabetic patients than diabetic with HTN patients. No significant difference was found (Table 1). Whereas, the mean values of a-b ridge count were lower in male diabetic and higher in female

diabetic than diabetic with HTN patients. A significant difference was found in the right hand of females (Table 2 and Figures 1 and 2).

The mean values of atd angle were higher in diabetic group than diabetic with HTN group except in left hand of male. The mean values of dat angle were lower in right hands and higher in left hands of diabetic group than diabetic with

Table 1: Comparison of TFRC and AFRC in DM and DM+HTN patients group

Parameters	Mean±SD			
	TFRC		AFRC	
	Male	Female	Male	Female
DM	87.54±19.88	81.76±29.36	116.36±34.90	104.20±45.78
DM+HTN	83.12±30.73	84.34±28.99	110.38±49.61	115.40±53.32
P value	0.324	0.585	0.438	0.226

DM: Diabetes mellitus, HTN: Hypertensive, TFRC: Total finger ridge count, AFRC: Absolute finger ridge count, SD: Standard deviation

Table 2: Comparison of a-b ridge counts of both hands of DM and DM+HTM groups

Parameters	Mean±SD			
	Right a-b ridge count		Left a-b ridge count	
	Male	Female	Male	Female
DM	20.54±8.14	21.46±8.52	20.68±7.31	21.22±8.83
Control	21.24±7.29	19.36±5.95	21.76±7.70	20.38±5.75
P value	0.539	0.049	0.388	0.468

DM: Diabetes mellitus, HTN: Hypertensive, SD: Standard deviation

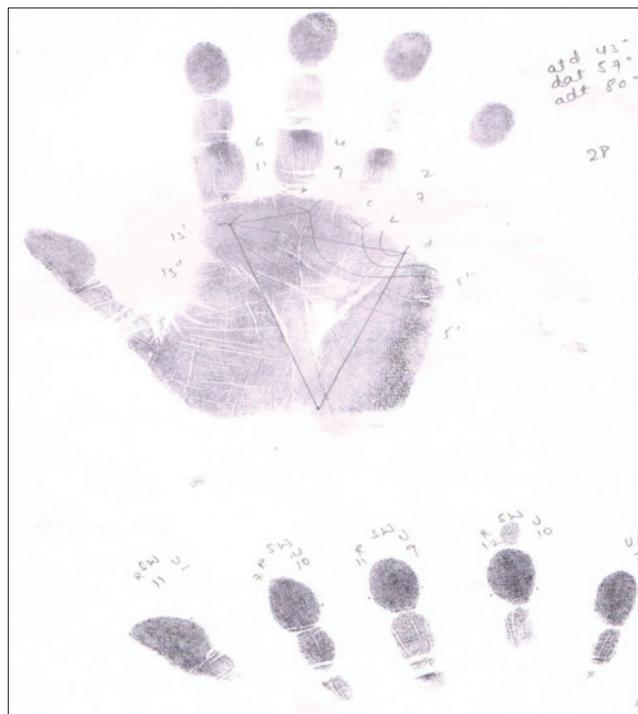


Figure 1: Dermatoglyphics patterns of right hand of diabetic group patient

HTN group. The mean values of adt angle were higher in males and lower in female's diabetic group than diabetic with HTN group. No significant difference was found (Table 3 and Figures 1 and 2).

In right hands, the mean values of fingertip ridge counts were lower in all digits except in 2nd, 4th, and 5th digits in male than diabetic with HTN group. In left hands, the mean values of fingertip ridge counts were lower in all digits of diabetic group than diabetic with HTN group except in 2nd, 4th and 5th digits. No significant difference was found (Table 4).

The mean values of pattern intensity index were higher in males and lower in females of diabetic group than diabetic with HTN group. No significant difference was found (Table 5).

The mean values of main line index were higher in right hands of male and left hands of females of diabetic group than diabetic with HTN. No significant difference was found (Table 6).

The most frequently occurring main line formula was 11-9-7, 11-7-7, 9-7-5, and 7-5-5. However, less frequently

occurring types were categorized under "rest." In diabetic males, the 9-7-5 (30%) was predominant followed by 7-5-5 (25%), 11-9-7 and 11-7-7 while in diabetic with HTN males, the 7-5-5 (29%) was predominant followed by 9-7-5, 11-9-7 and 7-5-5. In diabetic females, the 9-7-5 (28%) was predominant followed by 7-5-5, 11-7-7 and 11-9-7 while in diabetic with HTN females, the 9-7-5 (32%) was predominant followed by 7-5-5, 11-7-7, and 11-9-7 (Table 7 and Figures 1 and 2).

In the present study, we observed an increase in ulnar loops in the right hand of male diabetic and decreased frequency in the left hand of male and in both hands of female diabetic. In diabetic with hypertensive (HTN) patients, the frequency of the ulnar loop pattern was found to be increased in both male and female cases (Figures 1 and 2).

Table 3: Comparison of atd, dat and adt angles in the both hands of DM and DM+HTN groups

Parameter	Group	Mean±SD			
		Male		Female	
		Right hand	Left hand	Right hand	Left hand
"atd" angle	DM	41.48±7.31	40.86±5.02	43.38±6.46	43.56±6.39
	DM+HTN	41.66±6.05	42.44±7.73	41.92±6.42	42.28±5.91
	P value	0.894	0.201	0.266	0.331
"dat" angle	DM	58.48±4.58	59.08±4.22	56.94±4.36	57.06±5.75
	DM+HTN	59.42±4.25	58.96±6.75	57.28±4.69	57.00±5.38
	P value	0.258	0.900	0.712	0.959
"adt" angle	DM	79.80±7.16	79.86±5.54	79.28±6.09	79.34±6.04
	DM+HTN	78.94±6.18	78.44±6.16	80.84±5.92	81.12±5.22
	P value	0.482	0.193	0.231	0.118

DM: Diabetes mellitus, HTN: Hypertensive, SD: Standard deviation



Figure 2: Dermatoglyphics patterns of right hand of diabetic with hypertension group patient

Table 4: Comparison of fingertip ridge counts in the right hands of DM and DM+HTN groups

Parameters	Groups	Right hand			Left hand		
		DM	DM+HTN	P value	DM	DM+HTN	P value
D1	Male	14.16±6.55	14.42±8.18	0.850	11.58±7.50	11.82±6.26	0.412
	Female	12.56±6.89	13.44±6.55	0.483	11.06±6.68	13.88±6.95	0.471
D2	Male	11.68±5.77	10.64±7.18	0.453	9.80±7.20	9.68±5.30	0.149
	Female	9.62±6.78	12.18±8.09	0.053	11.68±7.29	11.72±6.13	0.414
D3	Male	10.04±4.94	10.04±6.26	1.000	10.68±6.75	11.00±6.44	0.761
	Female	10.86±5.71	11.98±7.96	0.430	10.92±7.48	11.92±6.70	0.396
D4	Male	14.66±6.73	13.58±7.21	0.445	13.76±7.61	12.22±6.36	0.957
	Female	13.24±7.15	14.72±7.49	0.233	13.12±7.49	13.62±7.00	0.733
D5	Male	9.12±3.93	7.92±4.45	0.178	9.06±5.43	8.14±3.75	0.426
	Female	7.90±4.40	8.82±4.90	0.262	7.86±3.68	8.30±4.29	0.441

DM: Diabetes mellitus, HTN: Hypertensive

Table 5: Comparison of pattern intensity index of both hands of DM and DM+HTN groups

Parameters	Mean±SD			
	Right pattern intensity index		Left pattern intensity index	
	Male	Female	Male	Female
Diabetic	1.48±0.31	1.33±0.38	1.39±0.37	1.30±0.40
DM+HTN	1.40±0.38	1.42±0.39	1.30±0.46	1.38±0.40
P value	0.241	0.219	0.241	0.369

DM: Diabetes mellitus, HTN: Hypertensive, SD: Standard deviation

Table 6: Comparison of MLI of both hands of DM and DM+HTN groups

Parameters	Mean±SD			
	Right a-b ridge count		Left a-b ridge count	
	Male	Female	Male	Female
Diabetic	9.04±1.88	8.56±1.84	8.02±1.64	8.44±1.94
DM+HTN	8.80±1.86	8.86±1.94	8.24±1.82	8.18±1.74
P value	0.538	0.455	0.908	0.504

MLI: Main line index, DM: Diabetes mellitus, HTN: Hypertensive, SD: Standard deviation

Table 7: Frequency of principal mainline formula

Parameters	Groups	Principal mainline formula (%)					
		DM			DM+HTN		
		Right hand	Left hand	Right+ left	Right hand	Left hand	Right+ left
11-9-7	Male	28	8	18	16	8	12
	Female	10	12	11	20	6	13
11-7-7	Male	8	12	10	8	12	10
	Female	30	24	15	26	8	17
9-7-5	Male	26	34	30	26	28	27
	Female	12	18	28	26	38	32
7-5-5	Male	20	30	25	24	34	29
	Female	32	26	28	26	28	27
Rest	Male	18	16	17	26	18	22
	Female	16	20	18	22	20	21

DM: Diabetes mellitus, HTN: Hypertensive

DISCUSSION

In the present study, we found increased frequency of ulnar loops in the right hand of diabetic patients which is similar to the studies of Ravindranath and Thomas, Chakravartii and decreased frequency of ulnar loops in left hand of diabetic male and both hands of diabetic female which is similar to results of Sant *et al.*⁶⁻⁸ However, we found decrease in whorls in diabetic of both sexes similar to Ravindranath and Thomas.⁶

In the present study, the mean TFRC was higher in diabetic patients. This was consistent with the findings of Ahuja *et al.*, Iqbal *et al.* and Barta *et al.* (1970).⁹⁻¹¹ While the mean values of AFRC was decreased in diabetics similar to

Ravindranath and Thomas, Sarthak and Jina, and Burute *et al.*^{12,13}

The present study has shown that the mean values of a-b ridge count were found lower in male diabetic and higher in female diabetic than control and significant in the case of females. This was similar to the findings of Ziegler *et al.*, Oladipo and Ogunnowo, whereas Tarca *et al.*, Dam *et al.*, Verbov found decrease a-b ridge count in diabetic patients.¹⁴⁻¹⁸

The present study showed the higher values of atd angle in diabetic group. Similar findings were reported by Ravindranath and Thomas, Sant *et al.*, Platilová *et al.* and Rajnigandha *et al.*, Sharma and Sharma, and Mittal and Lala.^{6,8,19-22} The values of atd angle in the present study are very close to the findings of Ravindranath and Thomas, Sharma and Sharma, Mittal and Lala as compared to other authors findings.^{6,21,22} The mean values of dat angle and adt angle showed lower values in the right hands and higher in left hands similar to the findings of Sharma and Sharma, and Mittal *et al.*^{21,22} There was no previous literature found on the diabetic with HTN patients pattern study and hence our present findings could not be compared.

CONCLUSION

The dermatoglyphic investigation is absolutely cost-effective and requires no hospitalization and it can help in predicting the phenotype of a possible future illness. This study would be helpful to formulate counseling messages based on dermatoglyphic pattern prevalent among young generation and their possible stimulation to determine the young people's likelihood to develop diabetes in their later age. It can be used for mass screening program for prevention of DM.

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How to cite this article: Bala A, Deswal A, Sarmah PC, Khandalwal B, Tamang BK. Comparative Study of Dermatoglyphic Patterns of Diabetes Mellitus and Diabetic with Hypertension Patients of Hilly Region. *Int J Sci Stud* 2016;3(11):108-112.

Source of Support: Nil, **Conflict of Interest:** None declared.

Isolation of Pathogenic Aerobic Organism from the Blood of Septicemic Neonates and the Susceptibility of Isolates to Various Antibiotics Attending in TMMC & RC, Moradabad, India

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Abstract

Introduction: Neonatal septicemia can be described as, systemic bacterial infection in neonates documented by positive blood culture. Neonatal septicemia is a major cause of morbidity and mortality among the neonates. It may be classified on the basis of onset of sepsis, <3 days as early onset sepsis (EOS) and >3-28 days as late onset sepsis (LOS). EOS and LOS are caused by organisms that are prevalent in the maternal genital tract and environmental factors, respectively.

Materials and Methods: Venous blood was collected aseptically and inoculated in the blood culture bottle. Further isolation and identification was done by Standard Microbiological Guidelines. Antibiotic susceptibility was detected according to CLSI guidelines.

Results: In our study, out of 388 clinically suspected septicemic neonatal cases, 140 (36.08%) was blood culture positive. In our study, out of 140 positive blood culture, 92 (65.71%) were males and 48 (34.29%) were female. Among positive blood culture 97 (69.29%) were EOS and 43 (30.71%) were LOS and out of 140 positive blood culture 83 (59.29%) were Gram-positive organism and 57 (40.71%) were Gram-negative organisms. In our study, the most common organism was *Staphylococcus aureus* 60 (42.85%) and *Klebsiella pneumoniae* 23 (16.43%) was a second most common causative organism of neonatal septicemia. Among Gram-positive organism, the most sensitive antibiotic was vancomycin 80 (96.39%) and linezolid 72 (86.74%). Among Gram-negative organism, the most sensitive antibiotic was polymyxin B (87.71%) and chloramphenicol, tigecycline, and meropenem (27.36%).

Conclusion: *S. aureus* is the most common Gram-positive bacterium, and *Klebsiella* is the most common Gram-negative bacterium causing neonatal sepsis. There is an increasing trend of antibiotic resistance against the commonly used first-line drugs. Continuous surveillance of antibiotic susceptibility is needed to ensure proper empirical therapy.

Key words: Early onset sepsis, Late onset sepsis, Neonatal intensive care unit

INTRODUCTION

Neonatal sepsis is defined as a clinical syndrome characterized by systemic signs of infection and bacteremia

during the first 28 days of life. It is a frequent cause of mortality and morbidity.¹ In India, 11-24.5/1000 live births were varied by the incidence of neonatal sepsis.² In the developing world, the major cause of morbidity and mortality among the newborns is neonatal sepsis.³

According to the age of onset, neonatal septicemia is divided into two types: Early-onset sepsis (EOS) (<72 h) and late onset sepsis (LOS) (≥72 h-28 days). EOS is acquired during delivery, fetal life, or at the nursery. Gram-positive as well as Gram-negative bacteria cause neonatal sepsis.⁴ There has been constantly changing the pattern

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Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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of the causative organism and frequent emergence of resistant bacteria.⁵

At birth, the neonate may be symptomatic in severe cases. Usually in EOS, neonates are present with respiratory distress and pneumonia. In general, the maternal genital tract is the source of infection.⁶ In LOS, the source of infection is either nosocomial or community acquired and usually presented with septicemia, pneumonia, or meningitis in infants.⁷ To select appropriate antimicrobial treatment, the knowledge of common pathogens causing neonatal septicemia and their antimicrobial susceptibility pattern is essential.

In neonates, the most common infection is blood stream infection. In the developing world, the most common reported organisms among LOS are *Escherichia coli*, *Klebsiella* species, and *Staphylococcus aureus*, whereas the most common pathogens among EOS, are *S. aureus*, *Streptococcus pneumoniae*, and *Streptococcus pyogenes*. *Klebsiella pneumoniae*, *S. aureus*, and *E. coli* are the three most common organisms, causing neonatal septicemia both in hospital and community, according to the National Neonatal Perinatal Database of India. In the developing countries, especially in the hospital setting, the causative agents of EOS and LOS sepsis are moreover similar. Geographically, antibiotic susceptibility pattern of pathogens are vary and are temporarily dependent on local pathogens and patterns of antibiotics use. Due to their weak immunity neonates are more prone to infection.⁸

There have been resistance bacteria of frequent emergency, and it has been changing constantly of causative organism pattern.⁵ The comparison of developed countries with developing countries like India there is a quite different organism's spectrum causing neonatal septicemia.⁹ The organism pattern differs from place to place, and it can change over a period of time in the same place.¹⁰

Moreover, a number of risk factors for the emergence and spread of antibiotic resistance are also home in developing countries. The reasons behind the emergence and spread of antibiotic resistance are over-the-counter and parallel market access, misuse of antibiotics, and counterfeit or poor quality drugs, combined with substandard hygiene and living conditions.^{11,12}

The isolation of bacterial agent from blood culture is a gold standard for diagnosis of septicemia.¹³

During the neonatal and pediatric age group, many infections can only be established on the basis of etiological agent recovered from blood,¹⁴ the possibility of neonatal sepsis does not rule by a negative blood culture.¹⁵

The prevalence of bacterial profile of blood cultures and their susceptibility patterns in an area, provide guidance to start empirical treatment which is the cornerstone in the management of sepsis.

Therefore, this study was aimed to determine the bacteriological profile and their antimicrobial susceptibility patterns in neonatal septicemia cases.

MATERIALS AND METHODS

The study is a 1-year, non-interventional prospective study of 388 patients suspected of septicemia visiting the neonatal intensive care unit in Teerthanker Mahaveer Medical College and Research Centre, Moradabad.

Collection of Blood Specimen

Blood samples were collected from the patients. First, 2-3 ml blood was drawn from the anti-cubital vein of each neonate into a sterile disposable syringe and then it is inoculated directly into BactAlert culture bottle by a trained study technician with all safety measures and then incubated at 37°C overnight for visible growth.

Subcultures were done on blood agar and MacConkey's agar. All positive blood cultures were identified by their characteristic appearance on their respective media, Gram-staining and confirmed by the pattern of biochemical reactions using the standard method. Members of Enterobacteriaceae were identified by indole production, citrate utilization, motility test, urease test, triple sugar iron test, and other relevant tests. For Gram-positive bacteria coagulase, catalase, and other tests were done.

Antimicrobial susceptibility test was performed by using modified Kirby-Bauer Disk diffusion method using Muller-Hinton agar and results were incorporated according to the CLSI, 2009. From pure culture 3-5, selected colonies of bacteria were taken with a sterile cotton swab and transferred to a tube containing peptone water, mixed well and incubated at room temperature for 30 min. Then swab was taken and the excess suspension removed by gentle rotation of the swab against the surface of the test tube. Then swab was used to evenly distribute the bacteria over the entire surface of Muller-Hinton agar. The inoculated plates were then left at room temperature to dry for 3-5 min and antibiotic discs were placed on the surface of Muller-Hinton agar plate.

For determining sensitivity, following antimicrobial disks were used such as ampicillin (10 µg), ampicillin/sulbactam (10/10 µg), cephalexin (30 µg), norfloxacin (10 µg), cotrimoxazole (25 µg), erythromycin (15 µg), gentamycin

(120 µg), ciprofloxacin (5 µg), levofloxacin (5 µg), linezolid (15 µg), tobramycin (10 µg), vancomycin (30 µg), amikacin (30 µg), pristinamycin (15 µg), teicoplanin (30 µg), chloramphenicol (30 µg), cefoperazone (75 µg), ceftazidime (10 µg), imipenem (10 µg), meropenem (10 µg), polymyxin B (300 units), tigecycline (15 µg), ceftriaxone (30 µg), ofloxacin (5 µg), tetracycline (30 µg), cefixime (5 µg), piperacillin/tazobactam (100/10 µg), and gatifloxacin (5 µg). The plates were then incubated at 37°C for overnight. Diameters of the zone of inhibition around the disc were measured to the nearest millimeter, and the isolates were classified as sensitive, intermediate, and resistant according to the standard table supplied by the CLSI guidelines.

RESULTS

In our study, the total number of culture positive cases was found to be 140 giving the culture positive rate of 35% (Table 1). Among culture, positive males were 92 (65.71%) and were females were 48 (34.29%), giving the male to female ratio was 1.91:1 (Table 1 and Figure 1).

The age of culture positive neonates ranged from 12 h to 28 days. Among culture positive neonates, 97 (69.29%) were having EOS and 43 (30.71%) were having LOS (Table 2 and Figure 2).

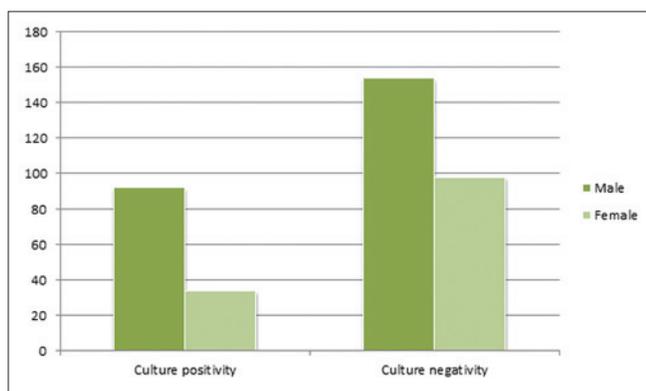


Figure 1: Blood culture positivity

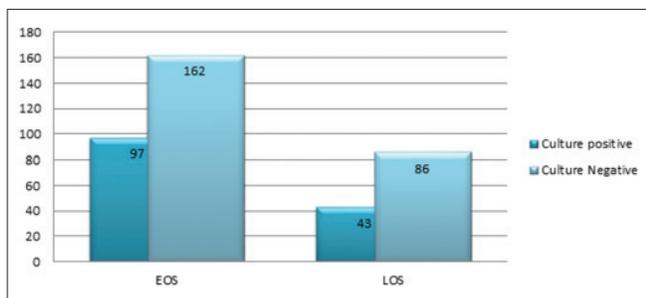


Figure 2: The distribution of cases according to the age of onset and culture positivity

Gram-positive organisms were more than Gram-negative organism, constituting about 60% of total isolates.

Most common pathogen identified was *S. aureus* 60 (42.8%) followed by *K. pneumoniae* 23 (16.43%), *Acinetobacter* 19 (13.57%), coagulase-negative *Staphylococci* 16 (11.43%), *Pseudomonas* 9 (6.43%), *Enterococcus faecalis* 5 (3.57%), *E. coli* 4 (2.86%), *S. pyogenes* 2 (1.43%) and *Enterobacter aerogenes* 2 (1.43%) (Table 3 and Figure 3). In this study, among *S. aureus*, methicillin-resistant *S. aureus* (MRSA) 34 (56.67%) were isolated.

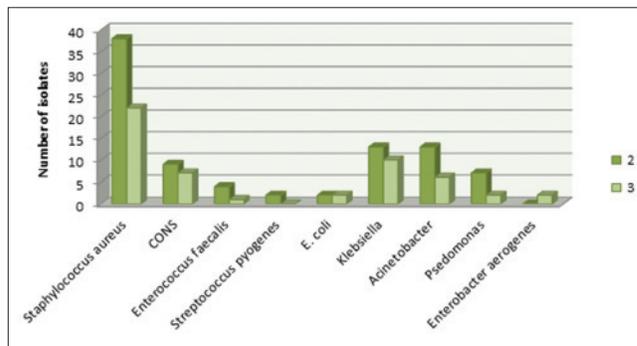


Figure 3: Bacterial isolates in blood culture

Table 1: Blood culture positivity

Blood culture	Male (%)	Female (%)	Total (%)
Culture positive	92 (65.71)	48 (34.29)	140 (36.08)
Culture negative	154 (60.10)	98 (37.90)	260 (63.92)
Total	254	146	400

Table 2: Distribution of cases according to age of onset and culture positivity

Age of onset	Culture positive (%)	Culture negative (%)	Total (%)
EOS	97 (69.29)	162 (65.32)	259 (66.75)
LOS	43 (30.71)	86 (34.68)	129 (33.25)
Total	140	248	388

EOS: Early onset sepsis, LOS: Late onset sepsis

Table 3: Bacterial isolates in blood culture

Organism	EOS (%)	LOS (%)	Total N (%)
<i>Staphylococcus aureus</i>	38 (63.33)	22 (36.67)	60 (42.85)
CONS	9 (56.25)	7 (43.75)	16 (11.43)
<i>E. faecalis</i>	4 (80)	1 (20)	5 (3.57)
<i>S. pyogenes</i>	2 (100)	0	2 (1.43)
<i>E. coli</i>	2 (50)	2 (50)	4 (2.86)
<i>Klebsiella</i>	13 (56.52)	10 (43.48)	23 (16.43)
<i>Acinetobacter</i>	13 (68.42)	6 (31.58)	19 (13.57)
<i>Pseudomonas</i>	7 (77.78)	2 (22.22)	9 (6.43)
<i>E. aerogenes</i>	0	2 (100)	2 (1.43)
Total	88	52	140

S. aureus: *Staphylococcus aureus*, CONS: Coagulase-negative *Staphylococci*, *E. faecalis*: *Enterococcus faecalis*, *S. pyogenes*: *Streptococcus pyogenes*, *E. aerogenes*: *Enterobacter aerogenes*, EOS: Early onset sepsis, LOS: Late onset sepsis

Among Gram-positive organism were found to be highly sensitive to vancomycin (96.39%) and linezolid (86.74%) followed by chloramphenicol (63.86%) and teicoplanin (67.47%) (Table 4 and Figure 4).

In our study, among *S. aureus* (60), 26 (43.33%) were methicillin sensitive *S. aureus* and 34 (56.67%) were MRSA, which is very high; it may be due to prolonged hospitalization, intake of broad spectrum antibiotics and nasal carriage.

Among Gram-negative organism were found to be highly sensitive to polymyxin B (87.71%) followed by meropenem (47.37%), chloramphenicol (47.37%), and tigecycline (47.37%) (Table 5 and Figure 5).

In our study, blood culture positivity rate in neonatal septicemia cases was 35% whereas in 65% of cases there

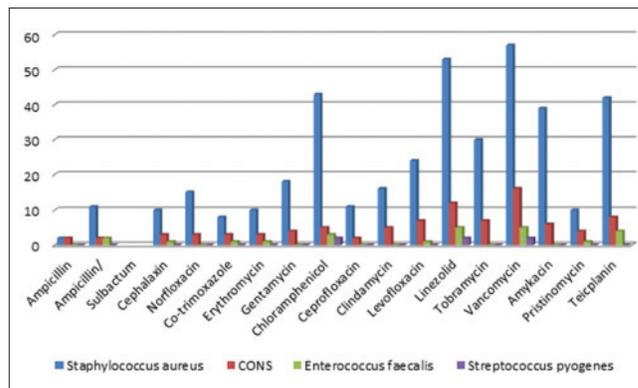


Figure 4: Antibiotic sensitivity of Gram-positive bacterial isolates

DISCUSSION

Throughout the world, developing countries share 99% of the estimated 4 million neonatal deaths, and the major contributor to it are sepsis, pneumonia, diarrhea, and tetanus infections¹⁶ being responsible for about 34/1000 live births compared to developed countries and among them the neonatal mortality due to sepsis is approximately 5/1000 live births.¹⁷

One of the major causes of neonatal morbidity and mortality is sepsis. The myriads of neonatal sepsis are risk factors and the clinical presentation, with differences in the usually responsible organism for the EOS and LOS.¹⁸ The gold standard for the confirmation of sepsis is blood culture.¹⁹

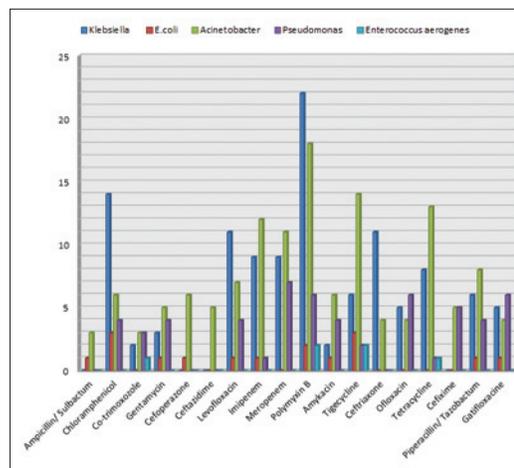


Figure 5: Sensitivity pattern of Gram-negative bacterial isolates

Table 4: Antibiotic sensitivity pattern of Gram-positive bacterial isolates

Antibiotics	N (%)				Total (83)
	<i>S. aureus</i> (60)	CONS (16)	<i>E. faecalis</i> (5)	<i>S. pyogenes</i> (2)	
Ampicillin	2 (3.33)	2 (12.5)	0	0	4 (4.82)
Ampicillin/Sulbactam	11 (18.33)	2 (12.5)	2 (40)	0	15 (18.07)
Cephalexin	10 (16.67)	3 (18.75)	1 (20)	0	14 (16.86)
Norfloxacin	15 (25)	3 (18.75)	0	0	18 (21.69)
Co-trimoxazole	8 (13.33)	3 (18.75)	1 (20)	0	12 (14.46)
Erythromycin	10 (16.67)	3 (18.75)	1 (20)	0	14 (16.86)
Gentamycin	18 (30)	4 (25)	0	0	22 (26.50)
Chloramphenicol	43 (71.67)	5 (31.25)	3 (60)	2 (100)	53 (63.86)
Ciprofloxacin	11 (18.33)	2 (12.5)	0	0	13 (15.67)
Clindamycin	16 (26.67)	5 (31.25)	0	0	21 (25.30)
Levofloxacin	24 (40)	7 (43.75)	1 (20)	0	32 (38.55)
Linezolid	53 (88.33)	12 (75)	5 (100)	2 (100)	72 (86.74)
Tobramycin	30 (50)	7 (43.75)	0	0	37 (44.58)
Vancomycin	57 (95)	16 (100)	5 (100)	2 (100)	80 (96.39)
Amikacin	39 (65)	6 (37.5)	0	0	45 (54.21)
Pristinomycin	10 (16.67)	4 (25)	1 (20)	0	15 (18.07)
Teicoplanin	42 (70)	8 (50)	4 (80)	2 (100)	56 (67.47)
Total	399	92	24	8	523

S. aureus: *Staphylococcus aureus*, CONS: Coagulase-negative *Staphylococci*, *E. faecalis*: *Enterococcus faecalis*, *S. pyogenes*: *Streptococcus pyogenes*, *E. aerogenes*: *Enterobacter aerogenes*

Table 5: Antibiotic sensitivity of Gram-negative bacterial isolates

Antibiotics	N (%)					Total (57)
	<i>Klebsiella</i> (23)	<i>E. coli</i> (4)	<i>Acinetobacter</i> (19)	<i>Pseudomonas</i> (9)	<i>Enterococcus aerogenes</i> (2)	
Ampicillin	0	0	0	0	0	0
Ampicillin/Sulbactam	0	1 (25)	3 (15.79)	0	0	4 (7.01)
Chloramphenicol	14 (60.87)	3 (75)	6 (31.58)	4 (44.44)	0	27 (47.37)
Co-trimoxazole	2 (8.70)	0	3 (15.79)	3 (33.33)	1 (50)	9 (15.79)
Gentamycin	3 (13.04)	1 (25)	5 (26.31)	4 (44.44)	0	13 (22.80)
Norfloxacin	0	0	0	0	0	0
Cefoperazone	0	1 (25)	6 (31.58)	0	0	7 (12.28)
Ceftazidime	0	0	5 (26.31)	0	0	5 (8.78)
Levofloxacin	11 (47.82)	1 (25)	7 (36.84)	4 (44.44)	0	23 (40.34)
Imipenem	9 (39.13)	1 (25)	12 (63.15)	1 (11.11)	0	23 (40.34)
Meropenem	9 (39.13)	0	11 (57.90)	7 (77.77)	0	27 (47.37)
Polymyxin B	22 (95.65)	2 (50)	18 (94.73)	6 (66.66)	2 (100)	50 (87.71)
Amikacin	2 (8.70)	1 (25)	6 (31.58)	4 (44.44)	0	13 (22.80)
Tigecycline	6 (26.08)	3 (75)	14 (73.69)	2 (22.22)	2 (100)	27 (47.37)
Ceftriaxone	1 (4.34)	0	4 (21.05)	0	0	5 (8.78)
Ofloxacin	5 (21.73)	0	4 (21.05)	6 (66.66)	0	15 (26.31)
Tetracycline	8 (34.78)	0	13 (68.42)	1 (11.11)	1 (50)	23 (40.34)
Cefixime	0	0	5 (26.31)	5 (55.55)	0	10 (17.54)
Piperacillin/tazobactam	6 (26.09)	1 (25)	8 (42.10)	4 (44.44)	0	19 (33.33)
Gatifloxacin	5 (21.73)	1 (25)	4 (21.05)	6 (66.66)	0	16 (28.07)
Total	103	16	134	57	6	316

E. coli: *Escherichia coli*

was no growth while that in Batt Sima *et al.*,²⁰ study was 56.67%, K. J. Desai *et al.*,²¹ study was 46.20%, Premlatha *et al.*,²² study was 82.35%. Sharma *et al.*,²³ study was 37.63%.

The incidence of neonatal septicemia is variable and differs from place to place because it depends on various factors such as fetal birth weight, gestational age, perinatal care and hygienic conditions, child health care facilities, and maternal nutrition.

In our study, males were more affected than females and male to female ratio was 1.91:1. This is comparable to other studies by Sharma *et al.*²³ The actual reason for the predominance of a male is not clear but its reason may be sex dependent factors.²⁴ X-linked immunoregulatory genes are probably regulate the synthesis of gamma globulins and as males contain one X-chromosome, hence, they are more susceptible to neonatal septicemia than females.²⁵

In our study, early onset septicemia (66.75%) was more than late onset septicemia (33.25%) which is comparable with the studies of Sharma *et al.*²³ in which 205 (56.32%) were aged <72 h (early onset) and 159 (43.68%) were aged >72 h (late onset).

Gram-positive bacterial isolates (59.29%) were more than Gram-negative bacterial isolates (40.71%) in our study and it is very similar to the study of Sodani and Mutha.²⁶

In our study, the most frequent isolate was *S. aureus* 66 (42.85%) in both EOS and LOS. This is very similar

to the study of Shaw *et al.*,²⁷ *K. pneumoniae* was the second most common organism followed by other organisms.

In our study, the Gram-positive organism was highly sensitive to vancomycin (96.39%) and linezolid (86.74%). This was comparable to the study of Bhurle and Solabannavar.²⁸

Among Gram-negative organism *K. pneumoniae* 23 (16.43%) was the predominant and second most causative organism of neonatal septicemia, which is followed by *Acinetobacter* 19 (13.57%), *Pseudomonas* 9 (6.43%), *E. coli* 4 (2.86%), and *E. aerogenes* 2 (1.43%) which is similar to the study of Sharma *et al.*,²⁴ in which also *Klebsiella* (27.01%) was the second predominant organism.

CONCLUSION

Our study showed that the neonatal septicemia causes life-threatening emergency in the world, and rapid treatment with antibiotics is essential for the favorable outcome. From this study, it is showed that Gram-positive bacteria were more commonly the cause of neonatal septicemia.

Our study showed that bacterial spectrum for sepsis could be different in different regions, and sensitivity pattern also differs accordingly. In our study, vancomycin and polymyxin B are the drugs that are susceptible among the Gram-positive and Gram-negative organisms, respectively. Neonatal septicemia is more prevalent among the EOS.

The positive blood culture with antibiotic sensitivity is the best guide to antimicrobial therapy. Hence, early diagnosis and judicious use of antibiotic therapy are a good solution to this problem.

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How to cite this article: Navdeep, Farooq U, Singh S, Bharti AK, Ahmed R, Singh K. Isolation of Pathogenic Aerobic Organism from the Blood of Septicaemic Neonates and the Susceptibility of Isolates to Various Antibiotics Attending in TMMC & RC, Moradabad, India. *Int J Sci Stud* 2016;3(11):113-118.

Source of Support: Nil, **Conflict of Interest:** None declared.

Clinico-Pathologic Study of Exfoliative Dermatitis in Patients Visiting a Tertiary Care Centre in South India

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Abstract

Introduction: Exfoliative dermatitis is an extreme state of skin irritation resulting in extensive erythema and or scaling of the body. More than 90% of skin surface involvement is considered as a salient pre-requisite to make a clinical diagnosis of exfoliative dermatitis. Histopathology aids in the diagnosis of many cases of exfoliative dermatitis.

Purpose: Exfoliative dermatitis can be caused by a wide range of pre-existing dermatosis or can develop *de novo*. Our study aimed at studying the clinical and pathological correlation in exfoliative dermatitis.

Materials and Methods: 50 patients with clinical diagnosis of exfoliative dermatitis who presented to our skin department were taken up, evaluated with lab tests and skin biopsies. Skin biopsies were classified as conclusive, compatible, and undefined according to the biopsy reporting.

Results: Psoriasis was the most common cause of exfoliative dermatitis, followed by atopic in the pre-existing dermatosis group leading to exfoliative dermatitis. Drug-induced erythroderma was seen in 24%. 26% of exfoliative cases were idiopathic. A skin biopsy was able to yield a diagnosis in 60% (36% biopsy were conclusive, 24% were compatible with a diagnosis). The rest 40% biopsy reports were undefined or non-specific findings.

Conclusion: Thus, in our series of patients presenting with exfoliative dermatitis, the etiologic diagnosis was defined in 60.0% of patients with the skin biopsy. The biopsy could not establish a definitive diagnosis in the remaining 40.0% patients. We would like to emphasize the importance of biopsy in a case of exfoliative dermatitis. Furthermore, in the population with undefined biopsy report, we would suggest follow-up biopsies 3 months later or so.

Key words: Erythroderma, Exfoliative dermatitis, Skin biopsy

INTRODUCTION

Exfoliative dermatitis is an extreme state of skin irritation resulting in extensive erythema and or scaling of the body.¹ More than 90% of skin surface involvement is considered as a salient pre-requisite to make a clinical diagnosis of exfoliative dermatitis.² Pre-existing dermatoses

is the single most common cause of adult exfoliative dermatitis followed by drugs, malignancies, and idiopathic cases.³ Erythroderma can be fatal even when properly managed, primarily because of its metabolic burden and complications. Hence, it is mandatory to establish its etiopathology to facilitate precise management. The prognosis of erythroderma is determined by its underlying cause. The clinico-histopathological correlation in erythroderma is usually poor because specific cutaneous changes of dermatoses or a drug reaction are obscured by the non-specific changes of erythroderma. A skin biopsy is an essential investigation in the clinical evaluation and management of patients with erythroderma, especially in those patients with an undetermined cause. Skin biopsies

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www.ijss-sn.com

Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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were helpful in determining the etiology in 60.0% of the patients in the present series of cases of exfoliative dermatitis.

MATERIALS AND METHODS

A total 50 patients of exfoliative dermatitis presenting to the Outpatient Departments of KMC, Mangalore and Government Wenlock Hospital between August 2008 and August 2010 have been enrolled for the study. Patients presenting with erythema and scaling involving more than 90% of the body surface area were included for the study.

Written and informed consent was taken from the patients intended to be included in the study. Details of the presenting complaints were taken with regards to the site of onset and progression as well as the presence of symptoms of itching, oozing, scaling, fever, and malaise. A detailed history of all pre-existing skin disorders, drugs taken, precipitating and exacerbating factors and of symptoms pertaining to malignancy was taken.

All vital parameters were noted, and a detailed physical examination was done. Patients were examined in detail for cutaneous and systemic manifestations. Nails, the oral cavity, genitalia, the scalp were examined for any involvement, and a rectal examination was carried out in all patients. A detailed systemic examination was carried out to rule out systemic involvement.

A detailed examination of all the lymph node groups (cervical, axillary, infraclavicular, pectoral, inguinal, and femoral) was carried out with respect to their size, consistency, and distribution. Fine-needle aspiration cytology and lymph node biopsy were done if there was clinical suspicion of malignancy. Investigations carried out in all patients included full blood count, liver function tests (LFTs), renal function tests, fasting and postprandial blood glucose, serum electrolytes, urine analysis, serum immunoglobulin E (IgE), HIV enzyme-linked immunosorbent assay, chest X-ray, electrocardiogram, and fungal scrapings. Skin biopsies from the interscapular areas of the back and lesions were carried out on all patients, and the histopathological changes were noted.

The histopathologic diagnosis was defined according to the features described in the biopsy reports and classified as:

- Conclusive, when the pathology gave the diagnosis
- Compatible, when it was not conclusive but highly suggestive; or
- Undefined when the changes found by pathology were non-specific.

The definite etiologic diagnosis was determined in cases where the histopathologic diagnosis was conclusive or compatible and coincident with the clinical diagnosis. The etiologic diagnosis was considered as undefined in cases where the histopathologic diagnosis was non-specific or did not coincide with the clinical diagnosis.

RESULTS

The prospective study was conducted between August 2008 and August 2010. 50 patients with erythroderma were included for the study. The male:female ratio was 1.8:1. The mean age of onset was 55 years. Most of the patients belonged to the age group of 51-60 (24.0%), and the majority of the patients were above 50 years of age (56.0%). Most of the patients were farmers (32.0%) by occupation. Most of the female patients were housewives (24.0%) (Table 1).

A pre-existing skin disorder was the most common predisposing factors leading to erythroderma in 25/50 (50.0%) patients. Of the pre-existing skin disorders, psoriasis was the most common, present in 11/50 (22.0%) patients, followed by atopic dermatitis in 5/50 (10.0%) patients, other eczemas in 8/50 (16.0%) patients, and pityriasis rubra pilaris (PRP) in 1/50 (2.0%) patients.

A history of drug intake was present in 12/50 (24.0%) patients. History of intake of anticonvulsant drugs was present in 5/50 (10.0%) patients of which intake of phenytoin was the most common, present in 3/50 (6.0%) patients followed by carbamazepine in 2/50 (4.0%)

Table 1: Predisposing factors

Predisposing factors	Male (32)	Female (18)	Total (n=50)	Percentage
Pre-existing skin disorder				
Psoriasis	8	3	11	22.0
PRP	1	0	1	2.0
Atopic dermatitis	3	2	5	10.0-50.0
Other eczema	7	1	8	8.0
Drug intake				
Carbamazepine	1	1	2	4.0
Phenytoin	2	1	3	6.0
Nevirapine (ART)	1	0	1	2.0
ACE inhibitors	0	1	1	2.0-24.0
Clavix	0	1	1	2.0
NSAID	0	1	1	2.0
Dapsone	0	1	1	2.0
Ayurvedic medication	0	1	1	2.0
Details unknown	1	0	1	2.0
Malignancy	0	0	0	0.0
Idiopathic	8	5	13	26.0

ACE: Angiotensin-converting-enzyme, NSAID: Non-steroidal anti-inflammatory drugs, ART: Antiretroviral therapy, PRP: Pityriasis rubra pilaris

patients. History of intake of nevirapine, angiotensin-converting-enzyme inhibitors, clavix (clopidogrel and aspirin), non-steroidal anti-inflammatory drugs, dapsone and ayurvedic medication was seen in 1/50 (2.0%) patient, respectively. The details of the drug intake in one patient were not known. Our study did not have any patients with a history of malignancy.

No cause for the erythroderma could be elicited in 13/50 (26.0%) patients, i.e., idiopathic.

The majority of the patients (27/50) had an acute presentation with a duration of illness of <3 months. A duration of illness between 3 months and 1 year was present in 14/50 (28.0%) patients. A duration of illness between 1 and 2 years was present in 2/50 (4.0%) patients and a duration of illness of more than 2 years was present in 7/50 (14.0%) patients.

On examination, erythema was present in 48/50 (96.0%) patients, followed by erosions in 46/50 (92.0%) patients, papules in 23/50 (46.0%) patients, plaques in 22/50 (44.0%) patients, pustule in 9/50 (18.0%) patients, vesicle in 3/50 (6.0%) patients, and petechiae in 3/50 (6.0%) patients.

Nail changes were seen in 27/50 (54.0%) patients. The most common change was discoloration in 20/50 (40.0%) patients, followed by ridges in 18/50 (36.0%) patients, dystrophy in 14/50 (28.0%) patients, pitting in 10/50 (20.0%) patients, onycholysis in 9/50 (18.0%) patients, shiny nails in 2/50 (4.0%) patients, and paronychia in 1/50 (2.0%) patients.

Lymph node involvement was present in 28/50 (56.0%) patients. Inguinal lymph nodes were involved in 23/50 (46.0%) patients, followed by femoral in 11/50 (22.0%) patients, axillary in 9/50 (18.0%) patients, cervical in 7/50 (14.0%) patients, infraclavicular in 5/50 (10.0%) patients, and pectoral in 2/50 (4.0%) patients.

Peripheral blood eosinophilia was present in 8/50 (16.0%) patients with drug-induced exfoliation. Deranged LFTs were seen in 6/50 (12.0%) patients with drug-induced exfoliation (Table 2).

An abnormal ultrasonography abdomen was seen in 3/50 (6.0%) female patients (altered echotexture of the liver in two patients and ascites in one patient) and 3/50 (6.0%) male patients (fatty hepatomegaly). The serum IgE levels were raised in 38/50 (76.0%) of the patients.

Classification of Skin Biopsies

Skin biopsies were classified as conclusive when the pathology gave the diagnosis, compatible when it was not conclusive but highly suggestive of the diagnosis;

or undefined when the changes found by pathology are non-specific.

Based on the histological features, skin biopsies were conclusive of the diagnosis in 18/50 (36.0%) patients, compatible in 12/50 (24.0%) patients, and undefined in 20/50 (40.0%) patients (Table 3).

The conclusive skin biopsies included psoriasis in 6/50 (12.0%) patients, PRP in 1/50 (2.0%) patients, drug induced in 5/50 (10.0%) patients, and eczema in 6/50 (12.0%) patients (Table 4).

The compatible skin biopsies included, drug induced in 4/50 (8.0%) patients, eczema in 7/50 (14.0%) patients, and psoriasis in 1/50 (2.0%) patient (Table 5).

Table 2: Histopathological change

Histopathological changes	Males (32)	Females (18)	Total (n=50)	Percentage
Hyperkeratoses	9	3	12	24.0
Acanthosis	15	10	25	50.0
Parakeratosis	10	5	15	30.0
Spongiosis	13	5	18	36.0
Elongated rete ridges	5	2	7	14.0
Perivascular lymphocytic infiltrate	18	7	25	50.0
Apoptotic keratinocytes	2	1	3	6.0
Eosinophilic infiltrate	2	4	6	12.0
Vascular change	2	3	5	10.0
Pigment incontinence	5	3	8	16.0

Table 3: Skin biopsies

Biopsy reports	Males (32)	Females (18)	Total (n=50)	Percentage
Conclusive	12	6	18	36.0
Compatible	8	4	12	24.0
Undefined	12	8	20	40.0

Table 4: Conclusive skin biopsies

Histopathologic Diagnosis	Male (32)	Female (18)	Total (n=50)	Percentage
Psoriasis	4	2	6	12.0
PRP	1	0	1	2.0
Drug induced	2	3	5	10.0
Eczema	5	1	6	12.0

PRP: Pityriasis rubra pilaris

Table 5: Compatible skin biopsies

Histopathologic Diagnosis	Males (32)	Females (18)	Total (n=50)	Percentage
Drug induced	2	2	4	8.0
Psoriasis	1	0	1	2.0
Eczema	5	2	7	14.0

Of the 11 patients who presented with a history of psoriasis, a conclusive skin biopsy was obtained in 6/50 (12.0%) patients, compatible in 1/50 (2.0%) patient, and undefined in 4/50 (8.0%) patients. A conclusive skin biopsy of platelet-rich plasma (PRP) was obtained in 1/50 (2.0%) patient, who on history and clinical examination had features suggestive of PRP. Of the 12/50 (24.0%) patients who had presented with a history of drug-induced exfoliation, a conclusive skin biopsy was obtained in 5/50 (10.0%) patients, compatible in 4/50 (8.0%) patients, and undefined in 3/50 (6.0%) patients. Of the 26/50 (52.0%) patients who on history and clinical examination had features suggestive of eczema, a conclusive skin biopsy was obtained in 6/50 (12.0%) patients, compatible in 7/50 (14.0%) patients, and undefined in 13/50 (26.0%) patients (Table 6).

DISCUSSION

The male:female ratio in our study was 1.8:1, this is comparable to the study by Akhyani *et al.*⁴ In our series, the mean age of onset was in the fifth decade, which is comparable to studies by Kondo *et al.*⁵ and Rym *et al.*⁶ The majority of the males were farmers (32%), and the majority of the females were housewives (24.0%).

Predisposing Factors

Pre-existing skin disorder

A pre-existing skin disorder was the most common predisposing factor leading to erythroderma, seen in 25/50 (50%) patients. This is comparable with most of the other studies.^{3,5,7-9} However, in studies by King *et al.*,¹⁰ drug reactions were the most common predisposing factor leading to erythroderma.

Of the pre-existing skin disorders, psoriasis was the most commonly implicated in this study (22.0%), which is comparable to most of the other studies.^{3,6,8} A history of atopic dermatitis predisposing to erythroderma was seen in 5/50 (10.0%) patients. In other studies,^{5,8} the percentage of patients with atopic erythroderma has been reported to vary from 4.76% to 23.9%. A history of non-atopic eczema was seen in 8/50 (16.0%) patients in this study. In other studies,^{3,6-9} the percentage of

patients with non-atopic eczema has been reported to vary from 5.12% to 25.3%. The high number of patients with non-atopic eczema in this study is explained by the presence of a greater number of manual laborers, who would be more occupationally exposed to dust and plant allergens.

A history of PRP was seen in 1/50 (2.0%) patient. In different studies,^{3,9} the percentage of patients with PRP has been reported to vary from 1.25% to 8.2%.

Drug Reactions

A history of a drug reaction leading to erythroderma was present in 12/50 (24.0%) patients in this study, which is comparable to studies by Seghal and Srivastava¹¹ (24.7%). The most commonly implicated drugs in this study were anti-epileptic medications in 5/50 (10.0%) patients, comparable to studies Akhyani *et al.*⁴ and Chaudary and Gupte.¹² A higher percentage was reported by King *et al.*¹⁰ (34.0%). Both these studies had included a higher number of patients (135 and 82 respectively).

Malignancy

None of the patients in this study had a history of malignancy. This is comparable to the study by Kondo *et al.*⁵

Idiopathic

No cause of the erythroderma could be elicited in 13/50 (26.0%) patients, i.e., idiopathic, which is comparable to several other studies.^{5,4,6,8} In different studies, the number of idiopathic cases has been reported to vary from 6.51% to 36.0%.^{6,8,9}

Skin Biopsy

Skin biopsies were able to yield a diagnosis in 30/50 (60.0%) patients, comparable to the study by Vasconcellos *et al.*¹³ In other studies,^{3-6,8} the percentage of diagnostic skin biopsies have been reported to vary between 27.7% and 83.3%.

Skin biopsies diagnostic of psoriasis were obtained in 7/50 (14.0%) patients comparable to the study by Nigam *et al.*¹⁴ In the study by Chaudary and Gupte,¹² diagnostic skin biopsies of psoriasis were obtained in all the patients with clinical features suggestive of psoriasis. In other studies,^{3,9} the percentage of skin biopsies diagnostic of psoriasis has been reported to vary from 5.35% to 40.0%. However, a smaller number of skin biopsies were carried out in these studies.

Skin biopsy diagnostic of PRP was obtained in 1/50 (2.0%) patients, comparable to the study by Jain *et al.*,¹⁵ in which 1/25 (4.0%) patient had a diagnostic skin biopsy of PRP. In other studies,^{3,5} the percentage of skin biopsies diagnostic of PRP have been reported to vary from 1.25% to 3.57%.

Table 6: Distribution of cases according to the etiologic classification of skin biopsies

Histopathologic Diagnosis	Conclusive	Compatible	Undefined
Psoriasis	6	1	4
PRP	1	0	0
Drug induced	5	4	3
Eczema	6	7	13

PRP: Pityriasis rubra pilaris

Skin biopsies diagnostic of drug-induced erythroderma was obtained in 9/50 (18.0%) patients, which is higher than that obtained by Chiratikarnwong.

Thus, in the series of patients presenting with erythroderma, the etiologic diagnosis was defined in 60.0% of patients and undefined in 40.0% patients.

CONCLUSION

Erythroderma, which may be referred to as exfoliative dermatitis, is an inflammatory disorder in which erythema and scaling occur in more or less generalized distribution.

The onset of the disease in the majority of the patients was acute, in contrast to most other studies. In accordance with other studies, a pre-existing skin disorder was the most common predisposing factor leading to erythroderma (psoriasis was the most common, atopic dermatitis, PRP) followed by drug-induced erythroderma. Among the drug reactions, anti-epileptics were most commonly implicated. There were no patients with malignancy in this study.

The clinico-histopathological correlation in erythroderma is usually poor because specific cutaneous changes of dermatoses or a drug reaction are obscured by the non-specific changes of erythroderma.

The skin biopsy is an essential investigation in the clinical evaluation and management of patients with erythroderma, especially in those patients with an undetermined cause. Skin biopsies were helpful in determining the etiology in 60.0% of the patients in the present series of cases of exfoliative dermatitis.

Close follow-up of erythroderma of unknown cause, by repeating cutaneous biopsies in time, will allow us to identify patients in the latter group for early diagnosis.

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How to cite this article: Mahabaleshwar G, Nayak K, Kuruvila M, Pai RR. Clinico-Pathologic Study of Exfoliative Dermatitis in Patients Visiting a Tertiary Care Centre in South India. *Int J Sci Stud* 2016;3(11):119-123.

Source of Support: Nil, **Conflict of Interest:** None declared.

Obstetrical and Perinatal Outcome in Rhesus Antigen Negative Pregnancy

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Abstract

Introduction: Incidence of Rh negativity in India is 5-10%. Rh negative pregnancy poses a risk only when there is incompatible mating, leading to antigen-antibody reaction, and hemolysis. However, it can be prevented by adequate measures.

Aims and Objectives: To assess obstetrical and perinatal outcome in terms of perinatal morbidity and mortality, to correlate maternal outcome with increased gravidity and impact of anti-D immunoglobulin (Ig) on the outcome of Rh negative pregnancy.

Materials and Methods: The prospective observational study was conducted in Rh negative pregnant women with incompatible mating attending the Department of Obstetrics and Gynecology, Rajendra Institute of Medical Sciences over a period of March 2013 to October 2014. Maternal outcome was assessed on the basis of mode of delivery and risk factors in present pregnancy. Neonatal outcome was assessed for weight, gestational age of birth, APGAR score, anemia, distal convoluted tubules positively, hyperbilirubinemia, need for phototherapy, and exchange transfusion.

Results: In the present study, 16% of patients in the study group were indirect coomb's test (ICT) positive, 84% were ICT negative. Isoimmunization was found to be significantly associated with increasing gravidity, *P* value being <0.05. Isoimmunization was found to be significantly less in mothers with a history of anti-D administration in previous pregnancies *P* value being <0.05. Of 150 births, 94% were live birth, 3.3% neonatal death, and 2.7% intrauterine death. Neonatal anemia (hemoglobin <18 g%) and hyperbilirubinemia (cord blood bilirubin ≥ 3.5 mg%) were significantly associated with isoimmunized mother, *P* value being <0.05. Association of isoimmunization with need of phototherapy (*P* < 0.5) and with exchange transfusion was highly significant (*P* < 0.01). In the present study, 48 out of 51 booked patients received routine antenatal anti-D prophylaxis in contrast to only 8 out of 99 unbooked patients. 3 of booked patients refused it because of the cost factor. 94 patients received post-natal prophylaxis with 300 mg anti-D. 61 patients did not receive because 24 were isoimmunized and 24 babies had Rh negative blood group. 10 patients refused to take anti-D, 6 because of the cost factor, and 4 as they adopted for permanent sterilization.

Conclusions: Though Rh hemolytic disease of the newborn forms common and preventable cause of maternal and perinatal morbidity, conditions are still encountered in India. Technically simple investigations and anti-D IgG when required decreases the burden of disease.

Key words: Erythroblastosis fetalis, Heterozygous, Hyperbilirubinemia, Isoimmunization, Perinatal, Rhesus, Utero

INTRODUCTION

Rhesus antigen negative pregnancy is one of the major causes of perinatal mortality and morbidity. "Rhesus

antigen" was named after monkey *Macacus rhesus* with whom about 85% human being shares this red cell antigen.¹ The incidence of Rh negative blood group is highest among Basques that is 34%. It is 13% among Caucasians, 7% among African-American, and 1% among Americans, Chinese, and other Asiatic peoples.² The incidence of Rh negative blood group in India varies between 3% and 5.7%.³⁻⁵ In general, 60% of Rh positive men are heterozygous, and 40% are homozygous.⁶ Rh negative pregnancy poses a risk to mother and baby only when there is incompatible mating, i.e., husband blood group is

Access this article online



www.ijss-sn.com

Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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Rh positive. If genotype of the husband is homozygous, all the babies will be affected by hemolytic disease and if heterozygous 50% of babies will be affected.

Before the discovery of Rh antigen by Landsteiner and Weiner in 1940, little was known about etiology of erythroblastosis fetalis, a condition in which fetus becomes edematous and dies in utero due to severe anemia and high output cardiac failure.⁷ Levine *et al.* in 1944 showed that in 90% cases of erythroblastosis fetalis, the mother was Rh negative.⁸ With discovery of Rh immune type of antibody by Race and Weiner (1944) which can cross placental barrier, it became evident that it is responsible for erythroblastosis fetalis.⁹

Rh disease accounts for 97% of hemolytic disease of the newborn (HDN), remaining 3% is caused isoimmunization against other fetal antigenic groups such as Kell, non-D Rh, Duffy, Kidd, and MNS.¹⁰ HDN is preventable disease when measures to prevent fetomaternal hemorrhage in Rh negative pregnancy and antenatal and post-natal immunoprophylaxis with anti-D immunoglobulin (Ig) are practiced correctly. HDN due to Rh isoimmunization is yet a significant health problem in India. The incidence of Rh sensitization during pregnancy is 1-9%⁵ and perinatal loss due to Rh alloimmunization has been reported to be between 1% and 2.5%.¹³ Risk of isoimmunization decreased 1.5% by post-natal anti-D prophylaxis and to 0.18% by additional routine antenatal anti-D prophylaxis (RAADP).¹⁴

The main cause of sensitization in present day practice is a lack of awareness in many places in India, particularly in rural areas where the mother is not routinely tested for their ABO Rh blood group, also in small rural areas where facilities for laboratory testing for Rh isoimmunization are non-existent. Finally, the benefits of protecting non-immune Rh negative mothers from isoimmunization with the use of prophylactic IM anti-D Ig are either unknown or ignored because of cost consideration.

While the prevention of Rh alloimmunization is the responsibility of all health care workers, the management of alloimmunized pregnancies requires specialized care. From a public health viewpoint, emphasis must be placed on prevention; hence, we have some areas to focus on. There must be increased awareness among doctors and patients about antenatal prophylaxis at 28 weeks or after any sensitizing event. The present study is done to show risk factors associated with isoimmunization, perinatal outcome, and impact of anti-D Ig on the outcome of Rh negative pregnancy.

MATERIALS AND METHODS

This was an observational study conducted in all Rh negative pregnant women with incompatible mating who presented in outdoor and emergency Department of Obstetrics and Gynecology, RIMS, Ranchi over a period of March 2013 to October 2014. Ethical approval from ethical committee was taken. Informed consent was taken from all the patients regarding the necessity of follow-up and compliance.

All pregnant women with Rh negative blood group irrespective to their age, parity, booking status, gestational age, and administration of Rh anti-D Ig in previous or present pregnancy were included in the study. Rh negative pregnant women with compatible mating were excluded. Those women who refused to comply with the follow-up visits were excluded from the study.

A proper history of patients was taken, and all the antenatal records were reviewed. Thorough general and obstetrical examination was done and all the routine antenatal investigations along with indirect coombs test were sent. The maternal chart was reviewed for parity index, gestational age, blood group, and history of anti-D administration in previous pregnancies. Neonatal outcome was assessed for weight, APGAR score, anemia, distal convoluted tubules (DCT) positively, hyperbilirubinemia, need for phototherapy and exchange transfusion.

RESULTS

In the present study, 44% belonged to age group 20-25 years followed by 38% in 26-30 years age group. This scenario was most probably due to early marriage and early childbearing among the Indian population. 42% mothers were primigravida, 24% were the second gravida, 14.7% were the third gravid, and only 9.3% were the fourth gravida. Only 4.1% of the populations were gravida 4 onward; this is most probably due to the adoption of family planning services. 62% of mothers presented to us at 37-40 weeks, 18% at 40-42 weeks, and 20% before 37 weeks. Most of them were in labor at the time of presentation. Only 34% of the patients were booked. Most of the unbooked patients presented to the hospital in labor. This is most probably due to illiteracy, lack of health facilities in rural areas, and loopholes in the implementation of the health program.

Among them, 36% patients were O negative, 30% B negative, 28% A negative, and only 4% AB negative. Husband's blood group in most, i.e., 39.3% was not

known. This is because all of these cases were unbooked and husband was not available at the time of presentation. Of those whose blood group was known 18.6% were A positive, 16.6% were B positive, 18.6% were O positive, and only 6.6% were AB positive. Husband's blood group was known in all of the booked cases.

Only 34% patients have received anti-D in previous pregnancies. 54% patients did not receive anti-D, this was either due to lack of awareness, home delivery or due to cost factor. Labor outcome shows that 37.3% delivered normally, 31.3% by emergency lower segment caesarean section (LSCS), and 16.7% by elective LSCS. Labor was induced in 12.7% patients, and 2% required instrumental delivery. The outcome of 141 (94%) pregnancy was live birth. 4 (2.7%) patients had intrauterine death (IUD), and 5 (3.3%) had early neonatal death. Out of 4 cases of IUD, one had features of hydrops fetalis. There are large number of Rh antigens due to its complex genetic makeup. Two Rh genes RhD and RhCE located on short arm of chromosome number 1 encodes for RhD antigen and E,e,C,c respectively.^{11,12}

39 (26%) of babies were A positive, 39 (26%) were B positive followed by 36 (24%) being O positive. Only 12 (8%) of babies were AB positive. 24 (16%) babies born were Rh negative, these babies were free from complications (Graph 1).

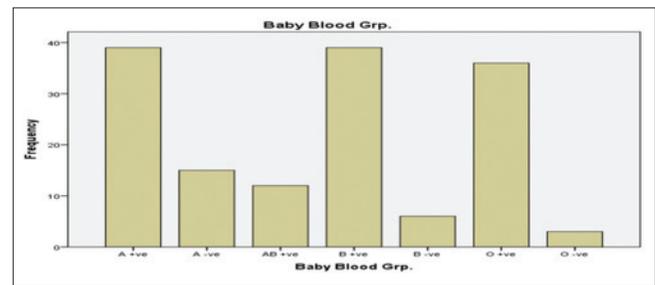
Out of 150 patients, 24 (16%) were indirect coomb's test (ICT) positive. Out of 24 ICT positive cases, only 1 was booked. Titer of booked case was 1:16 and was followed weekly but rising trend was not observed. Titer of 6 out of 24 was >1:32, one of these presented in active labor and delivered a dead baby with features of hydrops fetalis. One had IUD, 4 babies required exchange transfusion and phototherapy.

In the present study, 12 out of 24, i.e., (50%) isoimmunized patients belonged to 20-25 age groups. This is most probably because most of the patient in my study group belonged to this age group. It was also observed that isoimmunization is significantly associated with increasing gravidity, *P* value being <0.05. 9 out of 24 ICT positive cases were the third gravida. Association with gravida 4 onward is found to be comparatively less because of less number of patients in that age group, may be due to the adoption of family planning methods (Graph 2).

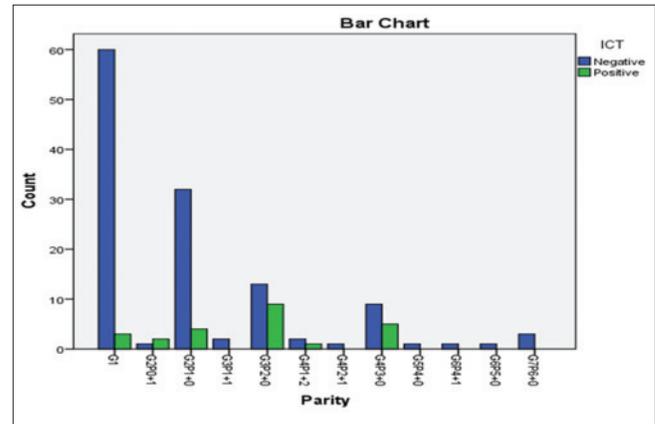
Isoimmunization was significantly associated with the unbooked status of the patient, *P* value being <0.01. 23 out of 24 ICT positive patients were unbooked as compared to

76 out of 126 ICT negative patients. It was more among unbooked patients. This was probably because most of the unbooked patients were illiterate belonging to remote areas; they were deprived of antenatal checkup and anti-D administration in previous pregnancies (Graph 3).

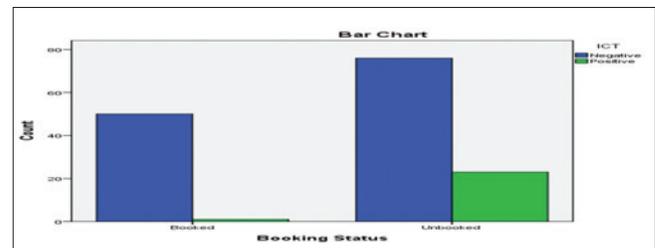
Isoimmunization was found to be significantly associated with mothers who did not have an anti-D administration in previous pregnancies, *P* value being <0.05. There was anti-D prophylaxis is a failure in 3 cases; all of these had a history of increased fetomaternal hemorrhage (FMH) in previous pregnancies. 1 of them had a history of mentally retarded offender program, 1 had a history of twin pregnancy, and other had a history of antepartum hemorrhage in the previous pregnancy (Graph 4).



Graph 1: Distribution of blood groups among newborns



Graph 2: Association of isoimmunization with parity



Graph 3: Association of isoimmunization with booking status of patients

In the present study, the neonatal outcome in terms of mortality at the time of birth was not significantly affected by isoimmunization, *P* value being >0.05. However, an adverse outcome like IUD was found more frequently in ICT positive cases. Neonatal death in ICT positive cases was due to severe HDN. Among ICT negative cases, death was due to other cause (Graph 5).

However, 5 min APGAR is <5 in 10 out of 24 ICT positive babies as compared to 5 out of 126 ICT negative babies. Thus, 5 min APGAR score was significantly low among isoimmunized babies, *P* value being <0.01. Furthermore, 6 out of 24 ICT positive babies and 9 out of 126 ICT negative babies were having birth weight <2.5 kg. Thus, low birth weight was also significantly associated with babies of isoimmunized mothers, *P* value being <0.01.

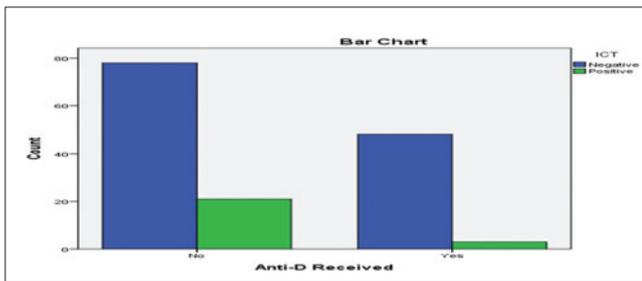
Hemoglobin (Hb) <12% was found in 3 out 24 ICT babies as compared to 1 out of 126 ICT negative babies. Hb between 12% and 18% was found in 12 out of 24 ICT

positive babies as compares to 14 out of 126 ICT negative babies. Thus, neonatal anemia was significantly associated in babies of isoimmunized mothers, *P* value being <0.01 (Graph 6).

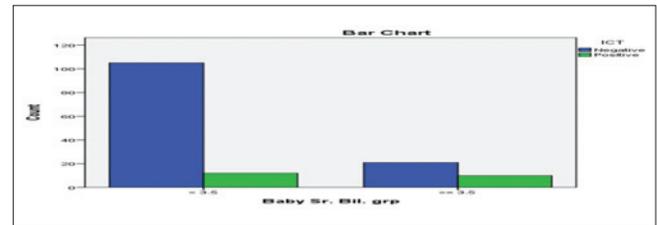
Furthermore, cord blood hyperbilirubinemia was found in 10 out of 24 ICT positive babies as compared to 1 out of 126 ICT negative babies and was found to be significantly associated with isoimmunization, *P* value being <0.05. All these babies developed pathological jaundice (Graph 7).

19 out of 24 babies of isoimmunized mother needed phototherapy as compared to 11 out of 125 non-immunized mothers. Thus, need for phototherapy was significantly associated with isoimmunization, *P* value being <0.05 (Graph 8).

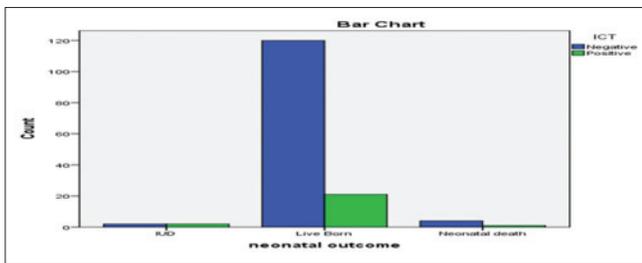
Four babies of isoimmunized mother needed exchange transfusion as compared to 1 out of 126 non-immunized mothers. Thus, need for exchange transfusion was significantly associated with isoimmunized mother, *P* value being <0.01 (Graph 9).



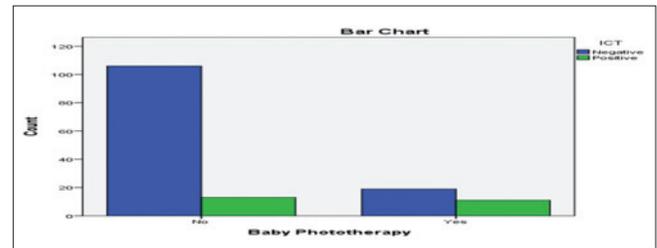
Graph 4: Association of isoimmunization with anti-D administration in previous pregnancy



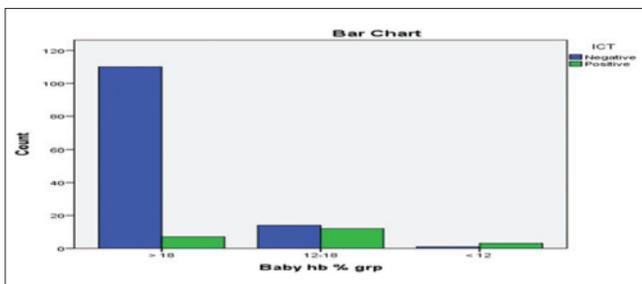
Graph 7: Cord blood bilirubin in isoimmunized and non-immunized pregnancy



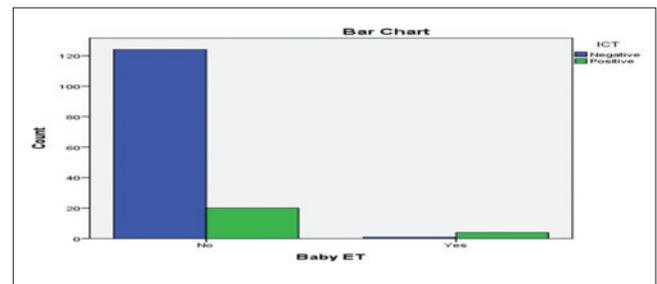
Graph 5: Neonatal outcome in isoimmunized and non-immunized pregnancy



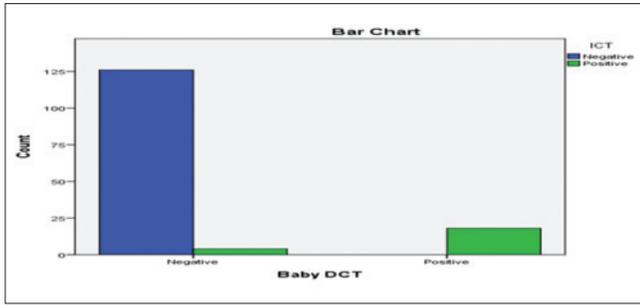
Graph 8: Need of phototherapy in isoimmunized and non-immunized pregnancy



Graph 6: Cord blood hemoglobin in isoimmunized and non-immunized pregnancy



Graph 9: Need of exchange transfusion in isoimmunized and non-immunized pregnancy



Graph 10: Distal convoluted tubules positivity in isoimmunized and non-immunized pregnancy

DCT positivity was significantly associated with babies of isoimmunized mother, P value being <0.01 (Graph 10).

Only 3 out of 51 booked patients in contrast to 91 out of 99 unbooked patients had not received anti-D prophylaxis in previous pregnancies. In the present pregnancy, 79 (52.6%) patients received post-natal anti-D prophylaxis. 61 patients did not receive because 24 were isoimmunized and 24 babies had Rh negative blood group. 6 patients refused to take anti-D due to the cost factor, and 4 were not prescribed as they adopted permanent sterilization.

DISCUSSION

Rhesus isoimmunization causing erythroblastosis fetalis is a distressing obstetric problem which is still seen in large numbers in India. It is the single most common yet preventable cause of HDN and also an important cause of neonatal hyperbilirubinemia.

Since post-natal anti-D prophylaxis was introduced to prevent sensitization of women lacking Rh antigens, the incidence of Rh hemolytic disease has markedly reduced. A further reduction will probably be achieved by proper and widespread antenatal anti-D prophylaxis. However, despite of these measures the incidence is unlikely to decline to zero. Factors contributing to the grave sequelae resulting from mismanagement of pregnancy in Rh negative women are: No prenatal care (home deliveries), non-availability of Rh testing in many health centers especially in peripheries; inadequate or no anti-D prophylaxis antenatally (after abortion including medical termination, ectopic pregnancy, threatened abortion, ante partum hemorrhage) or even post-natal many a times. The conventional treatment measures are appropriate hydration, phototherapy, and exchange transfusion. The number of affected cases is still at a stage where the management must be undertaken at a regional level, where the appropriate obstetrics, pediatric, and blood transfusion skill should be made available. Joshep from CMC Vellore used decision analysis technique in the year 2000 and found that there was gross underutilization

of anti-D prophylaxis in India.¹⁵ Deka *et al.* observed that failure to administer post-natal anti-D prophylaxis was responsible for Rh D alloimmunization in more than 50% cases followed by failure to administer anti-D after medical termination of pregnancy (MTP) (10%).¹⁴

In India, Federation of Obstetric and Gynaecological Societies of India guidelines suggest that all patients going for MTP should have documentary proof of blood group of both partners. It recommends routine antenatal prophylaxis by 100 mcg anti-D at 28 and 34 weeks or a single dose of 300 mcg at 28 weeks followed by post-natal prophylaxis by 300 mcg as soon as possible if the baby in Rh positive and DCT is negative. It also recommends 100 mcg anti-D after the sensitizing event of the first trimester. This post-partum anti-D dose is sufficient enough to neutralize 30 ml of fetal blood and is given without quantitative test for FMH. These test, i.e. Kleihauer test, flow cytometry, and rosette test is not readily available in India, also cost benefit of such testing has not been determined.¹⁶

The present study was undertaken to show the burden of HDN due to Rh incompatibility which is a preventable condition and to illuminates various causes for the persistence of this.

CONCLUSION

Over the 20th century, Rh alloimmunization was clinically recognized, its pathophysiology was understood, its treatment was established, and preventive measures were created to eliminate it. Unfortunately, the incidence of this disease is decreasing at a very slow place in India, in part because of lack of medical information and in part because of the high cost of medication used to prevent it. As shown in the present study, there is a risk of perinatal mortality of 12.5% among Rh negative isoimmunized mothers. Increased morbidity in term of congenital anemia and jaundice poses a great burden to medical professionals leading to increased NICU admissions, phototherapy and need for exchange transfusion. Anemia in newborn adversely affects the growth and development of the baby and increases the risk of neonatal sepsis. About 1/3rd of newborn of Rh negative mothers need treatment for hyperbilirubinemia. This risk is 3.8 times higher among multigravida.

All pregnant women at their first antenatal visit should have documentary proof of blood group; otherwise, a new test should be done. Rh negative mother should be counseled about the importance of Rh immunoprophylaxis and HDN. Routine antenatal prophylaxis with 300 mcg at or around 28th weeks or 100 mcg at 28th and 34th weeks followed by 300 mcg within 72 h of delivery is recommended. 100 mcg

of anti-D injection must be given after any sensitizing event in the first trimester. There should be increased awareness among doctors for RAADP and prophylaxis after MTP, abortion, ectopic pregnancy, etc., which is still lacking. In our country, the high cost of anti-D Ig and lack of its supply by government facilities amounts for significant risk of isoimmunization. While the public health system should guarantee the constant and adequate supply of Ig to all women who need it, physicians are responsible for its correct prescription to ensure the prevention of Rh disease. Family planning should also be encouraged for immunized women since the severity of hemolytic disease increases with consecutive pregnancies.

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How to cite this article: Shradha, Moitra B, Kumari A, Sahay PB. Obstetrical and Perinatal Outcome in Rhesus Antigen Negative Pregnancy. *Int J Sci Stud* 2016;3(11):124-129.

Source of Support: Nil, **Conflict of Interest:** None declared.

Morbidity Pattern in the Inmates of Residential Ashram in Rural Dakshina Kannada District, Karnataka

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Abstract

Background: India is projected to be the world's most populous country by 2025. Due to advents of urbanization, industrialization, education, and exposure to western lifestyles, the social values towards elderly are changing leading to a rapid breakdown from a joint family support system to nuclear family system. Finally, this unattended group of people lands up in places such as residential ashrams. The present study was undertaken to assess the health status and socio-demographic profile of inmates staying in the residential ashrams and planning of health care services for them.

Objectives: (1) To study health status of inmates residing in the ashram, (2) To study socio-demographic profile.

Materials and Methods: A cross-sectional study was done among the inmates of residential ashrams in rural field practice area of the Private Medical College in Mangalore, from June 2013 to May 2014. The study comprised a total of 179 inmates. A pretested semi-structured questionnaire was used to collect data regarding morbidity pattern and socio-demographic profile. Statistical analysis was performed using SPSS software version 16.

Results: The study comprised 179 inmates. 23.5% of the adults were illiterates. 22.3% of adults were suffering from 2 to 3 types of morbidities. The morbidity pattern of inmates was mainly anemia (64.2%) followed by hypertension (51.9%) and joint problems (44.1%). The other problems include gastrointestinal symptoms (27.4%), visual acuity problems (24%), respiratory symptoms (22.3%), obesity (20.7%), and diabetes (17.3%).

Conclusion: The study showed nearly all inmates suffered from one or more type of illness, the most common being anemia, hypertension, and joint problems. Hence, there is a need to address the health problems of inmates staying in residential ashrams.

Key words: Age group, Elderly, Health status, Morbidity, Old age home, Rural

INTRODUCTION

In India, in the last one and half decades, the longevity of the people has increased due to decline in mortality rate, better medical and health care facilities, and improvements in overall quality of life of people.¹ In 2001, geriatric population was 77 million in India and it is estimated that in India total number of elderly will rise to 150 million by 2025.² Due to advents of urbanization, industrialization, education, and exposure to western lifestyles, the social

values toward elderly are changing leading to a rapid breakdown from joint family support system to nuclear family system which further leads to problems such as economic insecurity, loneliness, lack of emotional support, lack of protection for their lives and property and dependency.³ Along with the social problems, aged people also suffer from many health problems. About 50% of the Indian elderly population has some or the other form of chronic disease and 5% suffer from immobility. Subsequently, these elderly are left over unattended and lands up in places such as residential ashrams.

Access this article online



www.ijss-sn.com

Month of Submission : 12-2015

Month of Peer Review : 01-2016

Month of Acceptance : 01-2016

Month of Publishing : 02-2016

MATERIALS AND METHODS

A cross-sectional study was done among the inmates of residential ashrams in rural field practice area of Private Medical College in Mangalore, from June 2013 to May 2014.

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The study comprised a total of 179 inmates. A pretested semi-structured questionnaire, clinical examination, investigation were used to collect data regarding morbidity pattern and socio-demographic profile. Statistical analysis was performed using SPSS software version 16.

Inclusion Criteria

All inmates of residential ashrams.

Exclusion Criteria

Inmates not willing to give their consent to participate in the study.

RESULTS

Table 1 represents the majority of the population ($n = 179$) belonged to the age group 60-69 (26.2%) years, followed by 20.1% in 50-59 years, and the least being 1.1% in the age group 90-99 years. The mean age of the group was 60.83 ± 14.28 years (males - 63.24 and females - 59.24).

Figure 1 represents study population ($n = 179$) consisted of 108 (60.3%) females and 71 (39.7%) males. In this study, females outnumbered the males.

Table 2 shows in this study ($n = 179$) in terms of religion, almost all (97.2%) residents were belonging to Hindu religion, followed by Muslims (2.2%) and least were Christians (0.6%). 36.3% of adults were married, 21.8% widow/widowers, 7.8% divorced/separated, and 34.1% were unmarried. About 27.7% of the married residents were living in the residential ashrams with their spouse. 23.5% of the adults were illiterates while the rest 76.5% were literate.

Table 3 represents the morbidity pattern of the population ($n = 179$) were mainly anemia (64.2%) followed by hypertension (51.9%) and joint problems (44.1%). The other problems include gastrointestinal symptoms (27.4%), visual acuity problems (24%), respiratory symptoms (22.3%), obesity (20.7%), diabetes (17.3%), urinary symptoms, cardiac illness, impaired hearing, and cerebrovascular accident.

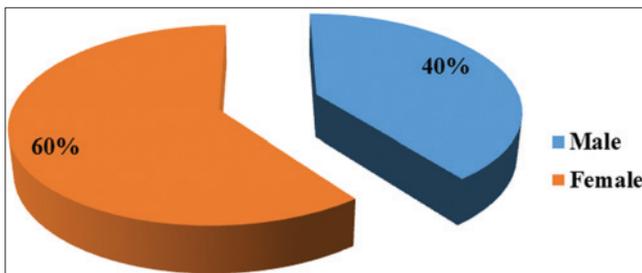


Figure 1: Pie chart representing the sex distribution of adult population (N = 179)

There was statistically significant difference in morbidity among males and females with respect to respiratory symptoms, cardiac illness, cerebrovascular accident, urinary symptoms, and impaired hearing. Joint problems and anemia were higher among females as compared to males.

Table 1: Age and sex distribution of the study population (N=179)

Age groups in years	N (%)		
	Males N=71	Females N=108	Total N=179
30-39	5 (7.0)	7 (6.4)	12 (6.7)
40-49	9 (12.6)	19 (17.5)	28 (15.6)
50-59	7 (7.0)	29 (26.8)	36 (20.1)
60-69	23 (32.3)	24 (22.2)	47 (26.2)
70-79	17 (23.9)	17 (15.7)	34 (18.9)
80-89	9 (12.6)	11 (10.1)	20 (11.1)
90-99	1 (1.4)	1 (0.92)	2 (1.1)
Mean age±SD	63.24±13.66	59.24±14.51	60.83±14.28

SD: Standard deviation

Table 2: Socio-demographic profile of the study population (N=179)

Variables	Categories	Total N (%)
Religion	Hindu	174 (97.2)
	Muslim	4 (2.2)
	Christian	1 (0.6)
Marital status	Married	65 (36.3)
	Alone	61 (34.1)
	Divorced/separated	14 (7.8)
	Widow/widower	39 (21.8)
Education status	Illiterate	42 (23.5)
	Literate	52 (29.1)
	Primary school	35 (19.6)
	Middle school	32 (17.9)
	High school	18 (10.1)

Table 3: Morbidity profile of the study population (N=179)

Morbidity condition	Total N=179 (%)	Male N=71 (%)	Female N=108 (%)	P value
Impaired vision	43 (24.0)	17 (23.9)	26 (24.0)	0.984
Impaired hearing	28 (15.6)	16 (22.5)	12 (11.1)	0.04*
Hypertension	93 (51.9)	35 (49.2)	58 (53.7)	0.564
Diabetes mellitus	31 (17.3)	14 (19.7)	17 (15.7)	0.491
Obesity (BMI>25)	37 (20.7)	15 (21.1)	22 (20.4)	0.952
Urinary symptom	26 (14.5)	17 (23.9)	9 (8.30)	0.004*
Respiratory diseases	40 (22.3)	23 (32.4)	17 (15.7)	0.009*
Cardiac illness	15 (8.40)	10 (14.1)	5 (4.60)	0.026*
Cerebrovascular accident	8 (4.5)	6 (8.5)	2 (1.90)	0.037*
Gastrointestinal symptoms	49 (27.4)	22 (31.0)	27 (25.0)	0.380
Joint pain/joint stiffness	79 (44.1)	25 (35.2)	54 (50.0)	0.051
Anemia	115 (64.2)	43 (60.6)	72 (66.6)	0.405

*p<0.05, Many of the subjects reported with multiple symptoms; Percentages are calculated on horizontal basis; P value analyzed by Chi-square test for 2x2 contingency table. BMI: Body mass index;

In the present study of morbidity among the adult population, one more age classification has been taken for the convenience of four groups for better comparison purposes.

DISCUSSION

The majority of the adult population in the present ($n = 179$) belonged to the age group 60-69 (26.2%) years, followed by 20.1% in 50-59 years, and the least being 1.1% in the age group 90-99 years.

In the study by Ramakrishna Reddy *et al.* in Bengaluru, Karnataka majority of the study population belonged to the age group 60-69 (49.3%) years, followed by 38.3% in 70-79 years, and the least being 12.1% in 80 years and above.⁴ In the study by Viveki *et al.*, in Belgaum city at old age homes, out of 73 elderly, majority were in the age group of 61-70 years (50.7%).⁵

In the study by Hegde *et al.* in Mangalore, the majority of the study population belonged to the age group 60-70 (46.91%) years, followed by 23.5% in 71-80 years, and the least being 7.2% in 80 years and above.⁶

In the study by Asadullah *et al.* in the OAHs of Udupi district, Karnataka, showed that majority (42.2%) were in the age group of 80 years and above. The mean age of male and female respondents were 75.3 (± 8.6) and 76.8 (± 7.7) respectively.⁷

In the present study, 108 (60.3%) were females and 71 (39.7%) were males. Females outnumbered the males. Similar findings were seen in the study by Banker *et al.* in Ahmadabad, the population consisted of 45.85% were males and 54.15% were females.⁸ In the study by Bansod and Paswan in the OAHs in Maharashtra, which also showed female predominance. Out of the 192 elderly, 45% were males and 55% were females.⁹ In the study by Jaiganesh *et al.* in Chennai, number of females are more than the number of males, i.e., females were 58.7%, and males were 41.3% in a total population of 450 individuals.¹⁰ In the study by Viveki *et al.* in Belgaum city at old age homes, out of 73 elderly, 54 were females (74.0%).⁵

In the present study, majorities (97.2%) were Hindus, followed by Muslims (2.2%), and least were Christians (6%). 36.3% of adults were married, 21.8% widow/widowers, 7.8% divorced/separated, and 34.1% were unmarried. About 27.7% of the married residents were living in the residential ashrams with their spouse. 23.5% of the adults were illiterates while the rest 76.5% were literate.

Similar results were seen, in the study by Rani *et al.* in OAHs of Chennai, and showed that around 71% belonged to

Hindu religion, 28% were Christians, and Muslims 1%.¹¹ In the study by Jaiganesh *et al.* in Chennai, majority were Hindus 62% followed by Christians 34% and Muslims 14%.¹⁰ In the study by All India Institute of Medical Sciences, New Delhi found majority of inmates were Hindus (73%) followed by Christians (21%) and Sikh (6%) in OAHs at New Delhi.¹²

In the present study morbidity, the pattern of the adult population was mainly anemia (64.2%) followed by hypertension (51.9%) and joint problems (44.1%). The other problems include gastrointestinal symptoms (27.4%), visual acuity problems (24%), respiratory symptoms (22.3%), obesity (20.7%), diabetes (17.3%), urinary symptoms, cardiac illness, impaired hearing, and cerebrovascular accident.

In the study by Viveki *et al.* in Belgaum city at old age homes, the prevalence of hypertension was (34.2%).⁵ In the study by Jaiganesh *et al.* in Chennai, the prevalence of hypertension was 54%.¹⁰ In other study by Kalavathy *et al.* in Kerala, found the overall prevalence of hypertension was 51.8%.¹³ In the study by Banker *et al.* in Ahmedabad, the prevalence of hypertension was 54.2%.⁸ In the study by Viveki *et al.* in Belgaum city at old age homes, the prevalence of locomotive and muscle disorders was 35.6%.⁵ Prevalence of musculoskeletal problems was 36.8% (males - 19.5% and females - 64.8%) and more in females in the study by Kishore *et al.*¹⁴ In the study by Ramakrishna Reddy *et al.* in Bengaluru, 17.8% of inmates had musculoskeletal problems.⁴

In the study by Hegde *et al.* in Mangalore, the prevalence of ophthalmological problems in 38.7% in the old age homes.⁶ In other study by Rani *et al.* in Chennai, the prevalence of visual problem was 35.1%.¹¹ In the study by Banker *et al.* in Ahmadabad impaired vision was found to be (44.2%), 82.3% were using spectacles followed by walking sticks.⁸

CONCLUSION

The study showed all inmates suffered from one or more type of illness, the most common being anemia, hypertension, and joint problems. Hence, there is a need to address the health problems of inmates staying in residential ashrams. Regular screening program should be done for detecting various diseases at an early stage among inmates of residential ashrams. Nutritional status of inmates should be checked at least once in a year.

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Singh and Kumar: Study of Morbidity Pattern in the Inmates of Residential Ashram

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How to cite this article: Singh DK, Kumar SN. Morbidity Pattern in the Inmates of Residential Ashram in Rural Dakshina Kannada District, Karnataka. *Int J Sci Stud* 2016;3(11):130-133.

Source of Support: Nil, **Conflict of Interest:** None declared.

Prevalence of Prostatic Intraepithelial Neoplasia in Patients Diagnosed as Benign Prostatic Hyperplasia Underwent Transurethral Resection of the Prostate at a Rural Teaching Hospital, India

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Abstract

Introduction: High grade prostatic intraepithelial neoplasia (HGPIN) is the most likely precursor of prostatic adenocarcinoma. In recent years, many studies have been shown that HGPIN is a major precursor of prostate cancer. It is very important to diagnose and correctly use the term HGPIN and to avoid confusion with other atypical entities of the prostate, which may differ with respect to clinical significance.

Purpose: To determine the prevalence of HGPIN in patients who underwent transurethral resection of the prostate (TURP) for benign prostatic hyperplasia (BPH).

Materials and Methods: It is a retrospective study, data collected from the medical records for the duration from January 2009 to September 2014, patients who underwent TURP for BPH at RL Jalappa Hospital, Kolar, India. Histopathology reports of all the patients who underwent TURP were analyzed, and reports with PIN tabulated.

Results: In the above study, 348 patients underwent TURP during the period enclosed. Among the above, a total 66 patients were found with histopathology showing with PIN ($n = 66$). Of which, HGPIN patients were 16 ($n1 = 16$) and Low grade PIN patients were 50 ($n2 = 50$).

Discussion: Earlier studies have shown that low grade PIN was significantly different from HGPIN in terms of cancer risk and was not associated with an increased risk of cancer any more than is the initial negative biopsy. Despite its histologic similarity to carcinoma *in situ*, a precursor to invasive cancer that arises in other organs (e.g. breast or skin). The finding of HGPIN with adjacent small atypical glands indicates a situation quite different from isolated HGPIN.

Conclusion: The study has conclusively shown there is a high prevalence of HGPIN in prostatic specimens and reported as BPH clinically in our hospital. The identification of increased number of HGPIN has an important implication for the management of the patient.

Key words: Benign prostatic hyperplasia, Neoplasia, Transurethral resection of the prostate

INTRODUCTION

High grade prostatic intraepithelial neoplasia (HGPIN) is a pathologic reading, something that the pathologist

might see on a needle biopsy or on a prostate that's been surgically removed. HGPIN is a most likely precursor of prostatic adenocarcinoma.^{1,2} The usual cell type comprising HGPIN is a glandular secretory epithelial cell. Squamous differentiation has been described in the benign prostate and prostatic carcinoma, but to our knowledge has not been previously reported in HGPIN. In recent years, many studies have shown that HGPIN is the major precursor of prostate cancer.

Most foci of PIN in young men are low grade, with increasing frequency of HGPIN with advancing age. The

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www.ijss-sn.com

Month of Submission : 12-2015

Month of Peer Review : 01-2016

Month of Acceptance : 01-2016

Month of Publishing : 02-2016

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volume of HGPIN also increases with patient's age.³ Race and geographic location may also influence the incidence of HGPIN. African and American men have a greater prevalence of HGPIN than whites in the 50-60 years age group. In contrast, Japanese men living in Osaka, Japan has a significantly lower incidence of HGPIN than men residing in the United States and Asians have the lowest clinically detected rate of prostate cancer.⁴

In contrast to HGPIN, the presence of low grade PIN is distinctly different and has no clinical significance. As a result, men with low grade PIN do not require a repeat biopsy unless other clinical indicators are present. In addition, using the term low grade PIN in the pathology report can lead to confusion with HGPIN.

PIN does not significantly elevate serum prostatic specific antigen (PSA) concentration and cannot be detected by ultrasonography.⁵ It is very important to diagnose and correctly use the term HGPIN and to avoid confusion with other atypical entities of the prostate, which may differ with respect to clinical significance. This study aims to clarify the diagnostic terms used in pathology reports and implications of the terminology upon clinical management.

Objective

To determine the prevalence of HGPIN in patients who underwent transurethral resection of the prostate (TURP) for benign prostatic hyperplasia (BPH).

MATERIALS AND METHODS

It is a retrospective study; data collected from the medical records for the duration from January 2009 to September 2014, in patients who underwent TURP for the BPH at RL Jalappa Hospital, Kolar, India.

Histopathology reports of all the patients who underwent TURP were analyzed and reports with PIN tabulated. In our study, total number of 348 patients who underwent TURP for BPH was included.

All the patient's reports are tabulated as different groups as reports patients with normal prostatic cells, reports with low grade PIN and HGPIN.

RESULTS

In the above study, out of 348 patients who underwent TURP during study period of four years 9 months, we found the following biopsy reports. Biopsy reports of TURP specimen: (1) BPH, (2) PIN, (3) adenocarcinoma, (4) squamous metaplasia, (5) basal cell hyperplasia, and (6) chronic prostatitis.

Among the above, a total 66 patients were found with histopathology showing with PIN ($n = 66$). Of which, HGPIN patients were 16 ($n1 = 16$), and low grade PIN patients were 50 ($n2 = 50$) (Figures 1 and 2) (Table 1).

DISCUSSION

HGPIN has a high predictive value as a marker for adenocarcinoma. A repeat biopsy is generally indicated in men with HGPIN. Earlier studies showed that low grade PIN was significantly different from HGPIN in terms of cancer risk $P < 0.05$, $P < 0.001$, and $P < 0.01$ and was not associated with an increased risk of cancer any more than is the initially negative biopsy.⁶⁻⁸

HGPIN is considered as a precancerous lesion. HGPIN is often diagnosed in a prostatic specimen obtained for a

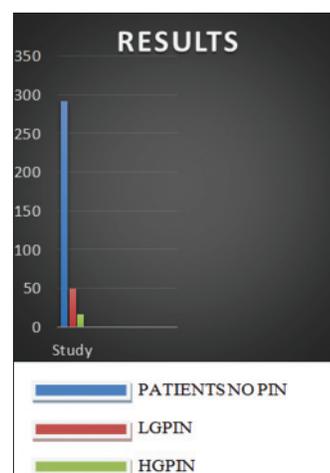


Figure 1: Number of patients with PIN

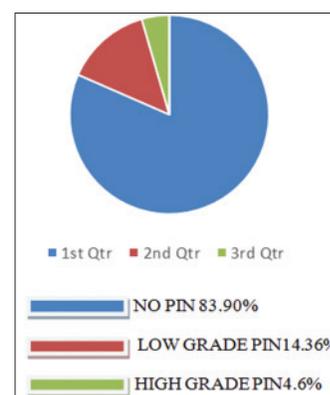


Figure 2: Percentage of patients with PIN

Table 1: Age distribution of patients studied

Years	N
61-70	124
71-80	157
81-90	52

diagnostic test (needle core biopsy) or for the treatment of non-neoplastic prostate pathology (such as TURP specimens for BPH). HGPIN is a non-invasive neoplastic process, which does not form a tumor mass or cause clinical symptoms.

Despite its histologic similarity to carcinoma - *in situ*, a precursor to invasive cancer that arises in other organs (e.g. breast or skin).⁹ PIN is a condition in which some prostate cells have begun to look and behaved abnormally. Abnormal cells located in two areas such as acini and ducts when PIN develops. The epithelial cells lining acini and ducts become abnormal, but lining itself remains intact. In contrast, when cancer develops, the epithelial lining is ruptured, and the malignant cells penetrate into the tissues of the prostate gland itself (Figures 3 and 4).

Originally, PIN was classified as Grades I, II, or III, according to increasing degree of abnormality. But 1989, a consensus conference recommended classification to low grade PIN (Grade I) and HGPIN (Grades II and III).¹⁰

This classification is important because low grade PIN does not increase developing cancer while HGPIN might. HGPIN is often multifocal and coexists with carcinoma in high frequency in radical prostatectomy specimens.¹¹⁻¹³

The reported incidence varies widely from 2.1% to 16.5%. Studies of men who have undergone prostate biopsies have found that anywhere from <1% to more than 20% had HGPIN.

Raviv *et al.* claimed that abnormal digital rectal examination (DRE) ($P = 0.008$), abnormal TRUS ($P < 0.001$) and

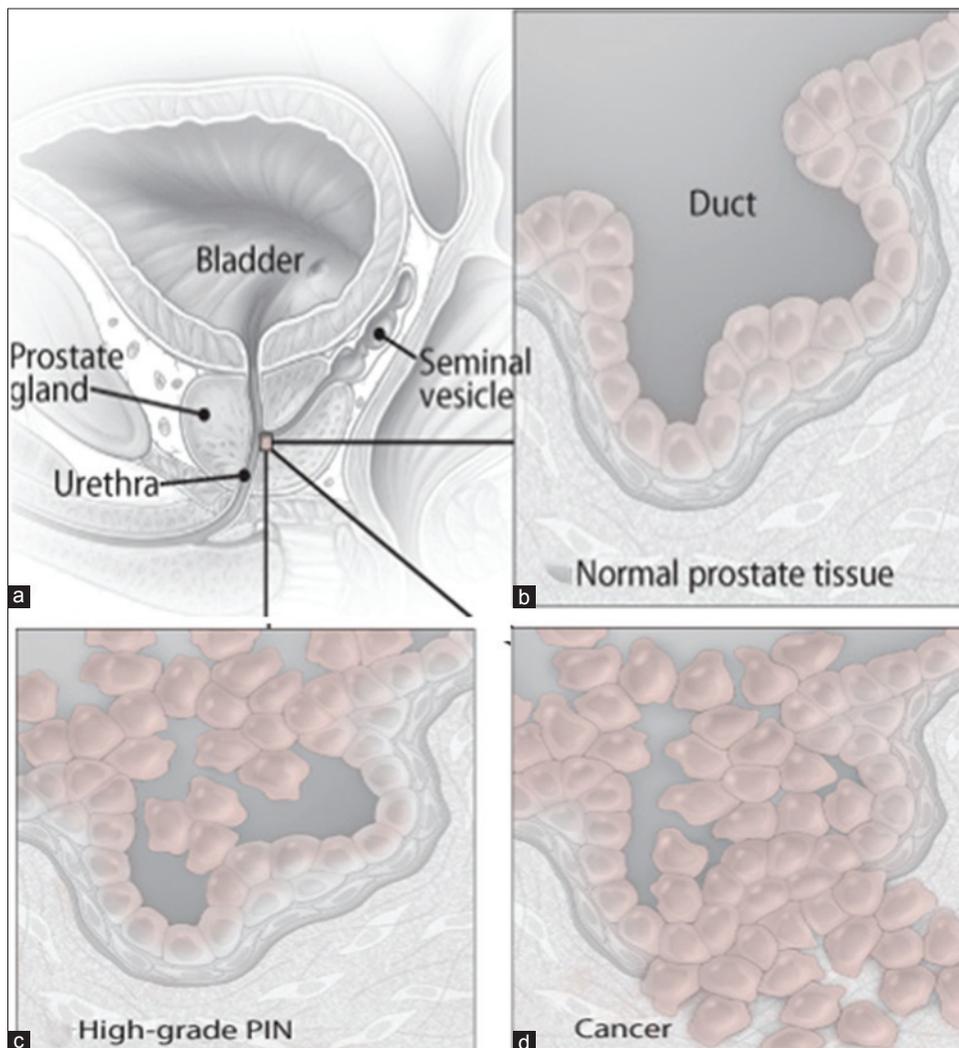


Figure 3: Normal epithelial cells line the ducts (a) that carry fluid from prostate gland to the main ejaculatory duct. In the case of high grade prostatic intraepithelial neoplasia (b), the cells become abnormally shaped. Their nuclei enlarge. Over time, these cells may become malignant and proliferate wildly, filling the duct and rupturing the epithelial lining (c). They can then penetrate into prostate gland tissue. (Source: 2014 Annual Report on Prostate Diseases by Harvard Medical School + Harvard Health Publications. Originally published Oct. 1, 2007)

Table 2: Incidence of isolated HGPIN in prostatic transurethral resections

References	Patient population	Men, n	Incidence of PIN (%)
Gaudin <i>et al.</i> , 1997 ¹⁴	Consecutive TURPs without cancer at Johns Hopkins Hospital	158	3.2
Pacelli and Bostwick, 1997 ¹⁵	Consecutive TURPs without cancer at Mayo Clinic	570	2.8
Skjorten <i>et al.</i> , 1997 ¹⁶	Consecutive TURPs from 1974-1975 at Ullevaal and Lovinsenbergs Hospitals, Oslo, Norway	731	33

HGPIN: High grade prostatic intraepithelial neoplasia, TURP: Transurethral resection of the prostate

Table 3: Incidence of isolated HGPIN in prostatic needle biopsies

Reference	Patient population	Men, n	Incidence of PIN (%)
Screening programs			
Mettlin <i>et al.</i> , 1991 ¹⁷	American cancer society National Prostate cancer Detection project	330	5.2
Feneley <i>et al.</i> , 1997 ¹⁸	Screening population in Gwent, England, 1991-1993	212	20
Hoedemaeker <i>et al.</i> , 1999 ¹⁹	PSA screening study in Rotterdam, The Netherlands	1824	0.7
Urology practice			
Lee <i>et al.</i> , 1989 ²⁰	Consecutive biopsies of hypoechoic lesions at St. Joseph mercy Hospital	256	11
Bostwick <i>et al.</i> , 1995 ²¹	Consecutive biopsies at Mayo clinic	200	16.5
Bostwick <i>et al.</i> , 1995 ²¹	Consecutive biopsies at Glendale Hospital, Calif	200	10.5
Langer <i>et al.</i> , 1996 ²²	Consecutive biopsies at University of Pennsylvania medical Centre	1275	4.4
Wills <i>et al.</i> , 1997 ²³	Consecutive biopsies at Johns Hopkins Hospital	439	5.5
Feneley <i>et al.</i> , 1997 ¹⁸	Consecutive biopsies at University College London Hospitals, 1988-1994	1205	11
O'Dowd <i>et al.</i> , 2000 ²⁴	Consecutive biopsies at UroCor Labs, Okla, 1994-1998	132, 426	2.3
Fowler <i>et al.</i> , 2001 ²⁵	Consecutive biopsies of men with suspected carcinoma at Veterans Affairs Medical Center, Miss, 1992-1998	1050	8.9

PSA: Prostate specific antigen, HGPIN: High grade prostatic intraepithelial neoplasia

Table 4: Incidence of prostate cancer on repeat biopsy²⁶

Initial biopsy finding	Percentage of men diagnosed with prostate cancer (%)	
	Repeat biopsy before 1995	Repeat biopsy between 1996 and 2000
Normal (benign) tissue	19	26.2
HGPIN	51	30.5

HGPIN: High grade prostatic intraepithelial neoplasia

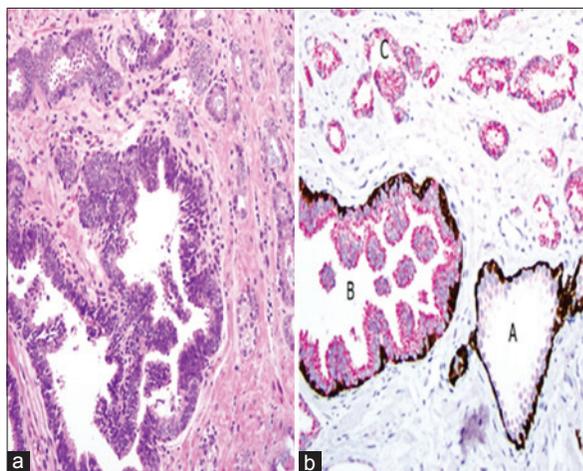


Figure 4: Triple antibody staining (AMACR, p63, and HMWCK).
 (a) Benign gland with basal cell staining (brown) minimal AMACR staining (red). (b) HGPIN gland with basal cell staining (brown) strong AMACR staining (red) in neoplastic acinar cells.
 (c) Adenocarcinoma with no basal cell staining but strong AMACR staining in acinar cells (red only)
 (Source: Int J Clin Exp Pathol 2009;2:327-338)

high PSA and predictive for carcinoma in the subsequent biopsy.⁵ The finding of HGPIN with adjacent small atypical glands indicates a situation quite different from isolated HGPIN. In rate of finding, cancer on biopsy is 50%. Hence, close follow-up with biopsy is recommended in men with HGPIN with small atypical glands (Tables 2-4).

CONCLUSION

The study has conclusively shown that there is a high prevalence of HGPIN in prostatic specimens and reported as BPH clinically in our hospital.

The identification of increased number of HGPIN has an important implication for the management of the patient.

Bearing in mind that HGPIN is strongly predictive as a precursor of prostatic carcinoma, patients with the finding of HGPIN report should be closely followed up with serum PSA, DRE and ultrasound, preferably transrectal ultrasound or repeated needle biopsy for a defined period of time.

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How to cite this article: Munireddy MV, Girish H, Prasad KK, Rajareddy H, Prevalence of Prostatic Intraepithelial Neoplasia in Patients Diagnosed as Benign Prostatic Hyperplasia Underwent Transurethral Resection of the Prostate at a Rural Teaching Hospital, India. *Int J Sci Stud* 2016;3(11):134-138.

Source of Support: Nil, **Conflict of Interest:** None declared.

Contrast-enhanced Computed Tomographic Evaluation of Acute Pancreatitis: An Exploratory Study

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Abstract

Introduction: Diseases of the pancreas have a very variable presentation and hence imaging plays an important role in the diagnosis and management of pancreatic disease, especially in acute pancreatitis. Computed tomography (CT) is the modality of choice as an evaluation of the pancreas.

Materials and Methods: A total of 30 patients who were clinically suspected of having acute pancreatitis attending our hospital were our study participants.

Results: The present study consisted of 30 patients who were suspected to have acute pancreatitis by clinical examination and laboratory parameters and referred for contrast-enhanced CT (CECT) examination of the abdomen. The peak age of incidence was noted in 30-40 years. 25 out of 30 patients had enlargement of the pancreas. 11 of these showed focal enlargement and the rest (14 patients) showed diffuse enlargement. Peripancreatic fat stranding was noted in 21 cases. Phlegmonous changes were evident in 14 patients with involvement of the lesser sac, mesentery transverse mesocolon, and anterior pararenal spaces. 7 cases showed the involvement of more than one anatomical site. In our study, 3 patients had Grade "A," 7 patients had Grade "B," 15 patients had Grade "C," 1 patient had Grade "D," and 4 patients had Grade "E" pancreatitis. In our study, CT severity index (CTSI) of 0-3 as seen in 16 patients, 4-6 was seen in 8 patients, and 7-10 was seen in 6 patients. Out of 4 patients who expired during the course of study, 3 had CTSI of more than 7 and those patients with CTSI of <3 had no complications, and there was no need of ICU stay for these patients.

Conclusion: In all the cases, CT scan revealed the exact morphological appearance of the disease. CECT was very useful in staging acute pancreatitis using various CT numerical grading systems.

Key words: Contrast-enhanced computed tomography, Grading of pancreatitis, Pancreas

INTRODUCTION

The pancreas was one of the last organs in the abdomen to receive the attention of anatomists, physiologists, physicians, and surgeons.¹ Diseases of the pancreas have a very variable presentation, and hence imaging plays an important role in the diagnosis and management

of pancreatic disease, especially in acute pancreatitis. Modalities for imaging of pancreas range from plain radiographs to contrast studies, ultrasonography, endoscopic ultrasound, endoscopic retrograde cholangiopancreatography (ERCP), computed tomography (CT), and magnetic resonance imaging. CT scan is the modality of choice as a non-invasive method of evaluation of the pancreas because it is unaffected by bowel gas or large body habitus. Among the diseases of the pancreas, pancreatitis is one of the most complex and clinically challenging of all abdominal disorders.^{2,3} During development of the pancreas, due to the differential growth of the gut wall, the ventral bud (along with the bile duct) shifts to the left side. Pancreatic tissue formed with respect to these two buds now fuses to form one mass. The ducts of the dorsal and

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Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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ventral buds anastomose with each other and open into the duodenum at ampulla of Vater.³ The most commonly seen developmental anomalies of the pancreas are - agenesis of dorsal or ventral pancreas, annular pancreas, pancreas divisum, and left sided pancreas.³ Out of these anomalies, pancreas divisum is commonly associated with recurrent pancreatitis.³⁻⁵ CT scan is the most useful modality in imaging a suspected case of pancreatitis. Ever since Mr. Hounsfield applied reconstruction technique to produce the world's first clinically useful CT image, it is extensively used/developed for imaging pancreatitis.⁴

Review of Literature

The pancreas is an exocrine and endocrine organ situated retroperitoneally in the left hypochondrium. It is descriptively divided into four parts *viz.* the head, neck, body, and tail (Figure 1).^{1,2,4} It is situated in the anterior pararenal space, by the posterior parietal peritoneum and dorsally by the anterior pararenal (Gerota's) fascia. The main pancreatic duct runs along the length of the pancreas and joins the common duct at the ampulla of Vater. In the head region, ranges 1-3 mm in diameter. The accessory pancreatic duct is more horizontal than the main duct. The CBD is seen within the pancreatic head close to its lateral and posterior surface, as a round or oval near water density structure.^{3,4} The attenuation of the pancreas is normally the same as that of soft tissue (30-50 HU). The normal pancreas increases in density after intravenous (IV) contrast administration. Pancreas is supplied by branches arising from the celiac and superior mesenteric arteries and drained by the tributaries of the superior mesenteric vein.

Acute pancreatitis is a common illness characterized by non-specific pancreatic inflammation associated with diverse etiologic factors, which include the following:⁵ (a) Metabolics such as alcoholic, hyperlipoproteinemia, hypercalcemia, drugs, scorpion venom, and genetic; (b) Mechanical such as cholelithiasis, post-operative (gastric/biliary), post-traumatic, retrograde pancreatography, pancreatic duct obstruction, pancreatic tumor, ascaris infestation, and duodenal obstruction; (c) Vascular such as post-operative (cardiopulmonary bypass), poly arteritis nodosa, and atheroembolism; and (d) Infections such as mumps and coxsackie virus. The most common etiologies found in 80% of patients are heavy alcohol abuse and cholelithiasis.⁵

The pathophysiology is still controversial but appears to be related to a temporary or permanent blockage of the pancreatic duct leading to a sudden release of enzymes into adjacent interstitial tissue. The activated extravasated enzymes lead to autodigestive fat necrosis and non-specific inflammation of the pancreas and peripancreatic tissues.⁶ The need for reliable imaging modality to diagnose and

confirm the clinical diagnosis of acute pancreatitis is evident when alternate methods of diagnosis are reviewed.^{7,8}

CT scanning is a reliable and non-invasive modality able to adequately evaluate the pancreas and the adjacent retroperitoneal structures in all most all individuals. The CT findings in acute pancreatitis reflect the presence and extent of the retroperitoneal inflammatory process.⁹⁻¹²

In patients presenting with milder clinical forms of pancreatitis, CT shows a relatively normal pancreas or a slight to moderate increase in the size of the gland. In most cases, the entire pancreas irregular and the parenchyma appears heterogeneous with areas of abnormal enhancement. Since pancreas does not have a well-developed fibrous capsule, extravasation of pancreatic secretions in and around the pancreatic gland occurs early. On CT, the peripancreatic fat becomes hazy and dirty, showing a slight increase in density and often mild thickening of adjacent facial planes.¹²

In the more severe forms of acute pancreatitis, small fluid collections are seen in the gland, and the amount of peripancreatic inflammatory exudates is increased. The gland may be massively enlarged and may show patchy areas of lack of enhancement, necrosis, and fragmentation.^{13,14} There is the total obliteration of the peripancreatic fat by large amounts of solid elements mixed with high density (20-40 Hu) fluid collections.

The sensitivity of CT to diagnose pancreatitis has been shown to be as high as 92%. The specificity of CT for acute pancreatitis is as high as 100%.^{13,14} Contrast-enhanced CT (CECT) accurately depicts the infected necrotic tissue and infected fluid collections and other complications of acute pancreatitis.¹⁵⁻¹⁹

Aims and Objectives

To study the use of CT for the detection and evaluation of acute pancreatitis.

To differentiate between acute edematous and acute necrotizing pancreatitis and to grade the severity of the disease using IV contrast-enhanced CT imaging features.

By follow-up imaging to detect any complications such as (a) Pseudocyst formation, (b) Pancreatic abscess formation, (c) Pancreatic phlegmon formation, (d) Vascular complications such as pseudoaneurysm of splenic, hepatic or pancreatico-duodenal arteries. To look for any associated conditions such as (a) Fatty liver, (b) Cholelithiasis, (c) Pancreatic calcifications, and (d) Pleural effusion; to plan the surgical intervention if indicated and CT guided aspiration of the abscess if any.

MATERIALS AND METHODS

A total of 30 patients who were clinically suspected of having acute pancreatitis attending Yenepoya Medical College Hospital, Mangalore were our study participants (Figure 2). The study was conducted for a period of 1-year from November 2014 to October 2015. Computed tomographic examinations were performed in the Department of Radio-diagnosis, Yenepoya Medical College Hospital, Mangalore. All cases referred for CT scan with clinical suspicion of acute pancreatitis were included in this study. Patients were selected on the basis of Clinical history, laboratory data suggestive of acute pancreatitis or findings of acute pancreatitis on other imaging modalities, especially ultrasounds scan.

Each patient underwent a thorough clinical evaluation including a detailed history and physical examination. All the patients underwent routine baseline blood investigations, which, however, did not form a part of the study. All the study participants were made to undergo CECT scan as the radiologic examination after taking proper informed consent for the same.

The study was performed using GE's 16 slice MDCT CT machine.

RESULTS

In our study, a total 30 patients were studied using CT scan, who were suspected to have acute pancreatitis. Among them, 24 (80%) were males and 6 (20%) were females (Table 1). In our study, 25 out of 30 (83.3%) patients had enlargement of the pancreas with focal enlargement seen in 11 patients (36.6%) (Figure 3) while the 14 patients (46.6%) showed diffuse enlargement. The contour of the pancreatic gland was irregular in 20 (66.6%) patients while in 10 (33.3%) it was regular. The density of the pancreatic gland was normal in 3 (10.0%) patients; focally hypodense in 20 (66.6%) of patients, generalized hypodensities in 5 (16.6%) patients, and the entire gland was distorted in 2 patients (6.6%). 21 of 30 patients (70%) showed peripancreatic fat stranding with or without phlegmonous changes (Figure 4).

Necrosis of the pancreatic gland parenchyma was seen in 14 (46.6%) patients. 8 patients (26.6%) showed <30% necrosis. 3 patients (10%) showed 30-50% necrosis, and 3 patients (10%) showed more than 50% necrosis (Figure 5 and Table 2).

By considering the grading and the extent of pancreatic necrosis CT severity index (CTSI) was calculated. CTSI = Grades A to E patients were assigned 0-4 points

plus 2 points for 30% necrosis, 4 points for 30-50% necrosis, and 6 points for more than 50% patients (Table 3). CTSI score of 0-3 was seen in 16 patients (53.3%), CTSI of 4-6 was seen in 8 patients (26.6%), and CTSI of 7-10 was seen in 6 patients (20%). 22 cases showed ascites and pleural effusion. However, the quantity of free fluid was more in

Table 1: Age and sex distribution of acute pancreatitis

Age (years)	Male (%)	Female (%)
0-10	0 (0)	0 (0)
10-20	2 (6.66)	0 (0)
20-30	4 (13.33)	0 (0)
30-40	7 (23.33)	0 (0)
40-50	4 (13.33)	1 (3.33)
50-60	4 (13.33)	2 (6.66)
60 and above	3 (10)	3 (10)

Table 2: CT signs of acute pancreatitis

Sign	N (%)
Gland	
Normal	5 (16.6)
Diffuse enlargement	14 (46.6)
Focal enlargement	11 (36.6)
Contour	
Regular	10 (33.3)
Irregular	20 (66.6)
Density	
Isodense	3 (10)
Focal hypodensity	20 (66.6)
Generalized hypodensities	5 (16.6)
Distorted architecture	2 (6.6)
Necrosis (%)	
<30	8 (26.6)
30-50	3 (10)
>50	3 (10)
Peripancreatic changes	21 (70)
Presence of gas/abscess	4 (13.3)
Phlegmonous changes	14 (46.6)
Pseudocyst formation	4 (13.3)
Pseudoaneurysm	1 (3.3)
Ascites	22 (73.3)
Pleural effusion	22 (73.3)

CT: Computed tomography

Table 3: Distribution of patient of acute pancreatitis according to the Grade of pancreatitis

Grade	No of patients (%)
A	3 (10)
B	7 (23.3)
C	15 (50)
D	1 (3.3)
E	4 (13.3)

Grade A: Normal pancreas, Grade B: Focal or diffuse enlargement of the gland, including contour irregularity, non-homogenous attenuation of the gland, dilatation of the pancreatic duct. Grade C: Intrinsic pancreatic abnormality associated with haziness and streaky densities representing inflammatory changes in the peripancreatic fat. Grade D: Single ill-defined fluid collection. Grade E: Two or multiple poorly defined fluid collections or presence of gas within the pancreas

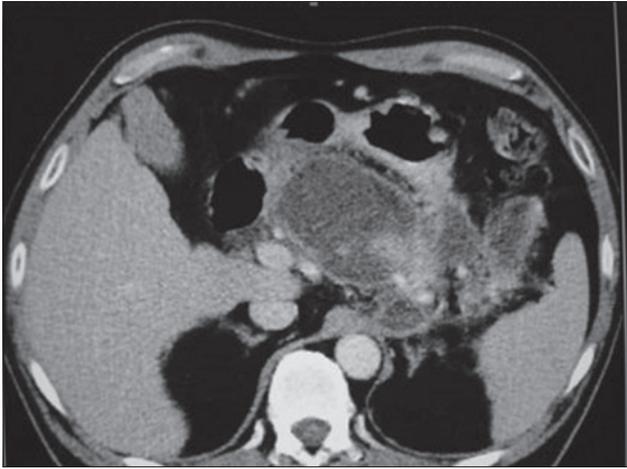


Figure 1: A case of resolving acute pancreatitis with developing pseudocyst in the body and tail regions of the pancreas

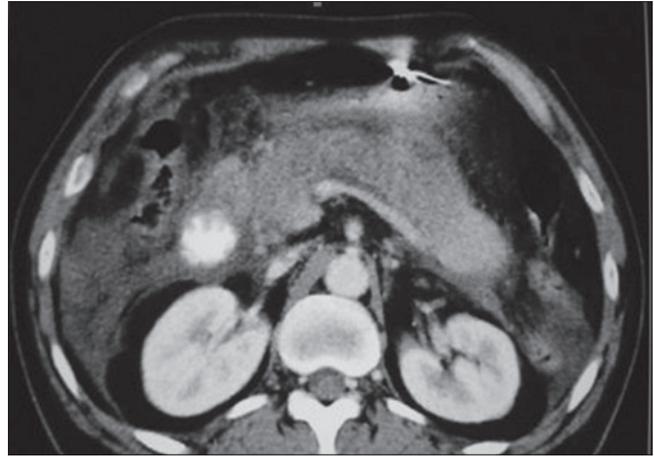


Figure 4: Mesenteric fat stranding with thickening of Gerota's fascia secondary to pancreatitis

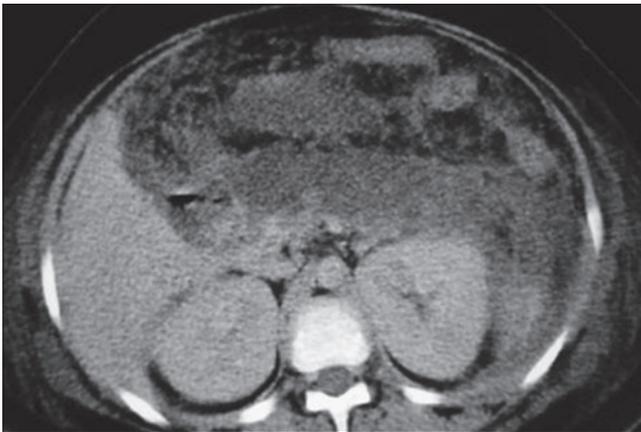


Figure 2: Mesenteric fat stranding with phlegmon formation in ongoing acute pancreatitis



Figure 5: Acute necrotizing pancreatitis with complete necrosis of pancreas

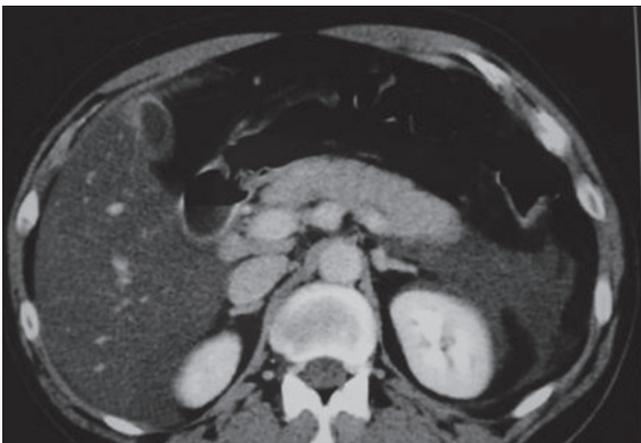


Figure 3: Case of Grade "B" pancreatitis with fatty liver with focal inflammation of peripancreatic fat around the tail of the pancreas due to alcoholic pancreatitis

severe cases, i.e., Grades C-E. Phlegmonous changes were seen in 14 cases, the lesser sac was involved in 12 cases, pararenal space was involved in 5 cases, and involvement

of mesocolon and mesentery was seen in 4 cases. Out of these 14 cases, 7 cases had shown the involvement of more than one anatomical site.

In cases of acute pancreatitis who had persistent symptoms or who were suspected to have pseudocyst, a repeat scan was performed. In our study, 4 cases showed pseudocyst formation. All the cases of pseudocyst were a complication of Grade "D" or Grade "E" pancreatitis. One case of Grade "C" pancreatitis had a complication in the form of pseudoaneurysm of the splenic artery. This case presented with persistence of pain abdomen following diagnosis of acute pancreatitis with an initial CT scan. 4 cases showed significant fatty liver. 5 cases showed gall bladder calculus. One case was a renal transplant recipient. This patient was thought to have azathioprine-induced acute pancreatitis. One case had pancreatic calcification. Abscess was seen within the pancreatic tissue in 4 cases (13.3%). In the plain and contrast-enhanced CT scan, all these findings were shown conclusively. All the cases in our study were followed till

recovery. The number of days of hospitalization was noted. Out of 30 patients, in our study, 4 cases were expired due to the complications of the disease. Out of these 4 cases, 3 were of Grade “E” pancreatitis. One case was of Grade “C” pancreatitis which was a case of post renal transplant recipient who was on azathioprine. In four cases, ERCP was performed, and removal of the bile duct calculus was performed. In 3 cases, surgical drainage of the collection was performed. One case of pseudoaneurysm of splenic artery was lost for follow-up (Figure 6). One patient developed partial thrombosis of the portal vein as a complication of acute pancreatitis (Figure 7). Though chronic pancreatitis was not part of our study, we had one case of acute pancreatitis that had preexisting asymptomatic pancreatic calcifications. It was a 28-year-old male, who was asymptomatic till then, presented with acute severe pain abdomen of 2 days duration. CT scan of the abdomen revealed normal sized pancreas with peripancreatic fat stranding, thickening of Gerota’s fascia, Ascites, and bilateral pleural effusion (Figure 8). Furthermore, there was a minimal area of necrosis. Multiple small areas of calcifications were noted in the body and tail region of the gland. The patient was hospitalized for 12 days and treated conservatively. The patient recovered completely without any residual exocrine or endocrine insufficiency.

DISCUSSION

Our study consisted of 30 patients who were suspected to have acute pancreatitis by clinical examination and laboratory parameters and referred for CECT examination of the abdomen.

We used non-ionic water-soluble contrast medium and were able to get good contrast enhancement of the normal pancreas. Since ours was an MDCT scan machine, our results were better than the results Zwicher *et al.*²⁰⁻²⁴

None of the 30 patients developed any adverse reaction to the IV contrast medium. All patients were observed for 3 h after injecting IV contrast medium.

Among these 30 patients, 24 were males and 6 were females. Thus, an increase in the percentage of males in the study could be attributed to alcoholism, which was the most common cause of pancreatitis.²⁵⁻²⁸

The peak age of incidence was noted in 30-40 years. This correlates with other studies²⁹⁻³³ in which mean age was 38 years. Two patients were in the age group of 10-20 years. Out of these, one was the recipient of transplant kidney and was on azathioprine. He had developed azathioprine-induced pancreatitis. The other patient was

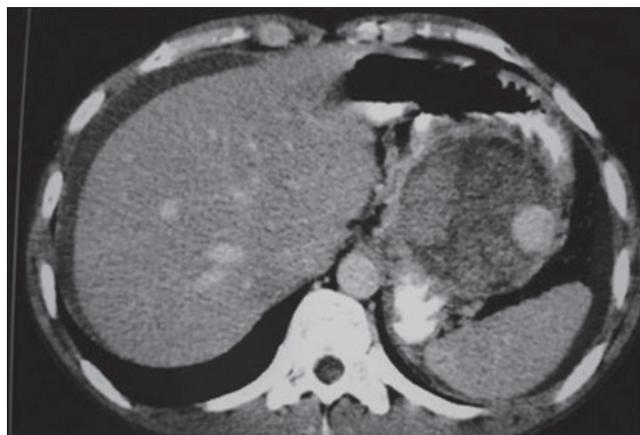


Figure 6: Pseudoaneurysm of splenic artery - a delayed complication of acute pancreatitis



Figure 7: Focal pancreatitis involving the head of the pancreas with dilated pancreatic duct. Note was made about portal vein thrombosis, as a complication of acute pancreatitis



Figure 8: Acute exacerbation of chronic pancreatitis

a 16-year-old boy who had developed post-traumatic pancreatitis.

25 out of 30 (83.3%) patients had enlargement of the pancreas. 11 of these (36.6%) showed focal enlargement and

the rest (14 patients - 46.6%) showed diffuse enlargement. This correlated with the previous studies^{14,34,35} that reported pancreatic gland edema in 90% of their patient (Table 4).

Peripancreatic fat stranding was noted in 21 cases (70%). Phlegmonous changes were evident in 14 patients (46.6%) with the involvement of the lesser sac, mesentery transverse mesocolon, and anterior Pararenal spaces. 7 cases showed the involvement of more than one anatomical site. These statistics are consistent with phlegmonous spread of pancreatitis described by other workers in 2/3rd of their patients (Table 5).^{14,35}

In our study, 3 patients (6.6%) had Grade “A,” (Figure 9) 7 patients had Grade “B” (23.3%) (Figure 10), 15 patients (50%) had Grade “C,” (Figure 11) 1 patient (3.3%) had Grade “D,” (Figure 12) and 4 patients (13.3%) had Grade “E” pancreatitis (Figure 13 and Table 6).

Balthazar *et al.* (1985)¹³ reported the following Grade “A” in 14.5%, Grade “B” in 29.9%, Grade “C” in 25%, Grade “D” in 14.5%, and Grade “E” in 27.7% of cases.

We calculated the CTSI as given by Balthazar *et al.* in their 1990 series.³⁶ Grades A to E patients were assigned 0-4 points plus 2 points for necrosis of <30%, 4 points for necrosis 30–50%, and 6 points for >50% necrosis of the pancreatic gland. This calculated CTSI grading into three categories (0-3, 4-6, and 7-10 points) more accurately reflects the early prognostic value of CT. They found that patients with a CTSI of 0-2 had no mortality and 4% morbidity. In contrast, a CTSI of 7-10 yields a 17% mortality and 92% complication rate.

In our study, CTSI of 0-3 as seen in 16 (53.3%) patients, 4-6 was seen in 8 patients (26.6%), and 7-10 was seen in 6 patients (20%).

Out of 4 patients, who expired, 3 had CTSI of more than 7. The other one was a boy with CTSI of 2 was organ transplant recipient. The correlation between CTSI and mortality is consistent with the results of Balthazar *et al.*

All the patients with CTSI of <6 recovered well (except the one who was the recipient of organ transplant who was on azathioprine - who expired).

Patients with CTSI of <3 had no complications and the number of days of hospitalization was less.

Ascites and pleural effusion of various severities were seen in 22 patients. Quantity of ascites and pleural effusion were more in Grades C, D, and E pancreatitis.

Table 4: Distribution of patients of acute pancreatitis according to CTSI

CTSI	No of patients (%)
0-3	16 (53.3)
4-6	8 (26.6)
7-10	6 (20)

CTSI: Computed tomography severity index

Table 5: Distribution of phlegmonous changes according to anatomical site

Site	No
Mesentery/mesocolon	4
Pararenal space	5
Lesser sac	12
Psoas muscle	0

Table 6: Distribution of mortality among cases of pancreatitis

Grade	Cases
A	0
B	0
C	1
D	0
E	3

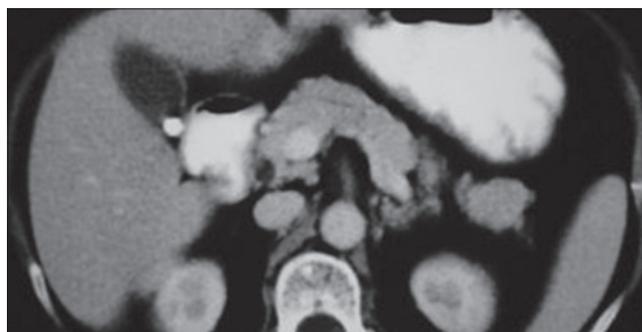


Figure 9: Grade “A” pancreatitis; normal contrast-enhanced computed tomography morphology of pancreas with elevated serum amylase. Incidental gallbladder calculus noted

Though chronic pancreatitis was not part of our study, we had one patient who had presented with acute severe pain abdomen for the first time in his life who did not have any risk factor for developing pancreatitis. He was diagnosed to have pancreatitis based on clinical parameters and serum amylase and lipase parameters. CT scan of the abdomen showed normal sized pancreas with peripancreatic fat stranding, ascites, and pleural effusion. There were multiple tiny areas of calcification in the body and tail region of the pancreas. Based on clinical and imaging parameters, he was diagnosed to have acute on chronic pancreatitis. According to various studies, pancreatic calcifications were the most consistent feature of chronic pancreatitis.³⁷⁻⁴⁶

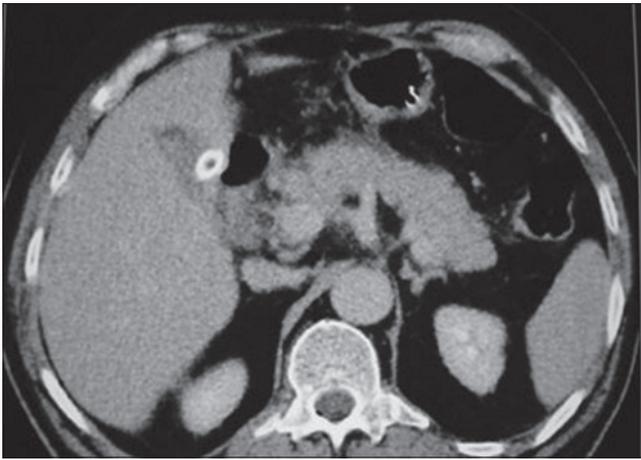


Figure 10: Grade “B” pancreatitis with cholelithiasis



Figure 12: Grade “D” pancreatitis

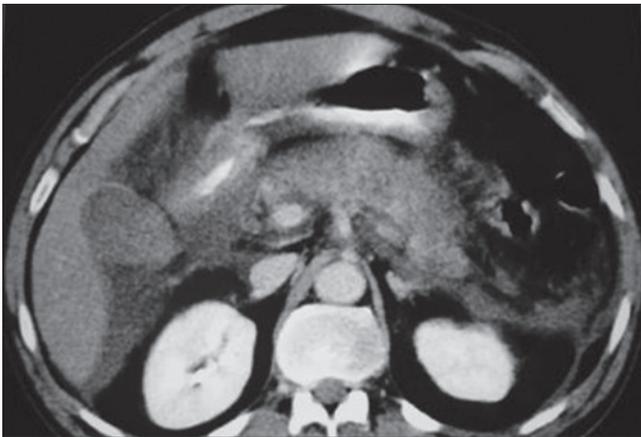


Figure 11: Grade “C” pancreatitis

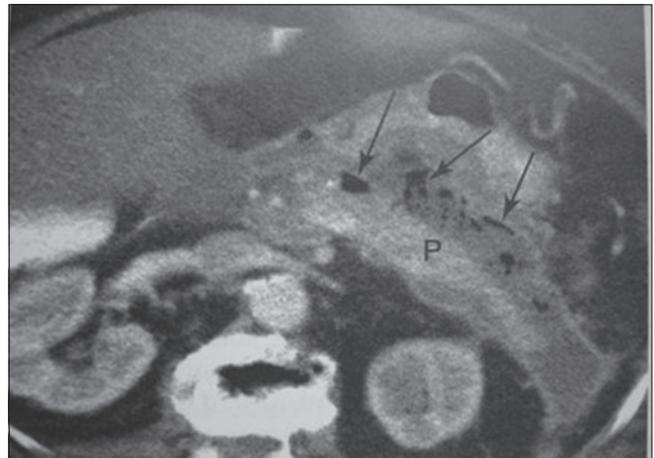


Figure 13: Grade “E” (emphysematous) pancreatitis

Limitations of the Study

Since ours was a tertiary care hospital, most of the cases had some data suggestive of pancreatitis before admission. So, all the cases, which are part of our study, had pancreatitis of various severities. In primary and secondary care centers, the clinically suspected cases of acute pancreatitis may turn out to some other diagnosis.

Our sample size was 30, which is relatively small in number.

Because we received most of our cases after a latent period of 24 h after the onset of symptoms, in our study, the CT scan was performed about 48-72 h after the onset of symptoms. If imaging was performed before 24 h of onset of symptoms, the changes of acute pancreatitis might not have developed.⁴⁵

CONCLUSION

This descriptive study of patients with clinically suspected acute pancreatitis using CT depicted full spectrum of appearances. In all the cases, CT scan revealed the exact morphological appearance of the disease. It also helped in diagnosing other associated findings such as fatty liver, gall bladder calculus, common bile duct calculus, pancreatic duct calculus, ascites, pleural effusion, portal vein thrombosis, and pancreatic duct dilatation. CT scan of the abdomen also revealed most of the local complications such as peripancreatic fat stranding, phlegmonous changes pancreatic pseudocyst, and pseudoaneurysm of the splenic artery. Furthermore, CT scan helped to rule out any other associated disease or complication suspected. CECT was very useful in staging acute pancreatitis using

various CT numerical grading systems. All the patients in our study were categorized into various stages based on Balthazar criteria and CTSI. The CT scan classification of the patients with acute pancreatitis into various grades helped in accurate prediction of prognosis in these patients.

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How to cite this article: Vinayaka US, Ravichandra G, Acharya KD, Muralidhara KN. Contrast-enhanced Computed Tomographic Evaluation of Acute Pancreatitis: An Exploratory Study. *Int J Sci Stud* 2016;3(11):139-146.

Source of Support: Nil, **Conflict of Interest:** None declared.

Evaluation of Dexmedetomidine-0.5 µg/kg and 1 µg/kg in Blunting the Responses to Laryngoscopy and Intubation

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ABSTRACT

Background: There is an on-going search for an ideal agent to blunt hemodynamic responses pertaining to tracheal intubation.

Objective: To compare the hemodynamic effects of intravenous (IV) dexmedetomidine in a dose of 0.5 µg/kg and 1 µg/kg body weight as premedicant.

Materials and Methods: 90 patients scheduled for various elective surgical procedures under general anesthesia belonging to ASA Class I and II and Mallampatti Grades I and II in the age group of 18 years to 60 years were included in the study. Patients with uncontrolled systemic disorders, difficult airways, and obesity were excluded from the study. The study population was randomly divided into three groups: (1) Group A: 30 Patients, receiving 10 ml of 0.9% saline IV, 10 min before induction. (2) Group B: 30 Patients, receiving 0.5 µg/kg dexmedetomidine IV, 10 min prior to induction (made to 10 ml with normal saline) (3) Group C: 30 Patients receiving 1 µg/kg dexmedetomidine IV 10 min prior to induction (made to 10 ml with normal saline). Patients of all the above-mentioned groups were premedicated with injection ondansetron 0.08 mg/kg IV and injection fentanyl 1.5 µg/kg IV prior to starting of infusion of the study drug.

Result: In our study, both the doses of IV dexmedetomidine blunted hemodynamic responses, however, IV dose of 1 µg/kg body weight was found more optimal with minimal incidence of side effects.

Conclusion: We conclude that dexmedetomidine in a loading dose of 1 µg/kg body weight significantly attenuates response to laryngoscopy and intubation with minimal incidence of side effects as compared with dexmedetomidine in a dose of 0.5 µg/kg which was found insufficient in majority of cases to cause complete attenuation of sympathetic response.

Key words: Intubation Blunting, IV Dexmedetomidine, General anaesthesia & Dexmedetomidine

INTRODUCTION

Laryngoscopy and tracheal intubation are invariably accompanied by an increase in arterial blood pressure and heart rate (HR). The peak rise in blood pressure and HR is usually transient, occurring 30 s after intubation and lasting for <10 min.¹

The magnitude of hemodynamic changes observed may be dependent on various factors such as depth of anesthesia, whether any measures are taken prior to airway manipulation, the anesthetic agent used, the duration of laryngoscopy and intubation. Until date, the exact mechanism of hemodynamic responses to laryngoscopy and intubation has not been clarified. The principle mechanism in hypertension and tachycardia is the sympathetic response^{2,3} which may be the result of increase in catecholamine activity.⁴

The increase in the pulse rate and blood pressure are usually transitory, variable, and unpredictable. Transitory hypertension and tachycardia are probably

Access this article online



www.ijss-sn.com

Month of Submission : 11-2015
Month of Peer Review : 12-2015
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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of no consequence in healthy individuals but either or both may be hazardous to those with hypertension, myocardial insufficiency or cerebrovascular diseases.⁴ This laryngoscopic response in such individuals may predispose them to development of pulmonary edema, myocardial insufficiency, and cerebrovascular accident.^{5,6}

Intravenous (IV) anesthetic induction agents do not adequately or predictably suppress the circulatory responses caused by endotracheal intubation.⁷ Hence, before initiating laryngoscopy, additional pharmacological measures such as use of volatile anaesthetics,⁸ topical and IV lidocaine,^{9,10} opioids,¹¹ vasodilators - sodium nitroprusside,¹² nitroglycerine,¹³ calcium channel blockers,¹⁴ and β -blockers¹⁵ have been tried by various authors.

None of the drugs mentioned above have been found to be completely effective in attenuating the sympathetic response to intubation.

α -2 agonists have been used for attenuating the sympathetic response¹⁶ and both clonidine and dexmedetomidine appear to fulfill all the above criteria. Both Clonidine and dexmedetomidine have actions on both α -1 and α -2 receptors, but dexmedetomidine is highly specific and selective α -2 adrenoceptor agonist with α 2: α 1 binding selectivity ratio of 1620:1 compared to 220:1 for clonidine.¹⁷

Various studies have also found that dexmedetomidine can decrease the hemodynamic response to laryngoscopy and intubation.^{18,19}

The advantages of IV dexmedetomidine as premedicant in anesthesia setting include anxiolysis, analgesia, sedation, improved hemodynamic stability, and no/minimal respiratory depression. These beneficial properties also result in decreased minimum alveolar concentration (MAC) of volatile anesthetics which decreases significantly up to 90% and hence decreases the requirement of anesthetics.²⁰

The present study, however, was aimed at attenuation of the hemodynamic response to laryngoscopy and intubation in adult patients posted for various surgeries under general anesthesia, with single IV bolus dose of 0.5 mcg/kg and 1 mcg/kg given over 10 min before induction.

Pharmacology

Dexmedetomidine

Dexmedetomidine is the S-enantiomer (dextroisomer) of medetomidine, a widely used anesthetic in veterinarian practice. Dexmedetomidine was first approved for use in 1999 by the FDA as a short term (<24 h) sedative and analgesic for use in the ICU in patients being mechanically ventilated.²¹

IV/Intramuscular dexmedetomidine causes anxiolysis, sedation, analgesia, and sympatholysis produced with minimal respiratory depression. It is used in ICU setting, as a premedication, as a sole anesthetic agent, in regional anesthesia, and in MAC.

Dose: Dexmedetomidine is initiated as 0.5-1 μ g/kg IV over 10 min followed by a maintenance infusion of 0.2-0.7 μ g/kg/h for a period not <24 h.

MATERIALS AND METHODS

A total of 90 patients scheduled for various elective surgical procedures under general anesthesia belonging to ASA Class I and II and Mallampatti Grades I and II in the age group of 18 years to 60 years were included in the study.

The detailed preanesthetic checkup was done on all patients, and relevant hematological, biochemical, and radiological investigations were carried out for all patients as per surgical requirements.

The study population was randomly divided into three groups:

Group A: 30 Patients, receiving 10 ml of 0.9% saline IV, 10 min before induction.

Group B: 30 Patients, receiving 0.5 μ g/kg dexmedetomidine IV, 10 min before induction (made to 10 ml with normal saline).

Group C: 30 Patients receiving 1 μ g/kg dexmedetomidine IV 10 min before induction (Made to 10 ml with normal saline).

Anesthetic Procedure

Patients of all the above-mentioned groups were premedicated with injection Ondansetron 0.08 mg/kg IV and injection fentanyl 1.5 μ g/kg IV prior to starting of infusion of the study drug.

Anesthesia was induced after the administration of the study drug using injection Propofol 2 mg/kg IV and injection Vecuronium 0.08 mg/kg IV. This was followed by 3 min of ventilation. Laryngoscopy and endotracheal intubation were done. After intubation, the patient was maintained on O₂:N₂O (1:1) and isoflurane (isoflurane was started 10 min post-intubation). The concentration of isoflurane was adjusted to maintain systolic blood pressure (SBP) within 20% of the preoperative values. Further neuromuscular block was maintained by injection Vecuronium 0.02 mg/kg body weight.

The SBP, diastolic blood pressure (DBP), mean arterial blood pressure (MAP), and HR were recorded. All these parameters were recorded as a baseline value,

T = 0 min, 5 min after starting dexmedetomidine infusion, preintubation (T = 10 min), immediately post-intubation, post-intubation 1, 3, 5 min, and at 10 min.

Adverse Effects

1. Hypotension was defined as SBP <90 mmHg or a DBP of <60 mmHg or MAP of <50 mmHg on any reading.
2. Bradycardia was defined as HR <50 b/min.
3. Arrhythmia was defined as supraventricular or a ventricular beats >3/min or a rhythm other than sinus.

Exclusion Criteria

- Patient refusal
- Patients with ASA Class III and above
- Patients on preoperative beta blockers
- Age <18 years and >60 years
- Pregnant or nursing women
- Any history of drug reactions
- Patients with anticipated difficult intubation
- Patient having hypovolemia, hypotension, and bradycardia
- Duration of laryngoscopy and endotracheal intubation >30 s
- Patients with systemic diseases, obesity.

DISCUSSION

Baseline Comparison of Groups

Demographic parameters

The study included patients in the age group ranging from age 18 to 60 years for all 3 groups. The mean values of the age were 38.33 ± 11.67 , 38.30 ± 9.45 , and 34.13 ± 11.42 years for Groups A, B, and C, respectively (Table 1). There was no statistical significance difference between the 3 groups with respect to age ($P = 0.234$).

Distribution of sex was also comparable (Table 2). In our study, Group A, 63.3% were males and 36.7% were females. In Group B, 46.7% were males and 53.3% were females. In Group C, 46.7% were males and 53.3% were females. No statistically significant difference was observed in sex distribution of the cases between the 3 groups ($P = 0.328$).

The mean weights of patients were 64.63 ± 10.42 kg, 61.87 ± 10.21 kg, 59.20 ± 10.17 kg in Group A, Group B, and Group C, respectively (Table 3). No statistically significant difference was observed in weight distribution of the cases between the 3 groups ($P = 0.128$).

Hemodynamic parameters

SBP

In Group A control, the mean baseline SBP was 124.13 ± 12.66 , which decreased by 3.1 mmHg after

completion of administration of study drug. Post-intubation, there was a rise in the mean SBP values from the pre-laryngoscopic values (T-10) by 29.64 mmHg immediately after intubation, 22.14 mmHg at 1 min, 15.3 mmHg at 3 min, 6.54 mmHg at 5 min, and 2.37 mmHg at 10 min (Table 4).

In Group B, the mean baseline SBP was 126.03 ± 11.62 which decreased by 6.66 mmHg after completion of administration of study drug. Post-intubation there was a rise in the mean SBP values from the Pre-laryngoscopic values (T-10) by 17 mmHg immediately after intubation, 12 mmHg at 1 min, 6.76 mmHg at 3 min, 1.3 mmHg at 5 min and decreased by 0.2 mmHg at 10 min as compared with pre-laryngoscopic values (Table 4).

In Group C, the mean baseline SBP was 126.67 ± 9.01 which decreased by 15.94 mmHg after completion of administration of the study drug. Post-intubation there was a rise in the mean SBP values from the pre-laryngoscopic values (T-10) by 7.87 mmHg immediately after intubation, 7.14 mmHg at 1 min, 1.90 mmHg at 3 min, and decreased by 0.3 mmHg at 5 min and 1.6 mmHg at 10 min as compared with pre-laryngoscopic values. However, at no point of time during the post-intubation period did the mean SBP rise above the Baseline mean SBP value of the study population in this group (Figure 1).

Group C demonstrated a better suppression of the pressor response to intubation compared with other two groups.

DBP

In Group A control, the mean baseline DBP was 78.00 ± 8.60 , which decreased by 0.4 mmHg after completion of administration of study drug. Post-intubation there was a rise in the mean SBP values from the Pre-laryngoscopic values (T-10) by 18.23 mmHg immediately after intubation, 13.77 mmHg at 1 min, 6.87 mmHg at 3 min, 1.73 mmHg at 5 min, and decreased by 0.17 mmHg at 10 min as compared with pre-laryngoscopic values (Table 5).

In Group B, the mean baseline DBP was 76.97 ± 8.28 which decreased by 1.2 mmHg after completion of administration of study drug. Post-intubation there was a rise in the mean DBP values from the pre-laryngoscopic values (T-10) by 11.96 mmHg immediately after intubation, 8.43 mmHg at 1 min, 1.66 mmHg at 3 min, and decreased by 0.24 mmHg at 5 min and decreased by 1.54 mmHg at 10 min as compared with pre-laryngoscopic values (Table 5).

In Group C, the mean baseline DBP was 78.87 ± 6.66 which decreased by 9.74 mmHg after completion of administration of the study drug. Post-intubation there was a rise in the mean SBP values from the pre-laryngoscopic values (T-10) by 6.04 mmHg immediately after intubation,

4.0 mmHg at 1 min, 0.4 mmHg at 3 min, and decreased by 0.7 mmHg at 5 min and 2.13 mmHg at 10 min as compared with pre-laryngoscopic values (Table 5). However, at no point in time during the post-intubation period did the mean DBP rise above the baseline mean DBP value of the study population in this group (Figure 2).

Group C demonstrated a better suppression of the pressor response to intubation compared to other two groups.

MAP

In Group A control, the mean baseline MAP was 93.30 ± 8.76 , which decreased by 1.0 mmHg after completion of administration of study drug. Post-intubation there was

a rise in the mean MAP values from the pre-laryngoscopic values (T-10) by 21.87 mmHg immediately after intubation, 16.3 mmHg at 1 min, 9.43 mmHg at 3 min, 3.23 mmHg at 5 min, and by 0.5 mmHg at 10 min (Table 6). In Group B, the mean baseline MAP was 92.97 ± 8.15 which decreased by 2.65 mmHg after completion of administration of study drug. Post-intubation there was a rise in the mean MAP values from the pre-laryngoscopic values (T-10) by 12.95 mmHg immediately after intubation, 8.71 mmHg at 1 min, 3.31 mmHg at 3 min, 0.25 mmHg at 5 min, and decreased by 1.11 mmHg at 10 min (Table 6).

In Group C, the mean baseline MAP was 94.53 ± 6.66 which decreased by 11.66 mmHg after completion of administration of the study drug. Post-intubation there was a rise in the mean MAP values from the pre-laryngoscopic values (T-10) by 6.83 mmHg immediately after intubation, 5.26 mmHg at 1 min, 1.1 mmHg at 3 min, and decreased by 0.24 mmHg at 5 min and 1.97 mmHg at 10 min as compared with pre-laryngoscopic values (Table 6). However, at no point of time during the post-intubation period did the mean MAP rise above the Baseline mean MAP value of the study population in this group (Figure 3).

Group C demonstrated a better suppression of the pressor response to intubation compared to other two groups.

HR

In Group A control, the mean baseline HR was 79.8 ± 11.06 , which remained the same after completion of administration of study drug. Post-intubation there was a rise in the mean HR values from the pre-laryngoscopic values (T-10) by 28.37 beats/min immediately after intubation, 21.67 beats/min at 1 min, 16.9 beats/min at 3 min, 9.07 beats/min at 5 min, and by 3.54 beats/min at 10 min (Table 7).

In Group B, the mean baseline HR was 80.73 ± 10.65 which decreased by 7.36 beats/min after completion of administration of study drug. Post-intubation there was a rise in the mean HR values from the Pre-laryngoscopic

Table 1: Age distribution of patients studied

Age groups (years)	Frequency (%)			P value
	Group A	Group B	Group C	
18-30	11 (36.7)	7 (23.3)	12 (40.0)	
31-40	8 (26.7)	12 (40.0)	11 (36.7)	
41-50	7 (23.3)	10 (33.3)	5 (16.7)	
51-60	4 (13.3)	1 (3.3)	2 (6.7)	
Total	30 (100)	30 (100)	30 (100)	
Mean±SD	38.33±11.67	38.30±9.45	34.13±11.42	0.234

SD: Standard deviation

Table 2: Gender distribution of patients studied

Sex	Frequency (%)			P value
	Group A	Group B	Group C	
Male	19 (63.3)	14 (46.7)	14 (46.7)	0.328
Female	11 (36.7)	16 (53.3)	16 (53.3)	
Total	30 (100)	30 (100)	30 (100)	

Table 3: Distribution of weight in three groups of patients studied

Weight (in Kgs)	Mean±SD			P value
	Group A	Group B	Group C	
Weight	64.63±10.42	61.87±10.21	59.20±10.17	0.128

SD: Standard deviation

Table 4: Comparison SBP mmHg in three groups of patients studied

SBP	Mean±SD			Group A vs. Group B	Group A vs. Group C	Group B vs. Group C
	Group A	Group B	Group C			
Baseline	124.13±12.66	126.03±11.62	126.67±9.01	0.789	0.657	0.974
T0	128.83±11.07	131.00±10.53	130.87±9.53	0.699	0.730	0.999
T5	124.40±10.18	124.20±12.66	117.30±11.43	0.997	0.048	0.057
T10	121.03±9.58	119.37±15.39	110.73±12.25	0.866	0.006	0.026
TP1	150.67±11.14	136.37±15.49	118.60±10.78	<0.001	<0.001	<0.001
T1	143.17±12.21	131.37±13.73	117.87±11.71	0.001	<0.001	<0.001
T3	136.33±11.24	126.13±12.03	112.63±10.76	0.002	<0.001	<0.001
T5	127.57±12.26	120.67±11.41	110.43±10.04	0.052	0.002	<0.001
T10	123.40±12.88	119.17±11.43	109.13±9.51	0.323	<0.001	0.003

SD: Standard deviation, SBP: Systolic blood pressure

Table 5: Comparison DBP mmHg in three groups of patients studied

DBP	Mean±SD			Group A vs. Group B	Group A vs. Group C	Group B vs. Group C
	Group A	Group B	Group C			
Baseline	78.00±8.60	76.97±8.28	78.87±6.66	0.868	0.905	0.621
T0	80.30±8.53	77.87±8.03	81.43±5.67	0.425	0.829	0.163
T5	77.33±9.60	74.87±9.30	72.73±8.01	0.540	0.123	0.630
T10	77.60±8.99	75.77±11.78	69.13±8.32	0.750	0.003	0.028
TP1	95.83±10.54	87.73±9.77	75.17±8.25	0.004	<0.001	<0.001
T1	91.37±9.52	84.20±9.06	73.13±9.68	0.011	<0.001	<0.001
T3	84.47±7.85	77.43±9.67	69.53±9.17	0.008	<0.001	0.003
T5	79.33±9.42	75.53±9.47	68.43±9.10	0.261	<0.001	0.011
T10	77.43±11.07	74.23±9.80	67.00±8.66	0.426	<0.001	0.016

DBP: Diastolic blood pressure, SD: Standard deviation

Table 6: Comparison MAP mmHg in three groups of patients studied

MAP	Mean±SD			Group A vs. Group B	Group A vs. Group C	Group B vs. Group C
	Group A	Group B	Group C			
Baseline	93.30±8.76	92.97±8.15	94.53±6.66	0.985	0.817	0.722
T0	96.43±8.26	95.30±7.56	97.87±5.31	0.813	0.719	0.351
T5	92.60±9.32	91.00±8.82	87.50±8.27	0.762	0.070	0.278
T10	92.30±8.33	90.32±12.22	82.87±9.05	0.725	0.001	0.014
TP1	114.17±10.20	103.27±10.62	89.70±8.60	<0.001	<0.001	<0.001
T1	108.60±9.56	99.03±9.48	88.13±9.87	0.001	<0.001	<0.001
T3	101.73±8.05	93.63±9.09	83.97±9.19	0.002	<0.001	<0.001
T5	95.53±9.56	90.57±9.19	82.63±8.88	0.099	<0.001	0.004
T10	92.80±10.86	89.21±9.33	80.90±8.25	0.317	<0.001	0.003

MAP: Mean arterial blood pressure, SD: Standard deviation

Table 7: Comparison of HR (bpm) in three groups of patients studied

HR	Mean±SD			Group A vs. Group B	Group A vs. Group C	Group B vs. Group C
	Group A	Group B	Group C			
Baseline	79.80±11.06	80.73±10.65	83.73±12.15	0.945	0.373	0.561
T0	87.00±11.16	83.23±13.52	88.53±13.51	0.491	0.888	0.248
T5	82.73±10.68	77.60±12.50	75.53±10.35	0.185	0.039	0.756
T10	79.83±9.97	73.37±12.23	68.50±9.50	0.054	<0.001	0.185
TP1	108.20±15.21	93.60±10.12	75.10±9.42	<0.001	<0.001	<0.001
T1	101.50±12.95	88.40±10.88	75.17±9.42	<0.001	<0.001	<0.001
T3	96.73±10.52	85.90±11.32	72.93±9.94	<0.001	<0.001	<0.001
T5	88.90±10.38	82.73±11.00	70.97±9.67	0.060	<0.001	<0.001
T10	83.37±10.50	79.77±10.34	69.83±9.78	0.364	<0.001	0.001

HR: Heart rate, SD: Standard deviation

Table 8: Comparison of side effects in three groups of patients studied

Side effect	Frequency (%)			P value
	Group A	Group B	Group C	
None	30 (100)	28 (93.3)	28 (93.3)	0.351
Bradycardia	0 (0.0)	2 (6.7)	2 (6.7)	
Hypotension	0 (0.0)	0 (0.0)	0 (0.0)	
Arrhythmias	0 (0.0)	0 (0.0)	0 (0.0)	
Total	30 (100)	30 (100)	30 (100)	

values (T-10) by 20.23 beats/min immediately after intubation, 15.03 beats/min at 1 min, 12.53 beats/min

at 3 min, 9.36 beats/min at 5 min, and 6.4 beats/min at 10 min (Table 7).

In Group C, the mean baseline HR was 83.73 ± 12.15 which decreased by 15.23 beats/min after administration of the study drug. Post-intubation there was a rise in the mean HR values from the pre-laryngoscopic values (T-10) by 6.6 beats/min immediately after intubation, 6.67 beats/min at 1 min, 4.43 beats/min at 3 min, 2.47 beats/min at 5 min and 1.33 beats/min at 10 min (Table 7). However, at no point of time during the post-intubation period did the mean HR rise above the T0 min mean HR value of the study population in this group (Figure 4).

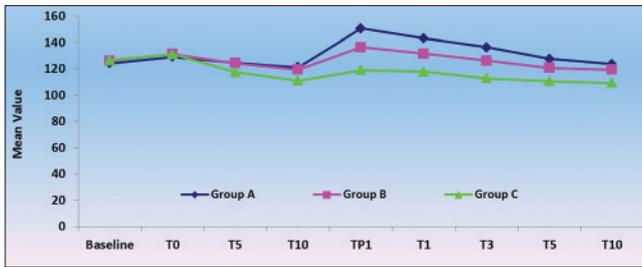


Figure 1: Comparison of mean systolic blood pressure among groups at different time points

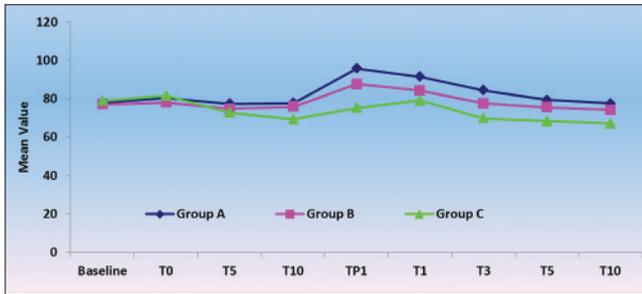


Figure 2: Comparison of mean diastolic blood pressure among groups at different time points

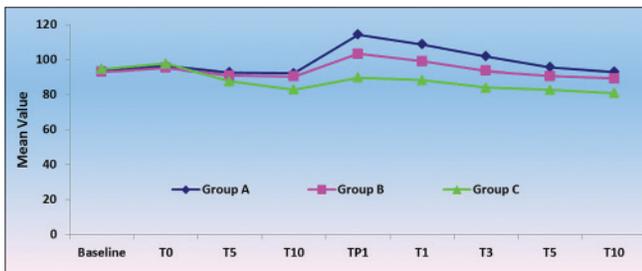


Figure 3: Comparison of mean arterial blood pressure among groups at different time points

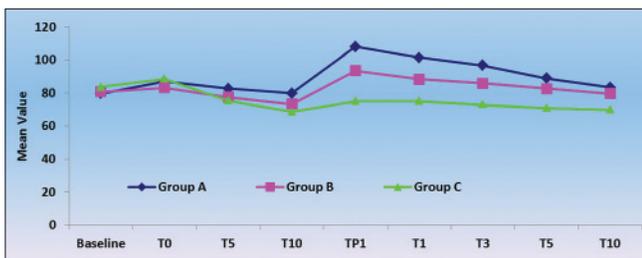


Figure 4: Comparison of mean heart rate among groups at different time points

Group C demonstrated a better suppression of the pressor response to intubation compared to other two groups.

Side effects

Group A, Group B, and Group C were statistically comparable in terms of side effects ($P = 0.351$). There

were 2 cases of bradycardia ($HR < 50/min$) in Group B, and 2 cases of bradycardia ($HR < 50/min$) in Group C, respectively. There were no other cases with hypotension or arrhythmias in terms of side effects (Table 8).

Comparison with Other Studies

In the study by Menda *et al.*,¹⁸ they found that the SBP, DBP, MAP, HR values were below the baseline values in the dexmedetomidine group at all measurement times,¹⁸ which was in accordance with our results.

Esra *et al.*²² observed in their study using dexmedetomidine $1 \mu g/kg$ that the mean SBP, DBP, MAP, and HR values were significantly lower at post-induction and 5 min after intubation compared to baseline values which were similar to the results of our study.

Our study results also concurred with the results of Keniya *et al.*²³ who observed an 8% increase in SBP and 11% for DBP, 7% for HR when compared with pre-laryngoscopic values in dexmedetomidine $1 mcg/kg$ group.

CONCLUSION

- Dexmedetomidine in a dose of $0.5 mcg/kg$:
 - Is insufficient to cause complete blunting of the hemodynamic response to laryngoscopy and intubation for 10 min in majority of cases.
- Dexmedetomidine in a dose of $1 mcg/kg$:
 - Significantly attenuates the hemodynamic response to laryngoscopy and intubation for 10 min.
 - Side effects observed were not statistically significant and comparable with side effects present in Group B.

No arrhythmias were seen during/after administration of study drug.

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How to cite this article: Rachit B, Nanda HS, Mahesh K. Evaluation of Dexmedetomidine-0.5 µg/kg and 1 µg/kg in Blunting the Responses to Laryngoscopy and Intubation. *Int J Sci Stud* 2016;3(11):147-153.

Source of Support: Nil, **Conflict of Interest:** None declared.

Prevalence of Multidrug-Resistant and Extensively Drug-Resistant *Proteus*, *Providencia* and *Morganella* Species in Burn Wound Infection

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Abstract

Background: The major challenge for a burn team is a nosocomial infection in burn patients, which is known to cause over 50% of deaths. The phenomenal evolution and increase of multidrug-resistance (MDR) of many bacterial pathogens is increasing and representing a growing public health problem in the world.

Subjects and Methods: A retrospective study was conducted among the patients admitted to the burn ward of our hospital, between January and December 2012. All the patients irrespective of age, sex, duration of hospital stay, percentage and degree of burn were included in our study. Wound swabs from 1294 patients hospitalized in burn ward were studied. The various isolates were analyzed for their antimicrobial susceptibility profile. Tribe *Proteaeae* was further classified into MDR, extensively drug-resistant (XDR), and pandrug-resistant (PDR) on the basis of standardized international criteria.

Results: Out of 883 isolates from 1294 patients, 71 were found to be *Proteus* species (8%), 15 *Providencia* species (1.7%), while only 1 *Morganella* species (0.1%) was isolated during the study period. Among the *Proteus* spp., 55% (39/71) were found to be MDR while 39.4% (28/71) were XDR. MDR and XDR *Providencia* were found to be 53.3% (8/15) and 46.6% (7/15), respectively. While the only *Morganella* spp. isolated was found to be MDR. None of the isolates were found to be PDR.

Conclusions: Although survival rates for burn patients have improved substantially in the past few decades, nosocomial infections still remain a major challenge in burn care. Resistance to antimicrobials is an increasingly common problem, and its management is a subject of concern. The present study highlights the alarming levels of antimicrobial resistance among members of tribe *Proteaeae*.

Key words: Burn wound infection, Extensively drug-resistant, Multidrug-resistant, Pandrug-resistant

INTRODUCTION

Despite significant advances in burn care, infection remains a major cause of morbidity and mortality in burn patients.¹ From time to time and from place to place, the invading microorganisms vary in their frequency and susceptibility to antibiotics. Therefore, it is desirable to conduct a periodic study to assess the infective agents

of burn wounds so that preventive measures could be modified accordingly.

The genus *Proteus* along with genus *Providencia* and *Morganella* belongs to the tribe *Proteaeae* of the family Enterobacteriaceae. Although the tribe concept was ruled out in the recent Centers for Disease Control and Prevention (CDC) classification, the terminology continues to be used until date. The phenomenal evolution and increase of multidrug-resistance (MDR) of many bacterial pathogens, including tribe *Proteaeae* is increasing and causing a growing public health problem in the world. Thus, a group of international experts came together through a joint initiative by the European Centre for Disease Prevention and Control and the CDC, to create a standardized international terminology to describe resistance profiles in bacteria often responsible

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Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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for healthcare-associated infections and prone to MDR.² They classified the organisms into MDR, extensively drug-resistant (XDR), and pandrug-resistant (PDR) on the basis of its antimicrobial susceptibility profiles.²

This study seeks to determine the prevalence of tribe *Proteaceae* in burn wound infections and their antibiotic resistance pattern.

MATERIALS AND METHODS

A retrospective study was carried out in the Department of Microbiology of a Tertiary Care Hospital in New Delhi, India. Wound swabs from 1294 patients hospitalized in the burn ward that came to our Microbiology Laboratory between January and December 2012 were analyzed. Various isolates and their antimicrobial susceptibility profile were studied. Antimicrobial resistance pattern of Tribe *Proteaceae* was further divided into MDR, XDR, and TDR. In our Microbiology laboratory, wound swabs are inoculated on blood agar (Nutrient agar [HIMEDIA Catalogue Number-M001] plus 10% sterile sheep blood), MacConkey agar (HIMEDIA Catalogue Number-M081B), and brain heart infusion broth (HIMEDIA Catalogue Number-M1037). Plates and the broth are incubated at 37°C for 24 and 48 h, respectively. All bacterial isolates examined for colony characteristics, Gram-staining, motility and biochemical tests. Tribe *Proteaceae* is identified on the basis of phenylpyruvic acid production, detected in the Phenylalanine deaminase test. Colonies which are non-lactose fermenting on MacConkey agar and show swarming on blood agar are isolated and identified by biochemical tests based on whether they are positive for phenylalanine deaminase production; H₂S gas production; and urease reactions. *Proteus vulgaris* produces indole which differentiated it from indole negative *Proteus mirabilis* and *Proteus penneri*. Similarly, identification of *Providencia* and *Morganella* spp. is done on the basis of biochemical tests. Antimicrobial susceptibility testing is done by modified Stokes disc diffusion method. A suspension of 0.5 McFarland standard prepared from colonies of the isolated organism and was inoculated along with control strains on Mueller-Hinton agar (MHA) plates (HIMEDIA Catalogue Number- M1084) with sterile cotton swabs. Antimicrobial discs applied on MHA and kept for overnight incubation. All Gram-negative bacilli tested for susceptibility to cephalexin (30 µg), ceftriaxone (30 µg) cefotaxime (30 µg), gentamicin (10 µg), amikacin (30 µg), ciprofloxacin (5 µg), amoxicillin-clavulanic acid (20/10 µg), imipenem (10 µg), meropenem (10 µg), piperacillin-tazobactam (100/10 µg), netilmicin (30 µg), polymyxin-B (300 units), colistin (10 µg) (HIMEDIA Laboratories Pvt. Ltd., Mumbai, India). *Escherichia coli* standard strain (NCTC 10418) used as a control.

The isolate was considered as MDR when non-susceptible to at least 1 agent in more than 3 antimicrobial categories/groups and XDR if bacterial isolate remains susceptible to only one or two antimicrobial categories. Isolate non-susceptible to all agents in all antimicrobial categories was considered as PDR.²

RESULTS

A total of 1294 pus swab specimens, from patients admitted to the burn ward, were received in our Microbiology laboratory between January and December 2012. The age range of the admitted patients was between 8 months and 55 years, and male to female ratio was 2:1. Out of 883 isolates obtained, 71 were found to be *Proteus* species (8%), 15 *Providencia* species (1.7%) while 1 was *Morganella* species (0.1%). Other isolates included *Pseudomonas* spp., *Klebsiella* spp., *Staphylococcus aureus* (56.7% methicillin-resistant *S. aureus* and 43.3% methicillin-susceptible *S. aureus*), *E. coli*, *Acinetobacter* spp., and *Citrobacter* spp. (Figure 1). The antimicrobial resistance profile of *Proteus*,

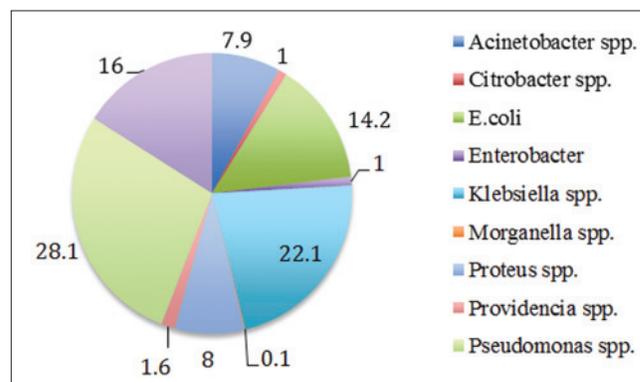


Figure 1: Percentage of different bacterial isolates from burn patients

Table 1: Percentage resistance of *Proteus*, *Providencia*, and *Morganella* isolates from burn patients

Antimicrobial (%)	Percentage of resistant isolates (%)		
	<i>Proteus</i>	<i>Providencia</i>	<i>Morganella</i>
Cephalexin	87.3	93	100
Ceftriaxone	45	80	0
Cefotaxime	71.8	80	100
Amoxicillin-clavulanic acid	94.3	100	0
Ciprofloxacin	86	86.7	0
Gentamycin	88.7	93	0
Amikacin	84.5	86.7	0
Imipenem	4.2	6.7	100
Meropenem	5.6	4.2	0
Piperacillin-tazobactam	9.8	4.2	0
Netilmicin	59	80	100
Polymyxin-B	59	26.7	100
Colistin	59	26.7	100

Providencia, and *Morganella* spp. is given in Table 1. Among the *Proteus* spp., 55% (39/71) were found to be MDR while 39.4% (28/71) were XDR. MDR and XDR *Providencia* were found to be 53.3% (8/15) and 46.6% (7/15), respectively. The *Morganella* isolate was found to be resistant to more than 3 classes of antimicrobial agents and thus classified as MDR.

DISCUSSION

A total of 1294 pus swab specimens, from patients admitted to the burn ward, were received in our Microbiology laboratory during a period of 1-year. Thus, compared to other studies, we employed a fairly large sample size, which is beneficial for accurate interpretation of results.^{3,4} In our study, the patient age ranged from 8 months to 55 years and male to female ratio was 2:1. This is similar to another Indian study conducted among burn patients.³ Similar results were also obtained in another study which reported male to female ratio of 1.45:1.⁵

Although survival rates for burn patients have improved substantially in the past few decades due to advances in modern medical care in specialized burn centers, still, nosocomial infections represent a major challenge for a burn team in burn patients, which are known to cause over 50% of burn deaths.⁶⁻⁸ In our study, the most frequent isolates was found to be *Pseudomonas* spp. followed by *Klebsiella* spp. this is similar to several other studies among burn patients.^{4,9-11} In our study, the prevalence of *Proteus* spp. was found to be 8% which was in contrast to 2.3% found in another study conducted in Chandigarh.¹² The variations may be due to differences in local conditions, prevention protocols, topical and systemic treatment of burn wounds as well as study lengths.¹³

In our study, we found very high-level of resistance, where 55% *Proteus* spp. were found to be MDR and 39.4% XDR while 53.3% and 46.6% of *Providencia* spp. were found MDR and XDR, respectively. The only *Morganella* spp. isolated was also identified to be MDR. However, none of the isolates were found to be PDR and most of the isolates were susceptible to piperacillin-tazobactam, imipenem, and meropenem which are the only options left for the treatment of these infections. Similar high-level resistance has been reported in other studies as well.¹⁴ This high-level resistance could be due to continuous usage of broad-spectrum antimicrobials and nonadherence to hospital antibiotic policy. This could also be explained by the fact

that our institution being a tertiary care referral institute, thus most patients would have been already harboring the resistant organisms.

CONCLUSION

Burns provide a suitable site for bacterial multiplication and infection, mainly because of the larger area involved and longer duration of patient stay in the hospital. To ensure early and appropriate therapy in burn patients, a frequent evaluation of the wound is necessary; all burn institutions should follow a strict antibiotic policy. Therefore, a continuous surveillance of microorganisms and a regular update of their antibiotic resistance pattern are essential to maintaining good infection control programs in the burn unit.

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How to cite this article: Perween N, Krishanprakash S, Bharara T. Prevalence of Multidrug-Resistant and Extensively Drug-Resistant *Proteus*, *Providencia*, and *Morganella* Species in Burn Wound Infection. *Int J Sci Stud* 2016;3(11):154-156.

Source of Support: Nil. **Conflict of Interest:** None declared.

Comparative Study between General Anesthesia and Combined General Anesthesia with Spinal Anesthesia in Laparoscopic Cholecystectomy

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Abstract

Background: The goal of anesthetic management in patients undergoing laparoscopic surgical procedures include management of pneumoperitoneum. Regional anesthesia such as epidural and spinal can be used with general anesthesia (GA) for laparoscopic surgery with standard pressure pneumoperitoneum.

Materials and Methods: A total of 60 patients of American Society of Anaesthesiologist physical Grades I or II undergoing laparoscopic cholecystectomy surgeries with standard pressure pneumoperitoneum (intraabdominal pressure = 12-15 mmHg) were randomly divided into 2 groups with 30 patients in each group. Group A underwent the procedure under GA as per preset protocol. Group B underwent the procedure under combined spinal anesthesia (SA) followed by GA. In both the groups, systolic and diastolic blood pressure, heart rate, bradycardia, hypotension, oxygen saturation (SPO₂), and electrocardiography with ST segment analysis were recorded. Patients were enquired about nausea and vomiting, headache, sore throat, transient neurological symptoms, and pain in post-operative area. Carbon dioxide insufflation pressure was 12-15 mmHg.

Results: Group B, receiving combined spinal with GA, was more hemodynamically stable as compared to the Group A. All three hemodynamic parameters pulse rate, systolic blood pressure, diastolic blood pressure were elevated throughout the procedure in the GA group. Bradycardia was seen in 2 and hypotension in 5 cases in the Group B group. The surgeons did not find any significant difference in the operating conditions or muscle relaxation between the two groups. Patients in both the groups maintained adequate SPO₂. Post-operative nausea and vomiting was seen in 30% cases in the GA group and in 6.7% in Group B. Post-operative analgesia was better in the Group B for duration of 6-h, after which there was not much difference in both the groups.

Conclusion: GA if combined with SA is a feasible, safe and effective alternative to GA alone, providing stable hemodynamics, less neuroendocrine stress response, good surgical conditions, pain-free post-operative period, and minimal post-operative sequel.

Key words: Combined spinal anesthesia with general anesthesia, General anesthesia, Laparoscopic cholecystectomy

INTRODUCTION

From the advent of the surgical era of medicine, there has been a constant search for better surgical modalities, techniques, and tools. The 20th century found the dawn of a new surgical modality, which gained rapid acceptance

from both the surgical fraternity and the patients. Minimally invasive surgery has virtually revolutionized the surgical therapy for a large variety of diseases, the most common used are endoscopic surgeries such as laparoscopic surgery. The first laparoscopic cholecystectomy, which might be regarded as the birth of minimally invasive surgery, was performed by Philippe Mouret in Lyons in March 1987.¹ The number of minimally invasive surgeries has increased exponentially worldwide over the past few decades as it provides less post-operative pain, decreased hospital stay, decreased cosmetic disfigurement and a quicker resumption of normal activities.² However, new surgical procedures translate to new anesthetic challenges demanding changes

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Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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in anesthesia techniques. Although it has many benefits than conventional surgeries, it still causes stress hormone responses (cortisol, epinephrine, and norepinephrine) to some extent, especially when carbon dioxide (CO₂) pneumoperitoneum is concomitantly used in laparoscopic surgery. Increased peripheral vascular resistance, elevated serum catecholamine level, and decreased cardiac output (CO) in laparoscopic procedures might entail hemodynamic fluctuation which, in turn, compromises tissue perfusion. In addition, ventilatory impairment and diaphragmatic dysfunction also occur after laparoscopic surgery. Hence, laparoscopy is only anatomically minimally invasive but physiologically it is otherwise. These insults if befall risky patients might sometimes court disaster, especially those with cardiopulmonary disease.

Increasing perioperative efficiency has become increasingly important in the modern day practice of anesthesiology. The role of the anesthesiologist has evolved from that of a physician primarily concerned with providing optimal surgical conditions and minimizing pain immediately after the operation, to that of a perioperative physician responsible for ensuring that patients with coexisting medical conditions are optimally managed before, during and after surgery.^{3,4} The evaluation of clinically meaningful outcomes (e.g, quality of recovery, resumption of normal activities of daily living) has increasingly become a focal point of anesthesia-related clinical research involving new drugs and techniques.⁵

Even though there are several advantage of laparoscopic procedures, the adverse effects during the procedure are related to the cardiopulmonary effects of pneumoperitoneum, systemic CO₂ absorption, venous gas embolism. Although the changes in CO and preload are still matters of debate, many studies have found a marked increase in systemic vascular resistance.^{6,7} These alterations in hemodynamic parameters need vigilant monitoring intra-operatively.

General anesthesia (GA) as the only suitable technique for laparoscopic procedures is a concept of the past. There is growing evidence suggesting that regional anesthesia has an important role to play in the care of patients undergoing laparoscopic procedures. Regional anesthesia such as epidural and spinal is can be used with GA for laparoscopic surgery with standard pressure pneumoperitoneum (intraabdominal pressure 12-15 mmHg). Key benefits of regional anesthesia if combined with GA include, decreased peritoneal stretch pain, decreased need for sedatives and narcotics and analgesics, better muscle relaxation and decreased surgical stress response and better hemodynamics, with post-operatives analgesia, improved bowel motility, and fast recovery.

Our study is designed to evaluate the feasibility of spinal anesthesia (SA) combined with GA in laparoscopic cholecystectomy and to compare the intra-operative surgical conditions, hemodynamic changes with GA and post-operative requirement of rescue analgesic and incidence of post-operative nausea and vomiting (PONV).

MATERIALS AND METHODS

The present study was carried out from June 2014 to May 2015, after taking the permission and approval from the departmental Ethical Committee and the written informed consent from the patients. It was a prospective, randomized, comparative clinical study. 60 American Society of Anaesthesiologist Physical status Grades I or II patients between 20 and 60 years, of either sex were posted for surgeries. A detailed pre-anesthetic evaluation was done to evaluate their basal heart rate (HR), blood pressure (BP). Patients were kept nil orally for 6-8 h prior to surgery and were randomly assigned to one of the two groups, either GA-Group A or combined SA with GA - Group B. On arrival in the operation theater, monitors were attached and baseline parameters such as HR, systemic arterial pressure, electrocardiograph (ECG), and peripheral oxygen saturation (SPO₂) were noted down. An appropriate sized intravenous cannula was placed *in situ*. Both the groups were preloaded with 10 ml/kg of ringer lactate.

In Group A patients, all patients underwent similar general anesthetic procedure. Patients were premedicated with ondansetron 4 mg, midazolam 0.05 mg/kg intravenously. Patients were induced with fentanyl 2 mcg/kg, thiopentone sodium 5 mg/kg, vecuronium bromide 0.1 mg/kg. Anesthesia was maintained with 40% oxygen in nitrous oxide and vecuronium bromide 0.05 mg/kg which was repeated every 20 min thereafter. Tidal volume and the ventilatory frequency was adjusted and intermittent positive pressure ventilation done to maintain end-tidal CO₂ between 32 and 36 mmHg. Pneumoperitoneum was created by insufflation of CO₂ and maintained at 12-15 mmHg. At the end of surgery, residual neuromuscular block was reversed by an appropriate dose of neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg intravenously and after extubation patients transferred to the recovery room.

In Group B patients, same protocols followed except after premedication patient was put to left lateral position and under strict aseptic precaution lumbar puncture was performed using 27-gauge disposable Quincke type of spinal needle at L3-L4 spinal intervertebral space by midline approach. After the free flow of cerebrospinal fluid, 3 cc of heavy bupivacaine hydrochloride was injected intrathecally,

the time and vital parameters noted after subarachnoid block (SAB). After the level of sensory blockade up to T4 was achieved, the patient was given GA as in Group A, vitals noted as preset proforma. During intra-operative period any hypotension, bradycardia were monitored during the surgical procedure. In both the groups, systemic blood pressure including the systolic blood pressure (SBP) and diastolic blood pressure (DBP), HR, SPO₂ and ECG with ST segment analysis were recorded at the following points of time: Prior to induction or pre-operative, at 1, 2, 3, 4, 5 min after intubation in Group A and after intubation of SA with GA in Group B, immediately after pneumoperitoneum and every 15 min thereafter. The intra-operative conditions and muscle relaxation was assessed by asking the surgeon to grade them as bad/good/excellent. In the post-anesthesia care unit, all the patients were monitored for any evidence of complications or adverse events. Patients were enquired about nausea and vomiting, headache, sore throat, transient neurological symptoms. Pain was analyzed using visual analog scale (VAS) and assessed at 1, 3, 6, 9, and 12 h. Intensity of pain was assessed by using 10-point VAS representing varying intensity of pain from 0 (no pain) to 10 (worst pain). Rescue analgesic diclofenac sodium 75 mg intramuscular was given when VAS was 6 or more. If any patient experienced nausea and/or vomiting, rescue antiemetic metaclopramide (0.1 mg/kg) intravenously was given. The results obtained in the study were presented in a tabulated manner.

RESULTS

The results obtained in the study were presented in the tabulated manner. A statistical analysis was done by sample “*P*” test. ANOVA and Chi-square test were performed for nonparametric values and corresponding *P* values was computed using SPSS for windows (statistical presenting system software version 17). *P* < 0.05 was considered statistically significant. 60 patients undergoing elective laparoscopic cholecystectomy over 1 year were randomly divided into two groups. Group A (*n* = 30) who underwent the procedure under GA and Group B (*n* = 30) who underwent the procedure under combined spinal with GA.

Age profiles were compared between the two groups of patients using Chi-square test, and no significant difference was found (Table 1).

Sex profiles were compared between the two groups of patients using Chi-square test, and no significant difference was found (Table 2).

Using 2 independent sample *t*-test *P* > 0.05, therefore, there was no significant difference between the two groups with respect to weight (kg) (Table 3).

Intra-operative comparison of mean pulse rate (PR) in Group A and Group B. Group B shows less tachycardia. The values at fixed intervals in both the Groups as shown in the observation table were observed. These values were compared using 2 independent sample *t*-tests. We found that there was a significant difference in PR values at post anesthesia intervals mentioned. Values were relatively lower in Group B and the difference was found to be statistically significant (*P* < 0.05) (Table 4).

Recorded the values at fixed intervals in both the Groups as shown in the observation table. These values were

Table 1: Age distribution

Age group (years)	n (%)	
	Group A	Group B
<30	15 (50)	16 (53.3)
31-45	13 (43.3)	12 (40)
45 and above	2 (6.7)	2 (6.7)
Total	30 (100)	30 (100)

$\chi^2=0.09, P=0.96$ (NS), NS: Not significant

Table 2: Sex distribution

Gender	n (%)	
	Group A	Group B
Male	10 (33)	11 (36.6)
Female	20 (67)	19 (63.7)
Total	30 (100)	30 (100)

$\chi^2=0.0733, P=0.78$ (NS), NS: Not significant

Table 3: Weight distribution

Group	Weight (kg) Mean±SD
Group A	58.56±5.16
Group B	57.72±5.25

t=0.57, *P*=0.58 (NS), NS: Not significant, SD: Standard deviation

Table 4: Changes in PR in two groups

Time interval (min)	Mean±SD		<i>t</i> value	<i>P</i> value	Significance
	Group A (PR)	Group B (PR)			
Pre-operative (PI)	80.5±9.2	74.6±8.5	2.37	0.02	S
1	105.7±10.5	77.8±10.4	9.42	0.00	S
2	103.5±10.1	76.0±7.1	11.16	0.00	S
3	104.1±9.9	73.5±7.0	12.62	0.00	S
4	103.4±9.0	72.2±6.9	13.79	0.00	S
5	101.4±9.5	74.4±8.0	10.88	0.00	S
At pneumo (PP)	114.7±11.4	81.4±5.9	13.01	0.00	S
15	112.4±8.3	75.0±10.3	14.14	0.00	S
30	105.9±10.3	71.4±10.2	11.91	0.00	S
45	105.0±11.6	71.7±6.2	10.34	0.00	S
60	100.7±6.7	72.9±6.5	11.35	0.00	S

NS: Not significant, S: Significant, PI: Post intubation, At pneumo: Pneumoperitoneum, PP: Post pneumoperitoneum, PR: Pulse rate, SD: Standard deviation

compared using 2 independent sample *t*-tests. We found that there was no statistical significant difference between Groups A and B with respect to SBP values at baseline. However, there was a significant difference in SBP values after anesthesia at mentioned intervals between the two groups. Values were relatively lower in Group B, and the difference was found to be statistically significant ($P < 0.05$) (Table 5).

Recorded the values at fixed intervals in both the Groups as shown in the observation table. These values were compared using 2 independent sample *t*-test. We found that there was no significant difference between Groups A and B with respect to DBP values at baseline ($P > 0.05$). However, there was a significant difference in DBP values in post anesthesia at mentioned intervals between the two groups. Values were relatively lower in Group B, and the difference was found to be statistically significant ($P < 0.05$) (Table 6).

Group A had 30% of patients with PONV as compared to 6.7% in Group B. However, the incidence was not statistically significant (Table 7).

Recorded the values at fixed intervals in both the Groups as shown in the observation table. These values were compared using 2 independent sample *t*-test. There was a significant difference between the two groups with respect to VAS values during post-operative period until 6-h. Values were lower in Group B, and the difference was found to be statistically significant ($P < 0.05$). We also found that there was no statistically significant difference between Groups A and B with respect to VAS pain score post-operative 9 and 12 h ($P > 0.05$) (Table 8).

DISCUSSION

GA has remained the most accepted modality of anesthesia for Laparoscopic cholecystectomy, while regional techniques have been shown to attenuate the metabolic and endocrine responses. However, the complications associated with GA has lead to the question whether the conventionally accepted sole modality of anesthesia, GA, is indeed a gold standard! The need for an additional modality of anesthesia with GA has led to studying various other options over the years. One of the most successfully used anesthesia with GA is spinal anesthesia. Various studies regarding its feasibility, patient comfort after the procedure, incidence of post-operative complications, recovery from anesthesia, ambulation, hospital stay and cost effectiveness due to decreased requirement of analgesia, have been conducted showing that it is indeed a good alternative to only GA, better than a sole, GA in various situations. All risks of SA are still

Table 5: Changes in SBP in two groups

Time interval (min)	Mean±SD		t value	P value	Significance
	Group A	Group B			
Pre-operative (PI)	121.8±11.2	121.3±7.4	0.18	0.86	NS
1	144.2±9.7	119.5±8.9	9.36	0.00	S
2	143.2±10.1	114.2±7.7	11.37	0.00	S
3	141.4±10.4	108.5±6.9	13.17	0.00	S
4	140.7±9.8	104.0±6.1	15.90	0.00	S
5	140.3±9.7	101.1±6.6	16.69	0.00	S
At pneumo (PP)	151.4±8.0	119.9±10.0	12.27	0.00	S
15	142.3±7.8	114.9±9.7	10.98	0.00	S
30	134.3±5.8	112.6±7.2	11.73	0.00	S
45	129.6±6.3	107.8±8.7	8.58	0.00	S
60	144.7±4.6	113.3±8.1	12.95	0.00	S

NS: Not significant, S: Significant, PI: Post intubation, At pneumo: Pneumoperitoneum, PP: Post Pneumoperitoneum, SD: Standard deviation

Table 6: Changes in DBP in two groups

Time interval (min)	Mean±SD		t value	P value	Significance
	Group A	Group B			
Pre-operative (PI)	74.8±7.0	79.0±3.3	2.70	0.01	NS
1	89.9±7.2	73.1±5.2	9.51	0.00	S
2	88.2±7.9	72.4±5.6	8.18	0.00	S
3	87.0±7.2	68.0±4.2	11.36	0.00	S
4	87.4±7.4	63.4±4.1	14.19	0.00	S
5	85.6±6.9	61.2±3.4	15.87	0.00	S
At pneumo (PP)	97.4±8.3	76.7±4.2	11.14	0.00	S
15	89.0±10.6	73.0±4.2	6.98	0.00	S
30	83.2±6.8	73.1±4.3	6.32	0.00	S
45	79.0±5.4	74.2±5.1	2.68	0.01	S
60	88.0±4.5	74.4±4.4	8.26	0.00	S

NS: Not significant, S: Significant, PI: Post intubation, At pneumo: Pneumoperitoneum, PP: Post Pneumoperitoneum, DBP: Diastolic blood pressure, SD: Standard deviation

Table 7: Post-operative nausea and vomiting

PONV	n (%)	
	Group A	Group B
Yes	9 (30)	2 (6.7)
No	21 (70)	28 (93.3)

$\chi^2=3.39, P=0.07, NS, NS$: Not significant, PONV: Post-operative nausea and vomiting

Table 8: Mean pain score (VAS) in two groups

Time interval (h)	Mean±SD		t value	P value	Significance
	Group A	Group B			
1	7.1±0.8	0.1±0.3	40.11	0.01	S
3	5.6±0.7	2.0±0.8	17.59	0.00	S
6	4.7±1.5	4.5±1.1	0.54	0.59	NS
9	5.3±1.5	4.6±1.0	1.85	0.07	NS
12	4.9±1.0	4.1±1.9	1.83	0.07	NS

NS: Not significant, S: Significant, VAS: Visual analogue scale, SD: Standard deviation

present, and side effects such as hypotension, bradycardia, urinary retention, and others, should be expected in their usual rates.

Our study compared GA with combined spinal with GA. As there are incidences of conversion of SA to GA in some previous studies^{8,9} due to intolerable pain after pneumoperitoneum with pressure of 12-15 mmHg, purpose of this study is to demonstrate that laparoscopic surgery done with standard pressure pneumoperitoneum can safely and effectively be performed with the patient under combined anesthesia, allowing the surgeon and anaesthesiologist a full complement of analgesia for the procedure.

In the present study, 60 patients undergoing laparoscopic cholecystectomy procedures were randomly assigned equally into GA Group (A) and combined spinal with GA Group (B). A statistical analysis of the age distribution ($\chi^2 = 0.09$, $P = 0.96$), sex distribution ($\chi^2 = 0.08$, $P = 0.78$), and weight distribution ($t = 0.57$, $P = 0.58$) all showed to be statistically insignificant. Hence, demographic characteristics are similar and comparable in both groups.

For each procedure, the surgeon was asked to opine regarding the surgical conditions and muscle relaxation as to whether it was bad/good/excellent. In all cases in the Group B, the surgeons did not find any difference in the operating conditions and muscle relaxation. Jesus de *et al.*,¹⁰ and Pamela *et al.*,¹¹ assessed the surgical conditions in patients given SAB and concluded that SAB provided good intra-operative conditions with muscle relaxation as good as GA.

Group B patients unlike Group A patient showed less tachycardia intraoperatively. The mean HR preoperatively was statistically insignificant. The mean HR at different time intervals intraoperatively was higher in the GA group and was statistically significant at all time intervals. Bradycardia was found in 2 patients (8%) in the SA group which was managed with intravenous glycopyrrolate 0.2 mg uneventfully. Mehta *et al.*,¹² and Gautam¹³ found no incidence of bradycardia in their studies, thus proving that bradycardia is not much of a threat.

Hypotension (i.e., >20% fall in BP) was noted in <20% cases, for which intravenous mephentermine 6 mg bolus was given in only 2 cases, and the rest were managed with intravenous fluids, while in group GA, hypotension was not seen in any patients. Sinha *et al.*,¹⁴ reported hypotension in 18.21%, Mehta *et al.*,¹² in 30% of the cases, Hartmann *et al.*,¹⁵ reported hypotension in 5.4% of their SA patients, Palachewa *et al.*,¹⁶ had an incidence of 15.7%, Throngnumchai *et al.*,¹⁷ 20.2%, and Hyderally¹⁸ reported a 10-40% incidence. This then conclusively proves that the incidence of hypotension is no different whether laparoscopic surgery or open surgery is being done with SA.

Mean SBP and DBP was found to be higher in Group A compared to Group B at all time intervals during the procedure. Thus, indicating that SA if combined with GA provides an overall better hemodynamic picture as compared to only GA. An added cardiovascular advantage cited has been the decrease in surgical bed oozing because of hypotension, bradycardia and improved venous drainage associated with SA.¹⁹

In the post-operative period after SA with GA, there was no restlessness as is commonly seen after GA, and the patient is always receptive and more compliant to suggestions. A specific advantage of SA component, seems to be the decrease in the requirement of post-operative analgesia. The injectable analgesic was usually required early in post-operative period after extubation when only GA was used. The benefit of prolonged analgesia after SA has also been noted in other studies.^{9,20,21} Intensity of pain was less in Group B as compared to Group A during early post-operative period until 6-h. There was no significant difference seen after this period.

Postural headache, one of the complications of SA was not seen in our study group B. The incidence of spinal headache has been variously quoted as 3.3%²² 7.7%,²³ and 14%²⁴ after SA in open surgery.

There was no difference in occurrence of complications such as sore throat, relaxant-induced muscle pain, dizziness in both groups. But PONV was significantly low in Group B. It often create high morbidity after GA. In this context, PONV is, particularly, troublesome, and antiemetics may be required in as many as 50% of patients²² and can delay discharge from the hospital in 7% of patients.²³ The problem with PONV was seen 8% in SA patients, but has been reported as high as 8.1% in another study of SA.²² However, PONV is the highest after only GA, especially when high amounts of nitrous, opiate are used. In their presence, the rate can vary up to 60-70%.^{24,25} Even with the newer agents like propofol and isoflurane, the incidence is as high as 30% and substantially increase the cost of anesthesia.²⁶ Our GA patients had an incidence of 20% of PONV, which was significantly higher compared with that in Group B patients. No significant difference was found in occurrence of sore throat in both the group.

Our initial experience with laparoscopic surgery under combined spinal with GA appears promising. We conclude that procedure is technically safe and feasible with excellent recovery and high degree of satisfaction in selected patients.

CONCLUSION

Our initial experience with laparoscopic surgery under combined spinal with GA appears promising. We conclude that procedure is technically safe and feasible with excellent recovery and high degree of satisfaction in selected patients. Large randomized control trials are needed before recommending this technique in larger population.

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How to cite this article: Sale HK, Shendage VJ, Wani S. Comparative Study between General Anesthesia and Combined General Anesthesia with Spinal Anesthesia in Laparoscopic Cholecystectomy. *Int J Sci Stud* 2016;3(11):157-162.

Source of Support: Nil, **Conflict of Interest:** None declared.

Evaluation of Peripheral Arterial Disease of Lower Extremity by Doppler Imaging

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Abstract

Background: Doppler ultrasonography has earned recognition as the optimal screening technique for the detection of peripheral arterial disease (PAD). Doppler using color Doppler, pulse wave Doppler, and power Doppler combined with baseline grayscale ultrasound has proved to be very useful, sensitive, and cheap tool to identify and characterize lesions of PAD.

Materials and Methods: A total of 50 patients with symptoms of PAD were subjected to Doppler examination, and the pathoanatomy of the lesions of PAD was mapped along with a study of their risk factors during the period from December 2011 to December 2013.

Results: The risk factors and Doppler features of 60 limbs affected with PAD were reviewed. 90% cases were above the age of 40 years with mean age of presentation being 52.12 years. Among all patients of PAD male to female ratio was around 2:1. Symptomatically intermittent claudication was the most common symptom seen in 62% cases followed by color and temperature changes (COLD), gangrene (GG), and rest pain. Evaluation of risk factors identified 60% were having hypertension while 52% had diabetes mellitus. Nearly 50% patients had the habit of smoking. The other risk factors found in our study were hyperlipidemia, alcohol intake (ALC), and ischemic heart disease. Femoral segments were most commonly affected with 43.33% in superficial femoral artery followed by 30% in popliteal artery and 20% in the common femoral artery. Below knee involvement was seen in 21 cases. Hemodynamically significant stenosis 74.25% had involvement of the femoropopliteal segment, 7% in the iliac segment, and 18.59% of infrapopliteal segments. 34 cases had plaques identified in them, low echogenicity plaque was seen in 23.68% cases while moderate to severely echogenic plaques that are seen as the disease progresses were seen in 76.32% cases. Peak systolic velocity ratios of <2 were obtained in 21.6%, 2-4 in 30%, >4 in 11.66%, and total block in 36.66%.

Conclusion: Doppler examination proves to be a valuable modality of imaging in evaluating the characteristics, distribution, localizing, and assessing the extent of lesions of PAD.

Key words: Claudication, Doppler, Ischemia, Peripheral arterial disease

INTRODUCTION

Lifestyle diseases such as diabetes mellitus (DM), hypertension (HTN), and obesity predispose the individual peripheral arterial diseases (PAD) of the lower limb.^{1,2} PAD is the most common disease affecting lower limb arteries and

causes a reduction in arterial supply secondary to stenosis and occlusion. PAD can be asymptomatic or have symptoms such as claudication, rest pain (RP), local ulcerations, and gangrene (GG). In late stages, it can even necessitate limb amputation. Atherosclerosis is the most common cause of PAD. Other causes include thromboembolism, inflammation of vessel walls, micro embolism, and trauma.³ Initial luminal narrowing by the deposition of atheromatous plaques is compensated by dilatation of vessel lumen. The plaque may rupture with the formation of thrombus and embolism phenomenon downstream; the ruptured plaque heals by fibrosis causing permanent stenosis of the lumen. This hemodynamic compromise is the cause of the clinical manifestations of PAD.⁴

Access this article online



www.ijss-sn.com

Month of Submission : 12-2015

Month of Peer Review : 01-2016

Month of Acceptance : 01-2016

Month of Publishing : 02-2016

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Invasive contrast-based investigations, such as arteriography and ankle-brachial index computed tomography angiography, are the various modalities used for PAD. Ultrasonography combined with Doppler imaging has been found to be useful in the mapping of the vascular anatomy of lower limbs. Advantages are it is very sensitive to identify thrombus, stenosis, and provide a dynamic assessment of the hemodynamic status of the vessel. It is radiation free, portable, cheap, and easily available. The Doppler findings in PAD are helpful for planning surgical versus medical management and for post procedure surveillance.^{5,6} This study aims to study the risk factors and evaluate the role of Doppler ultrasound (US) examination to study characterization, classification, distribution of lower limb PAD.

MATERIALS AND METHODS

A hospital-based descriptive study was conducted on 50 patients with clinical diagnosis of PAD. This study was done in the Department of Radio-diagnosis and Imaging of Dr. Vaishampayan Memorial Government Medical College, Solapur in a period of 2-year from December 2011 to December 2013. Patients who were pregnant, suffering from lower limb trauma or degloving injuries or burns were excluded from the study. The US Doppler examination was performed on Siemens Acuson X300 US machine with color Doppler. Patient demographic and clinical history was noted, and images were evaluated for location, plaque characterization, degree of stenosis, peak systolic velocity (PSV) ratio, and sites of significant stenosis.

RESULTS

The data were entered in the master chart and analyzed using Statistical Package. The results were converted in the form of graphs and pie diagrams for easy understanding and comparison. The results are displayed from Figures 1-8.

In our study of 50 patients, 10 patients had bilateral disease so in total 60 limbs affected with PAD were evaluated. The range of presenting age was 13-82 years (Figure 1). 90% cases were above the age of 40 years with mean age of presentation being 52.12 years. It is a known fact that prevalence of PAD increases with increasing age and is in correlation with the studies done by Hughson *et al.*,⁷ Fowkes,⁸ and Vogt *et al.*⁹ 72% patients were males while only 28% were females (Figure 2). Hughson *et al.*⁷ in their study found that 2% males and 1% females had symptoms of PAD in the community. Our findings also show a male to female ratio of around 2:1. Symptomatically, we found

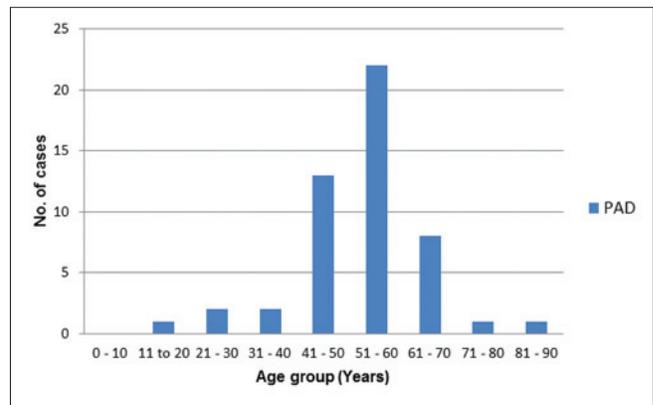


Figure 1: The age wise distribution of patients affected with peripheral arterial disease

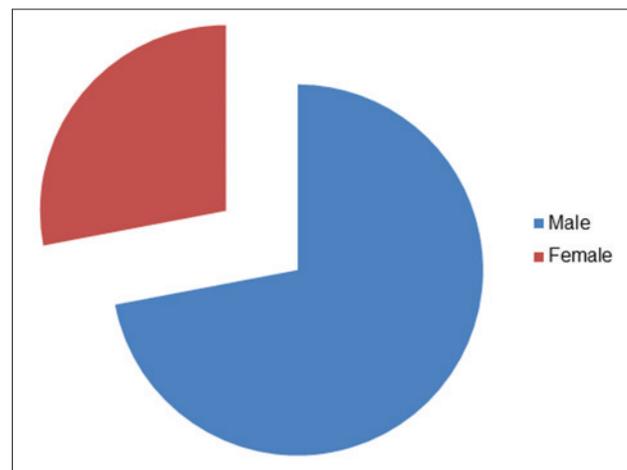


Figure 2: Sex wise distribution of peripheral arterial disease

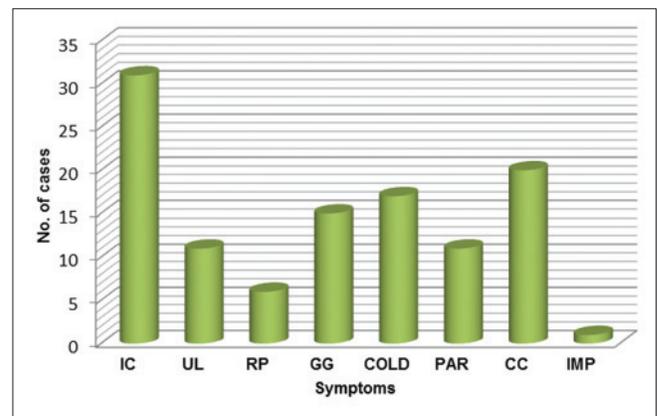


Figure 3: Symptom wise distribution of peripheral arterial disease

intermittent claudication (62%) being the most common symptoms. Color and temperature changes, GG, and RP were the other common presentations. Impotence was found in a single case, and it was associated with DM (Figure 3). Kannel and McGee¹⁰ in their study stated that IC is the most common manifestation of PAD. Rajan¹¹

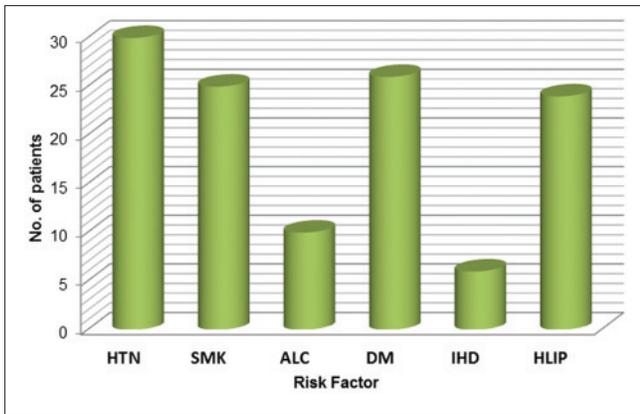


Figure 4: Risk factor wise distribution of peripheral arterial disease

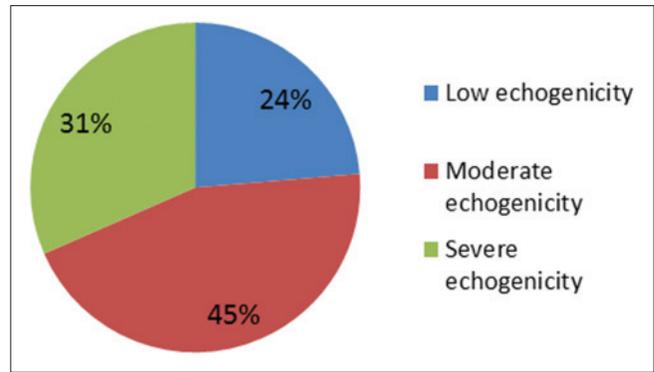


Figure 7: Echogenicity wise distribution of plaques

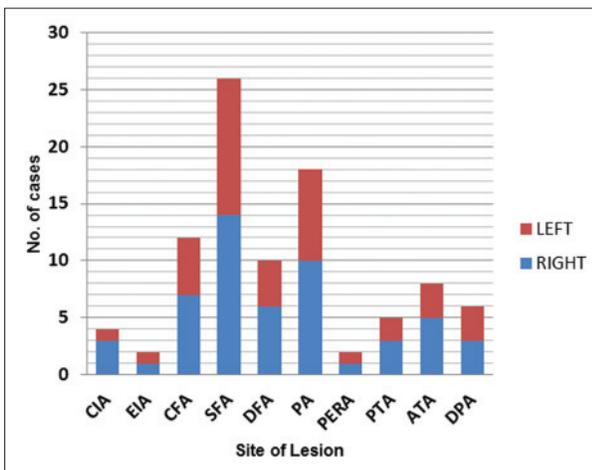


Figure 5: Anatomic segment wise distribution of peripheral arterial disease

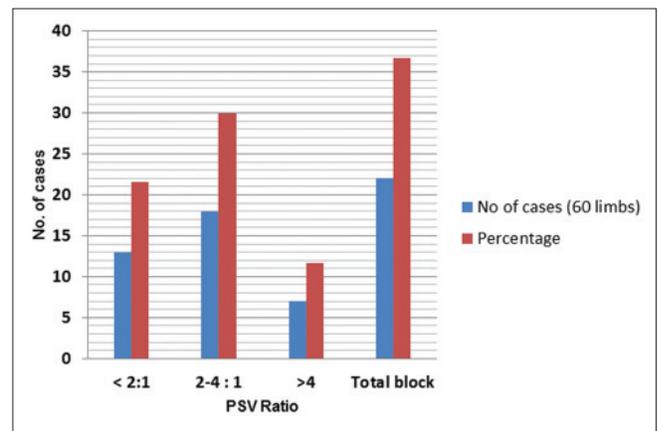


Figure 8: Distribution based on peak systolic velocity ratio

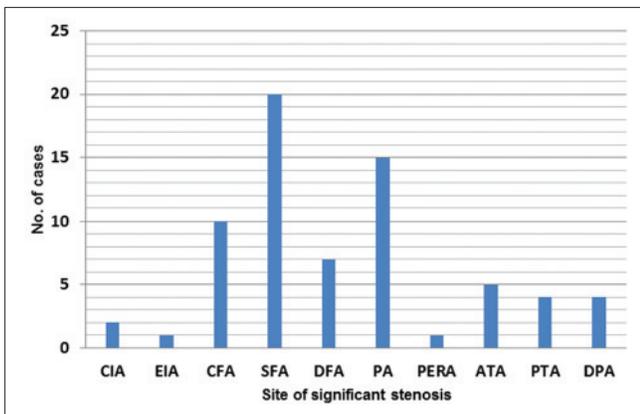


Figure 6: Distribution based on site of significant stenosis

in his study of 188 cases of PAD reported 32% had GG while it was found in 30% patients of our study. Evaluation of risk factors identified 60% were having HTN while 52% had DM. Nearly 50% patients had the habit of smoking (SMK) with half of them smoking more than 20-30 cigarettes daily for more than two

decades. The other risk factors found in our study were hyperlipidemia (HLIP), alcohol intake and ischemic heart disease (IHD) (Figure 4). Krishnaswamy *et al.*¹² in their study found HTN in around 29.3% and DM in 30.3% of patients with PAD. In their study, Gordon and Kannel¹³ found the relative risks of developing PAD in smokers being 1.7-7.5 times. The other risk factors found in their study were HLIP, alcohol intake, and IHD. Similar findings were observed in the study of Hughson *et al.*⁷ where they also found that when present together these factors had a multiplicative effect. In our study, the majority of the lesions were involving the femoral segments with most of them (43.33%) in superficial femoral artery followed by 30% in popliteal artery and 20% in the common femoral artery. Below knee involvement was seen in 21 cases (Figure 5). Among patients with hemodynamically significant stenosis, 74.25% had involvement of the femoropopliteal segment, 7% in the iliac segment, and 18.59% of infrapopliteal segments (Figure 6). Ahchong *et al.*¹⁴ in their study of severely stenosed cases of PAD found 76% had femoropopliteal involvement. In patients with complete occlusion who had significant collaterals had the severest symptoms. This is in correlation with the study of Suzuki *et al.*,¹⁵ who stated poor prognosis in cases with collaterals and absence of flow in the main trunk. 34 cases

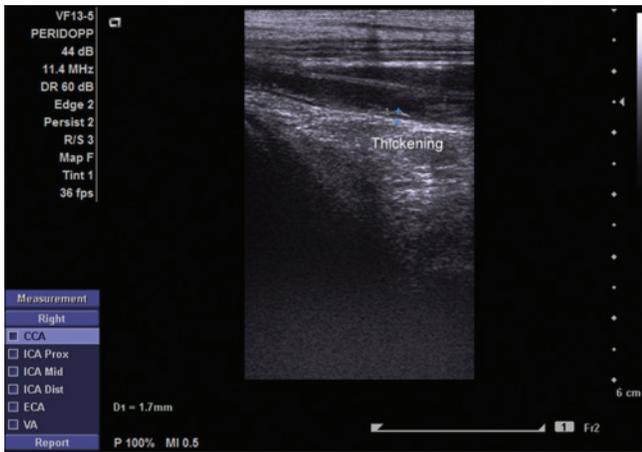


Image 1: Longitudinal grayscale image showing intimal thickening involving Dorsalis pedis artery

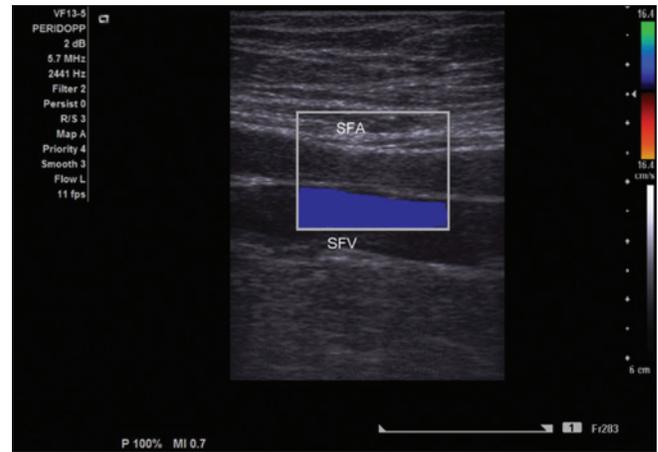


Image 4: Longitudinal color Doppler image of chronic thrombosis of superficial femoral artery with thickened walls

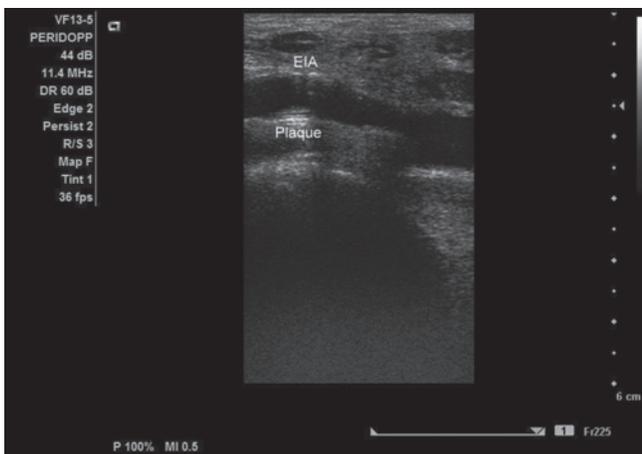


Image 2: Longitudinal grayscale image showing chronic calcified plaque in external iliac artery

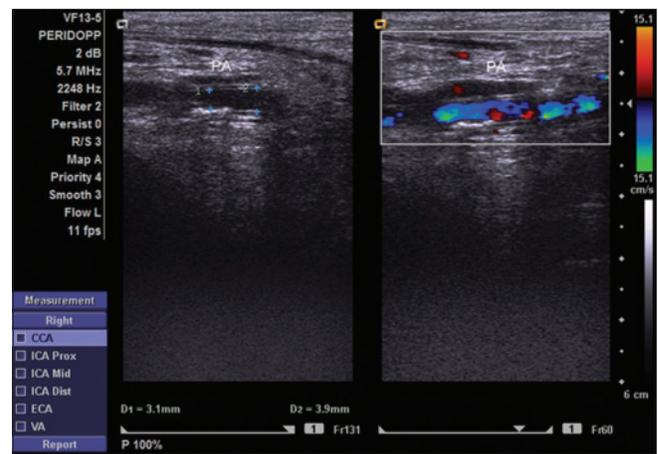


Image 5: Longitudinal grayscale and color Doppler images of popliteal artery with mild stenosis showing turbulent color flow at site of stenosis

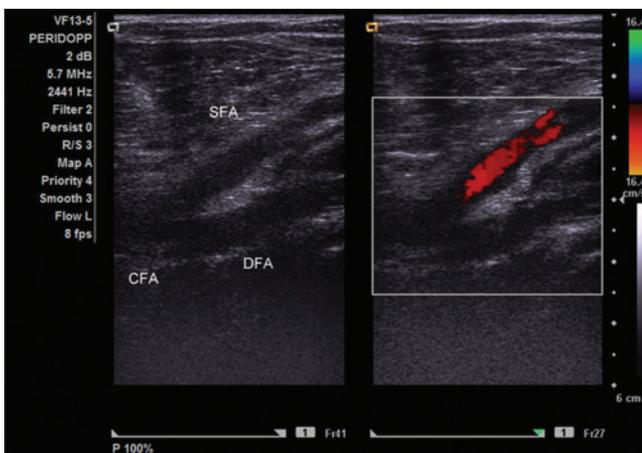


Image 3: Longitudinal grayscale and color Doppler images of acute thrombosis of common femoral artery and deep femoral artery with normal color flow in superficial femoral artery



Image 6: Transverse grayscale and color Doppler images showing thrombosed popliteal artery with collateral formation

had plaques identified in them; low echogenicity plaque was seen in 23.68% cases while moderate to severely echogenic plaques that are seen as the disease progresses

were seen in 76.32% cases (Figure 7). Hughson *et al.*⁷ found atherosclerosis to be a most important factor associated in IC and subsequently with PAD. Thus, the atherosclerotic

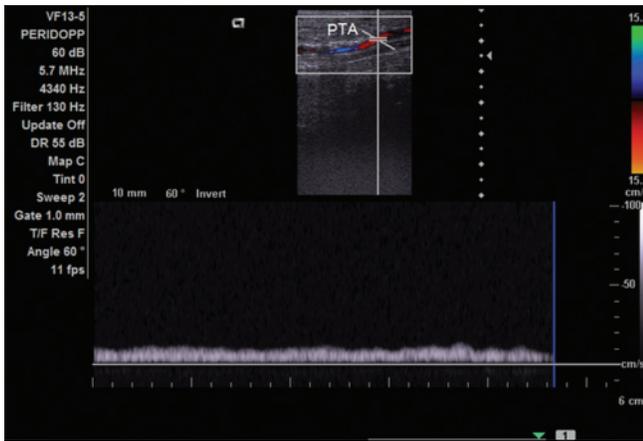


Image 7: Longitudinal color Doppler image of post-thrombotic posterior tibial artery showing monophasic waveform

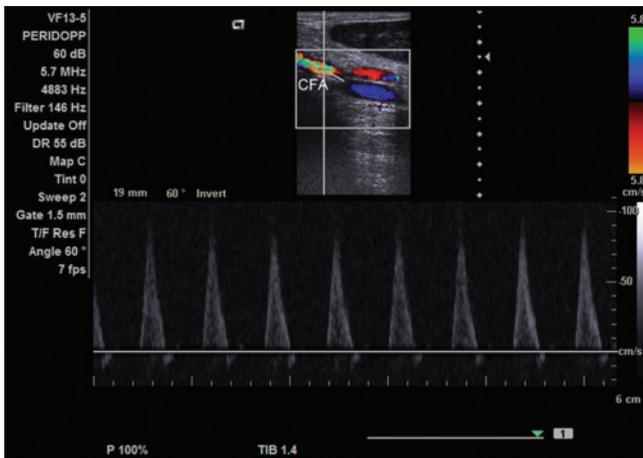


Image 8: Longitudinal color Doppler image showing moderately stenotic common femoral artery with biphasic waveforms

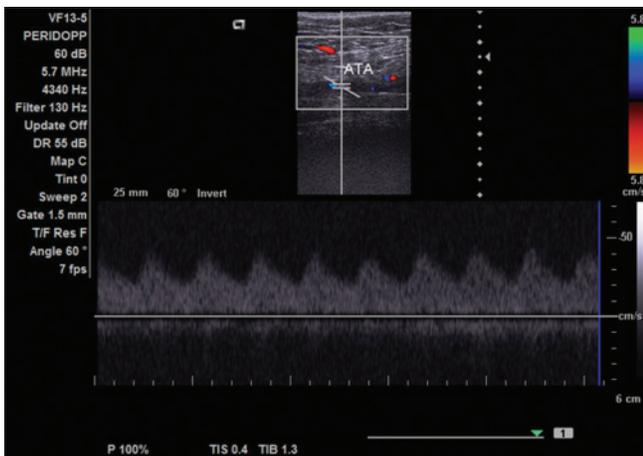


Image 9: Longitudinal color Doppler image of post-stenotic segment of anterior tibial artery showing low resistance flow pattern

lesions of PAD are mostly chronic and this is similar to the study of Maseri and Fuster,¹⁶ who found chronic plaques to predominate in settings of PAD. Out of the 50 patients of PAD, PSV ratios of <2 were obtained in 21.6%, 2-4 in

30%, >4 in 11.66%, and total block in 36.66% (Figure 8). In our study, among the 25 patients who had PSV ratio more than 2, 60% had hemodynamically significant stenosis. As per the study done by Cossman *et al.*,¹⁷ a PSV ratio more than 2 is seen in hemodynamically significant lesions and severity of stenosis is proportional to the PSV ratio. Using PSV ratio in Doppler reports is easy to remember, provides standardization, and clinically comparable.

Images (1-9) explain the various findings that can be demonstrated using doppler imaging.

CONCLUSION

In this study using Doppler examination, it was possible to categorize the diseases as PAD along with their pathoanatomy mapping. The lesions could be also classified as acute versus chronic, significant versus non-significant stenotic. We also studied the age and sex wise distribution of the lower limb vascular diseases with the underlying risk factors for them. Thus, color Doppler imaging is an excellent modality for PAD of lower limbs. Finally, the findings of this study correlate well with many other studies reported in the literature.

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How to cite this article: Choudhary VA, Patil SS, Shah VR. Evaluation of Peripheral Arterial Disease of Lower Extremity by Doppler Imaging. *Int J Sci Stud* 2016;3(11):163-168.

Source of Support: Nil, **Conflict of Interest:** None declared.

Maternal and Fetal Outcome in Pregnancy with Fibroids: A Prospective Study

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Abstract

Background: Fibroid (myomas) is the most common benign tumors of the uterus. Complications occur in approximately 10-40% in the presence of fibroids. The aim of our study was to evaluate the maternal and fetal outcome in antenatal women with fibroids.

Methods: A prospective study was carried out over a period of 1-year in 30 women admitted with the diagnosis of pregnancy with fibroid. Duration of study was from 1.08.2014 to 30.07.2015, 1 year in a tertiary care medical college hospital, Raja Mirasdar Hospital attached to Thanjavur Medical College, Thanjavur, Tamil Nadu, India. Routine basic investigations were done for all the women included in the study. Ultrasonogram was done at booking visit and during subsequent visits to assess the increase in the size of the fibroid and degeneration and other obstetric complications such as malpresentation and placenta previa.

Results: Major proportion was in the younger age group of 25-35 years. Fibroids were more frequent in multigravidae 22 (73.3%), and primigravidae were 8 (26.6%). The reported incidence of fibroid in pregnancy ranges from 0.01%-10.7%. 10 (33.3%) women were asymptomatic during pregnancy. Out of 30 women, 10 (33.3) were known the case of fibroid became pregnant, remaining 20 (66.6%) were diagnosed as having fibroid during routine antenatal visits. 7 women (23.3%) had pain, 4 of them (13.3%) had threatened preterm labor, 3 (10%) had spontaneous miscarriage, and 3 (10%) had anemia, and placenta previa was diagnosed in 3 patients (10%). 27 women (90%) were crossed 37 completed weeks of gestation. Out of 27, 8 (29.6%) women had vaginal delivery, outlet forceps applied in one woman (3.7%), and ventouse applied in one woman (3.7%). Lower segment cesarean section done in 16 women (59.2%), and cesarean hysterectomy proceeded in one woman (3.7%).

Conclusion: Pregnancies with fibroids are associated with complications during the antepartum, intrapartum, and postpartum period. They need frequent follow-up and evaluation. Most of the fibroids are asymptomatic but may adversely affect the course of pregnancy and labor depending on their location and size.

Key words: Fibroid, Leiomyoma, Myoma, Myomectomy, Obstetric complications

INTRODUCTION

Myomas are a common benign smooth muscle tumor of the uterus. They are found in approximately 35-77% of women of reproductive age.¹ They have been found to be associated with menstrual disorders and pelvic pain and can negatively affect fertility and pregnancy outcome. The reported incidence of fibroids in pregnancy ranges from 0.1 to 10.7% of all pregnancies.² Incidence of fibroids

increases with maternal age who are older than 35 years of age and in nulliparas.³ Pregnant women with myoma are at increased risk of cesarean delivery, breech presentation, malposition, and preterm delivery. Fibroid <5 cm in diameter tend to remain stable or decrease in size^{4,6} and, larger fibroids (>5 cm) tend to grow during the pregnancy.⁶ The risk of adverse events in pregnancy increases with the size of the fibroid. Different complications with variable rates of incidence have been reported in pregnancy with fibroids which include antepartum hemorrhage, acute abdomen, laparotomy, preterm labor, fetopelvic disproportion, malposition of the fetus, retention of the placenta, postpartum hemorrhage (PPH), red degeneration, dysfunctional labor, retained placenta, and retained products of conception, intrauterine growth restriction.⁷⁻¹¹ These complications are more commonly seen with large submucosal and retroplacental fibroids.¹² Even though

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Month of Submission : 12-2015

Month of Peer Review : 01-2016

Month of Acceptance : 01-2016

Month of Publishing : 02-2016

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there is higher cesarean section rate in women with fibroids, the presence of uterine fibroids should not be regarded as a contraindication to a trial of labour.¹³ Cesarean rate is higher particularly in women with large fibroids.

METHODS

The present study was a prospective study carried out over a period of 1-year on 30 women admitted with the diagnosis fibroid with pregnancy. The study period was from 1.08.2014 to 30.07.2015 for the period of 1-year in a Tertiary Care Medical College Hospital, Raja Mirasdar Hospital attached to Thanjavur Medical College, Thanjavur, Tamil Nadu, India. During our study period, the total number of deliveries were 14199, and a total number of antenatal outpatients were 39490, and the incidence in the hospital is 0.075%. Ultrasonogram done at booking visit and patients with fibroid of 5 cm and above were included in the study. The mean age group was 28 years. In our study, 8 were primigravidae and 22 were multigravidae. Out of 8 primigravidae, 2 women were with larger fibroid more than 15 cm and other 6 were with fibroids of <7 cm and between 5 and 7 cm one had multiple fibroids and remaining 7 were with single fibroid. All the primigravidae were diagnosed during routine antenatal booking visits. Among 22 multigravidae, 7 had multiple fibroids more than 3 in number and 15 had a single fibroid. Out of 22 multigravidae, 10 were referred from outside and 12 were diagnosed at our hospital.

RESULTS

Myomas are the most common benign smooth muscle tumors of the uterus. They have been found to be associated with pain, degeneration and can negatively affect fertility and pregnancy outcome. In our study, we included 30 women who were having pregnancy with uterine fibroids. We included 30 women who were having pregnancy with fibroids. Women with fibroids of more than 5 cm were included in the study. A major proportion was in the younger age group of 25-35 years (Table 1). The mean age in our study population is 29.5 years. Fibroids were more frequent in multigravidae 22 (73.3%), and primigravidae were 8(26.6%) (Table 2). The reported incidence of fibroid in pregnancy ranges from 0.01% to 10.7%. In our study, the incidence is 0.075%. 10 (33.3%) women were asymptomatic during pregnancy. Out of 30 women, 10 (33.3) were known the case of fibroid became pregnant, remaining 20 (66.6%) were diagnosed as having fibroid during routine antenatal visits (Table 3). 7 women (23.3%) had pain, 4 of them (13.3%) had threatened preterm labor, 3 (10%) had spontaneous miscarriage, and 3 (10%) had anemia, and placenta previa was diagnosed in

3 patients (10%) (Table 4). 27 women (90%) were crossed 37 completed weeks of gestation. Out of 27, 8 (29.6%) women had a vaginal delivery, outlet forceps applied in one woman (3.7%), and ventouse applied in one woman (3.7%). Lower segment cesarean section (LSCS) done in 16 women (59.2%), and cesarean hysterectomy proceeded in one woman (3.7%) (Table 5). Indications for LSCS were breech presentation in 2 (7.4%) women, 2 women were with post-cesarean pregnancy (7.4%) transverse lie in 2 (7.4%), placenta previa in 3 (11.1), premature rupture of membranes (PROM) with poor bishops score in 2 (7.4%), uterine inertia in 3 (11.1%), and non-progressive labor in 3 (11.1%) (Table 6). 5 (18.5%) had PPH and myomectomy

Table 1: Age of study population (n=30)

Age in years	n=30	Percentage
20-25	5	16.6
26-30	10	33.3
31-35	13	43.3
>36	2	6.61

Table 2: Parity wise distribution (n=30)

Gravidity	n=30	Percentage
Primigravida	8	26.6
Multigravida	22	73.3

Table 3: Duration of gestation at diagnosis (n=30)

Gestational age (weeks)	n=30	Percentage
Pre-pregnancy diagnosis	10	33.3
<12	12	40
13-20	3	10
21-28	3	10
29-36	2	66

Table 4: Complication during pregnancy (n=30)

Complication	n=30	Percentage
Asymptomatic	10	3.3
Spontaneous miscarriage	3	10
Pain abdomen	7	23.3
PP	3	10
Threatened PTL	4	13.3
Anemia	3	10

PP: Postpartum, PTL: Preterm labor

Table 5: Mode of delivery (n=27)

Mode of delivery	n=27	Percentage
SVD	8	29.6
Outlet forceps	1	3.7
Vacuum application	1	3.7
LSCS	16	59.2
Cesarean hysterectomy	1	3.7

SVD: Spontaneous vaginal delivery, LSCS: Lower segment cesarean section

Table 6: Indication for LSCS (n=17)

Elective cesarean section	n=17	Percentage
Malpresentation	4	14.8
Placenta previa	3	11.1
Post-cesarean pregnancy	2	7.4
PROM with poor Bishop score	2	7.4
Uterine inertia	3	11
Non progressive labor	3	11.1

PROM: Premature rupture of membranes, LSCS: Lower segment cesarean section

done in 3 (11.1%) patients. All 27 babies were with weight above 2.5 kg with good Apgar score. There was no perinatal and maternal mortality in our study.

DISCUSSION

We have conducted this study to evaluate the maternal and fetal outcome in pregnancies complicated by leiomyomas. Mean maternal age in our study was found to be 28.9 years, which is comparable to other studies, showing occurrence of leiomyomas in second and third decades of life.¹

In our study, we found that fibroids were less frequent in the first primigravidae compared to multigravidae. This is inconsistent with earlier studies by Sarwar *et al.*¹⁴ (63% multigravida and 37% primigravida). Regarding obstetric complications, in our study, 3 out of 30 patients (10%) had a spontaneous abortion. High incidence of abortions in patients with fibroids is in agreement with results from earlier studies.⁹ The proposed mechanism is compressed endometrial vascular supply, affects the fetus adversely resulting in abortion.⁹ In our study, 7/30 (23%) had pain abdomen, which is inconsistent with earlier studies.^{9,14}

Pain is the most commonly reported complaints and is seen most often in women with larger fibroids (more than 5 cm) during 2nd and 3rd trimesters of pregnancy. Fibroids may grow quickly and cause intense pain during pregnancy.⁸ Patients with pain were managed conservatively. Cause of pain was due to red degeneration, which is thought to be result of effect of progesterone on fibroids, and occurs more commonly in pregnancy.¹⁵

Though 4/30 (13.3%) patients had a history of threatened preterm labor during pregnancy, all the four patients had continued their pregnancy until term. The incidence of preterm delivery was nil in our study compared to study by Sarwar *et al.* (33.3%).¹⁴ The incidence of PROM, (4/30, 14.8%) is slightly higher in our study when compared to Sarwar *et al.* (10%). 3 patients (10%) had anemia.

Regarding the mode of delivery, 10 patients (37.03%) had spontaneous onset of labor and vaginal delivery. Out of 27 patients, 17 had LSCS (63%). Women with fibroids have

a 3.7 fold increased risk of cesarean delivery. Cesarean incidence in our study is similar to studies by Klatsky *et al.*⁹

Indications for LSCS were breech presentation in 2 (7.4%) women, transverse lie in 2 (7.4%), placenta previa in 3 (11.1), PROM with poor bishops score in 4 (14.8%), uterine inertia in 3 (11.1%), and non-progressive labor in 3 (11.1%). 5 (18.5%) had PPH and myomectomy done in 3 (11.1%) patients. Among women, transverse lie in 2, placenta previa in 3 (11.1), PROM with poor bishops score in 4 (14.8%), uterine inertia in 3 (11.1%), and non-progressive labor in 3 (11.1%). In our study, 5/27 (18.5%) had PPH, which is slightly high, compared with 14% in the study by Lam *et al.*¹⁶ and myomectomy done in 3 (11.1%) patients.

Among 3 cases of myomectomy, one patient was a primigravida with myoma of 30 cm × 30 cm in the lower segment of the uterus more close to the line of the incision and was easily removed, and approximation of the uterine wound was also perfect after removal of the fibroid. The second case of myomectomy was a multigravida with a very large subserous fibroid of 30 cm × 35 cm in fundus of uterus in the anterior wall and it was removed without any difficulty.⁷ The third case of myomectomy was a multigravida with previous cesarean delivery and the fibroid of 10 cm size located in the vicinity of lower uterine segment scar and was easily shelled out during surgery. During surgery blood transfused for all 3 myomectomies. Post-operative blood transfusion was not needed in all three. Before proceeding myomectomy, bilateral uterine artery ligation was done in all three myomectomies. All 3 were genuine indications for myomectomy.¹⁷ No case of placental abruption and only one woman with very large fibroid and uncontrolled PPH ended up in cesarean hysterectomy in our study.

All 27 babies were with weight above 2.5 kg with good Apgar score. There was no perinatal and maternal mortality in our study.

CONCLUSION

Pregnancies with fibroids are associated with complications during antepartum, intrapartum, and PP period. They need frequent follow-up and evaluation. Most of the fibroids are asymptomatic, but may adversely affect the course of pregnancy and labor depending on their location and size. These pregnancies are associated with increased incidence of cesarean delivery and PPH and considered as high risk.

ACKNOWLEDGMENTS

I gratefully acknowledge and express my sincere thanks to our Dean, Thanjavur Medical College and Hospital,

Thanjavur, for allowing me to do this study and utilizing the Institutional facilities. I would also like to thank all the medical and para-medical staffs who have helped me complete this study.

Special thanks to all the patients who willingly co-operated and participated in this study. I would like to thank all my colleagues and friends who have been a constant source of encouragement to me.

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How to cite this article: Poovathi M, Ramalingam R. Maternal and Fetal Outcome in Pregnancy with Fibroids: A Prospective Study. *Int J Sci Stud* 2016;3(11):169-172.

Source of Support: Nil, **Conflict of Interest:** None declared.

Non-stress Test and Vibroacoustic Stimulation Test in High-risk Pregnancies and its Relation to Perinatal Outcome

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Abstract

Introduction: Non-stress test (NST) is commonly performed fetal surveillance test, but shows low sensitivity and positive predictive value. Vibroacoustic stimulation test (VAST) improves the sensitivity and specificity in high-risk pregnancies.

Objective: (1) To evaluate the efficacy of VAST in antenatal fetal assessment in high-risk pregnancy, (2) to correlate the VAST results with the perinatal outcome, and (3) to compare efficacy of VAST over NST.

Materials and Methods: This study was conducted on 100 women with high-risk pregnancies fulfilling inclusion criteria. NST was performed and results were obtained. Patients with nonreactive NST underwent VAST. The perinatal outcome was noted as any one of: (a) Caesarean section (CS) for fetal distress, (b) 5 min APGAR score <7, (c) admission to the neonatal intensive care unit (NICU) for more than 24 h, and (d) neonatal mortality.

Results: About 48 patients with reactive NST were in Group I and 52 with nonreactive NST in Group II. In Group II after subjecting to VAST, 27 patients became reactive. 11.12% of VAST reactive (VAST-R) and 88% of VAST nonreactive (VAST-NR) underwent emergency CS, 11.12% VAST-R, and 76% of VAST-NR had a 5 min APGAR <7 (both $P < 0.001$); 7.4% VAST-R, 44% VAST-NR required NICU admission ($P = 0.009$); there were two neonatal mortalities. 88.89% of VAST-R group had a favorable outcome, 92% of VAST-NR group had an unfavorable outcome ($P < 0.001$). 52% of NST-R had a favorable outcome, 50% of NST-NR had an unfavorable outcome (P - not significant). The sensitivity, specificity, positive and negative predictive value of NST was 50.98%, 51.02%, 50% and 52.1% and of VAST was 88.46%, 92.3%, 92% and 88.89%, respectively.

Conclusion: VAST is easy to perform adjunct to NST, in the antenatal fetal assessment of high-risk pregnancy with higher specificity, sensitivity, positive and negative predictive value in predicting perinatal outcome.

Key words: Antenatal fetal surveillance, Fetal acoustic stimulation test, High-risk pregnancy, Non-stress test, Vibroacoustic stimulation test

INTRODUCTION

High-risk pregnancies require sophisticated maternal and fetal surveillance and on many occasions, difficult management decisions to optimize the outcome. Fetal

morbidity and mortality are greater in high-risk women, such as those with prolonged pregnancy, intrauterine growth restriction (IUGR), hypertension, or other risk factors.¹ The test commonly used for antepartum fetal assessment is the non-stress test (NST) which looks for the presence of spontaneous temporary accelerations in the fetal heart rate (FHR) associated with fetal movements perceived by the mother or observed by the obstetrician. Fetal heart accelerations associated with fetal movement is a reflex that is affected by pathological and physiological influences on the fetal brain. The most common physiological condition being the fetal sleep states and most common pathological condition being

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www.ijss-sn.com

Month of Submission : 12-2015

Month of Peer Review : 01-2016

Month of Acceptance : 01-2016

Month of Publishing : 02-2016

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fetal asphyxia. Due to which, NST has been shown to have a low sensitivity.

The vibroacoustic stimulation test (VAST) aims to assess the functional state of the fetal central nervous system and its reflex cardiovascular response. The test is based on the observations that (1) the fetal cochlear apparatus gets mature enough to appreciate acoustic stimulation from 28 weeks, (2) auditory sensation is one of the first to get affected by hypoxia.² Due to the affection of the auditory system in a hypoxic fetus, a compromised fetus does not show a reflex cardiovascular response of fetal heart acceleration in response to acoustic stimulation.

To perform VAST, at the end of 10 min of plain cardiotocography (CTG), a vibroacoustic stimulation is given by placing an acoustic stimulator near baby's vertex, for a period of a maximum of 3 s. In a healthy fetus, cardiac acceleration occurs almost instantaneously on giving the stimulus. If it fails to occur with one stimulus, the stimulus may be repeated at 1 min intervals for a maximum of 3 times.²

Hence, it may help obstetricians to discover unsuspected cases of chronic fetal distress. It has been shown to reduce the number of nonreactive tests and testing time.³ The addition of VAST as a component of the biophysical profile for the fetal assessment in high-risk pregnancies has also been proved to be of reliable diagnostic approach due to higher accuracy, ease of administration, and shorter testing time.⁴ Hence, the present study has been undertaken to study the efficacy of VAST as a test of antenatal fetal surveillance in various high-risk pregnancy conditions, and its advantages over NST.

Objectives

(1) To evaluate the efficacy of VAST in antenatal fetal assessment in high-risk pregnancy, (2) to correlate the VAST results with the perinatal outcome, and (3) to compare efficacy of VAST over NST.

MATERIALS AND METHODS

This was a prospective study carried out on 100 high-risk pregnancies admitted from September 2011 to September 2013 in a tertiary hospital. Women with high-risk factors fulfilling the inclusion criteria admitted in the antenatal wards were randomly selected. The procedure was explained and informed consents were obtained from the patients. After examining the patients, necessary investigations were performed, including Doppler studies in patients of

IUGR and pregnancy induced hypertension (PIH). Electronic Fetal Monitor of Bionet Company, Twin view FC 14000, model MW 160KA1803F52 was used. Vibroacoustic Stimulator belonging to Maestro Mediline Company, giving a stimulation of 75 db intensity at 1 meter at 75 hz was used to perform CTG. Inclusion criteria: (1) Post datism, (2) prolonged pregnancy, (3) prelabour rupture of membranes, (4) gestational diabetes, (5) bad obstetric history, (6) IUGR with at least 2-3 weeks head circumference/abdominal circumference lag, (7) PIH, and (8) oligohydramnios, not in labor, with singleton pregnancy of gestational age more than 34 weeks, with cephalic presentation. Exclusion criteria: (1) Patients in labor, (2) preterm labor, (3) multiple gestations, (4) malpresentations, (5) cases requiring immediate emergency caesarean section (CS) for placenta praevia or placental abruption and cord prolapse, (6) eclampsia, and (7) thick meconium stained liquor.

NST was observed for: (a) Basal heart rate, (b) variability, (c) presence of at least 2 accelerations and absence of decelerations. Patients with reactive NST were allotted Group I, and those with nonreactive or equivocal results in Group II. Group II was followed by a vibroacoustic stimulus for 3 s. In the absence of response, another stimulus was given at an interval of 1 min for maximum three stimuli over a 10 min trace. The presence of FHR acceleration in response to stimulus was considered reactive or VAST negative. The absence of FHR acceleration at the end of three stimuli was considered VAST nonreactive (VAST-NR) or VAST positive. With a reactive VAST, no attempts at termination of pregnancy were made. The tests were performed twice a week until patient landed up in spontaneous or induced labor. Perinatal outcome was noted in all three groups.

Table 1: Distribution of high-risk factors

High-risk factors	NST-R Group I n=48	NST-NR Group II n=52		Total
		VAST R Group II A n=27	VAST NR Group II B n=25	
		PIH	16	
IUGR	17	11	10	38
Oligohydramnios	16	9	4	29
PROM	9	3	3	15
Postdatism	15	6	7	28
GDM	2	1	1	4
BOH	1	4	0	5
Others	5	7	7	19

PIH: Pregnancy induced hypertension, IUGR: Intrauterine growth restriction, PROM: Prelabour rupture of membranes, GDM: Gestational diabetes mellitus, BOH: Bad obstetric history, NR: Non-reactive, R: Reactive, NST: Non-stress test, VAST: Vibroacoustic stimulation test

Table 2: Distribution of perinatal outcome

Outcome	NST-R Group I n=48 (%)	NST-NR Group II n=52		Total	Chi-square Df=2	P value
		VAST-R Group II A n=27 (%)	VAST-NR Group II B n=25 (%)			
Intrapartum fetal distress fetal distress/MSL/tachycardia	21 (43.75)	3 (11.1)	23 (92)	47	34.5	<0.001**
CS-for fetal distress	20 (41.66)	3 (11.12)	22 (88)	45	31.4	<0.001**
APGAR at 5 min<7	11 (22.91)	3 (11.12)	19 (76)	33	28.9	<0.001**
NICU Admission>24 h	12 (25)	2 (7.40)	11 (44)	25	9.27	0.009#
Neonatal Mortality	1	0	1	2		

CS: Caesarean section, **Highly significant, #Significant, R: Reactive, NR: Non-reactive

OBSERVATIONS AND RESULTS

Out of 100, 48 patients had a reactive NST throughout pregnancy and were allotted Group I. Of the 52 patients with nonreactive NST in Group II, 27 became VAST reactive (VAST-R) when subjected to vibroacoustic stimulus and allotted Group IIA while 25 remained VAST nonreactive and were allotted Group IIB. Observations were noted and Chi-square test was applied. $P < 0.05$ was considered significant. The age group and parity in each group were comparable. High-risk factors in each group were as follows: (Table 1).

Although the study included patients beyond 34 weeks of gestation, many high-risk pregnancies were identified near term. In Group I, a total of 35 (72%) and in Group II, a total of 22 (42.3%) patients required induction of labor. The perinatal outcome was as follows: (Table 2).

Two patients with reactive NSTs had an instrumental vaginal delivery due to second stage fetal distress which though an adverse outcome, was not included in the present study. A total of 25 neonatal intensive care unit (NICU) admissions were observed in the study. Although NST was reactive in 48 patients, there were 12 NICU admissions. 52.08% of NST-R had a favorable outcome and 50% of NST-NR had an unfavorable outcome (P value - not significant, Table 3). 88.89% of VAST-R group had a favorable outcome while 92% of VAST-NR group had an unfavorable outcome ($P < 0.001$, Table 4).

The sensitivity, specificity, positive predictive value and negative predictive value of NST were 50.98%, 51.02%, 50% and 52.1%, respectively. The sensitivity, specificity, positive predictive value and negative predictive value VAST was, 88.46%, 92.3%, 92% and 88.89%, respectively (Table 5).

DISCUSSION

In the study, it was found, out of the 52 patients which had a nonreactive NST, 27 became reactive after VAST. During

Table 3: Non stress test outcome

NST results	Unfavorable outcome (%)	Favorable outcome (%)	Total	Chi-square Df=1	P value
NST-NR	26 (50)	26 (50)	52	0	1.0**
NST-R	23 (47.91)	25 (52.08)	48		
Total	51	49	100		

**Not significant, R: Reactive, NR: Non-reactive, NST: Non-stress test

Table 4: Vibroacoustic stimulation test outcome

VAST results	Unfavorable outcome (%)	Favorable outcome (%)	Total	Chi-square Df=1	P value
VAST-non reactive	23 (92)	2 (8)	25	30.8	<0.001*
VAST-reactive	3 (11.12)	24 (88.89)	27		
Total	26	26	52		

*Highly significant, R: Reactive, NR: Non-reactive. VAST: Vibroacoustic stimulation test

the period of antenatal surveillance, in 9 patients when VAST became reactive, the pregnancy was continued, and biweekly tests were continued. Out of these patients only 1 had an unfavorable perinatal outcome.

In 1986, Smith *et al.*,³ performed a retrospective analysis of the adjunctive use of acoustic stimulation in the study group and found a 50% reduction in the number of nonreactive test. Consequently, a prospective study was conducted to compare the standard NST with VAST, in which it was found that the incidence of the nonreactive test in the control group of NST was 14% while in the study group was 9%. Chen,⁵ (1991) studied 103 pregnant females and found a reduction in the number of falsely nonreactive test from 26 with non stress test, to zero with vibroacoustic stimulation test (Table 5).

Perez-Delboy *et al.*,⁶ studied 113 pregnant patients, and randomized them into VAST group and NST group. He found that 5 (9.6%) patients subjected to NST alone had persistent nonreactive NST while no patients in the Group subjected to vibroacoustic stimulus had persistent

Table 5: Comparison of VAST over NST

Study	Test	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Present study (2013) n=100	VAST	88.46	92.3	92	88.89
	NST	50.98	51.02	50	52.1
Nyman <i>et al.</i> , ⁹ n=517	VAST	81	89%	12	99.69
	Saraçoglu <i>et al.</i> , ¹¹ n=400	VAST	85.7	94	54.5
Tannirandorn and Kittipibul ¹² n=604	NST	87.5	88	38.8	98
	FAST	66.7	99.8	85.7	99.5
Batcha and Goonewardene ¹³ n=423	VAST	93	79	67	96
	NST	100	45	50	100

VAST: Vibroacoustic stimulation test, NST: Non-stress test

nonreactive test ($P = 0.0002$). Tongsong and Piyamongkol⁷ studied the incidence of nonreactive tests, which was 6.8% in the Acoustic stimulation test group and 13.8% in the NST group ($P < 0.001$). Due to fetal sleep-activity cycles, the testing time for NST is also longer. With the application of VAST, there is a reduction of the testing time due to modification of the behavioral cycle.^{5,6} In the present study, the time to reactivity was not studied. However, by reducing the number of nonreactive tests, the need for performing extended NSTs and repeat NSTs was avoided. Furthermore, the need for further evaluation in the form of biophysical profile or Doppler and the related costs were avoided.

Out of patients with nonreactive VAST, maximum patients developed intrapartum fetal distress out of which 22 underwent emergency CS. Furthermore, with reactive NST up to 43.75% patients developed intrapartum fetal distress.

Serafini *et al.*,⁸ studied the FHR acceleration response to an acoustic stimulation, which was compared to the traditional NST in regard to pregnancy outcome, as reflected by the incidence of intrapartum fetal distress, meconium staining of the amniotic fluid, 1 and 5 min APGAR scores, and perinatal mortality. They found that fetuses with spontaneous or sound-generated reactivity had comparably good outcomes with respect to all outcome measures investigated. Fetuses which lacked spontaneous or sound-stimulated reactivity had an increased risk for intrapartum fetal distress.

Nyman *et al.*,⁹ studied 517 patients of high-risk pregnancies. In five cases, where the FHR tracings were pathological, stimulation nonetheless, produced fetal movements, and the fetal outcome was good. 30 cases had pathological fetal heart tracing with no fetal movement on vibroacoustic stimulus, out of which 7 had 5 min APGAR < 7 . This shows that fetal movement in response to vibroacoustic stimulus in spite of pathological fetal tracing has a good perinatal outcome. They also observed that there was no habituation to the vibroacoustic stimulus.

Salamalekis *et al.*,¹⁰ studied a series of 180 cases of high-risk pregnancies in order to assess if a NST taken 24 h

before delivery is of any prognostic significance. They concluded that the nonreactive test could identify a population at risk but it was not helpful as a “stand-alone” modality in decision making because of the low sensitivity and positive predictive value rates (40.9% and 28.1), respectively. Various studies have compared. Tannirandorn *et al.*¹², have studied reactive response to short Fetal acoustic stimulation test (FAST), in 604 high risk pregnancies after 28 weeks of gestation. Fetal heart rates were recorded 3 minutes before and 5 minutes after fetal acoustic stimulation. The results of the tests performed within a week of delivery were compared with perinatal outcomes (Table 5).

CONCLUSION

VAST is an easy to perform, bedside test and cost-effective adjuvant to NST, in the antenatal fetal assessment of high-risk pregnancy with higher specificity, sensitivity, positive and negative predictive value in predicting perinatal outcome.

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Sambarey and Bilagi: Study of Non-stress Test and Vibroacoustic Stimulation Test in High-risk Pregnancies

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How to cite this article: Sambarey P, Bilagi DM. Non-stress Test and Vibroacoustic Stimulation Test in High-Risk Pregnancies and its Relation to Perinatal Outcome. *Int J Sci Stud* 2016;3(11):173-177.

Source of Support: Nil, **Conflict of Interest:** None declared.

Solitary Extramedullary Plasmacytoma of Nasal Cavity: An Emerging Differential Diagnosis of Nasal Masses

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Abstract

Background: This study was carried out with an aim of studying the characteristics of solitary extramedullary plasmacytoma (EMP) of the nasal cavity and reporting it as an emerging differential diagnosis of nasal masses.

Materials and Methods: A hospital record-based analysis was performed with case sheets of 197 patients who underwent surgery for nasal masses, over a period of 2-year ranging from July 2012 to June 2014. The findings pertaining to the clinical picture and treatment response of cases diagnosed as solitary EMP of nasal cavity were analyzed and compared with the available literature.

Results: There was 4 (80%) male and 1 (20%) female patient with a mean age of 54.4 years, of which 2 (40%) cases had a history of removal of a nasal mass within last 2 years. The main presenting symptoms were nasal obstruction (80%), nasal bleeding (60%), visible mass in nose (40%), and pain in nose (20%). The mean tumor size was 4.7 cm. After a median follow-up period of 24-month, 3 (60%) patients are alive and disease-free, 1 (20%) patient is alive with multiple myeloma and 1 (20%) patient died of multiple myeloma. There were no cases of loco-regional recurrence following radiotherapy until the documentation of this study.

Conclusion: Solitary EMP of the nasal cavity presents with nonspecific clinical and radiological features. It should be considered in the differential diagnosis of nasal masses. Surgery followed by radiotherapy gives promising results. However, in lieu of its propensity for local recurrence and progression to multiple myeloma, a long-term follow-up is mandatory.

Key words: Multiple myeloma, Nasal mass, Plasma cell, Plasmacytoma, Solitary extramedullary plasmacytoma

INTRODUCTION

Plasmacytomas are uncommon hematologic neoplasms, characterized by monoclonal proliferation of plasma cells that elaborate a single homogeneous immunoglobulin molecule or fragment. They originate in either bone (solitary osseous plasmacytoma) or in soft tissues (extramedullary plasmacytoma [EMP]).¹ Depending on their origin they present either as a localized disease

(solitary medullary or solitary EMP) or a widespread disease as a part of a systemic process during the evolution of multiple myeloma.²

EMP is of special interest to an otorhinolaryngologist because of its long history and the associated diagnostic challenge. EMP represent <1% of all head and neck malignancies.³ The post-diagnosis clinical course is unpredictable and varies among individuals.⁴ Between 10% and 32% of all patients develop multiple myeloma following diagnosis, which dramatically decreases the mean survival time from 8.3 years to 20 months.⁵

The optimal management of EMP is controversial. Surgery can achieve high rates of local control in certain situations. However, radical excision is often impossible due to size or the location of the tumor.⁶ Based on the well-known

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Month of Submission : 12-2015

Month of Peer Review : 01-2016

Month of Acceptance : 01-2016

Month of Publishing : 02-2016

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radiation sensitivity of plasma cell tumors, radiotherapy is generally, accepted as the treatment of choice for EMP, while the role of chemotherapy in these tumors is not well-defined.⁷ In this article, we present the characteristics and treatment outcome of solitary EMP of the nasal cavity along with a brief literature review.

Aim of Study

1. To study the various presentations of EMP of nasal cavity
2. To establish extramedullary plasmactoma of nasal cavity as an emerging differential diagnosis of nasal masses.

MATERIALS AND METHODS

The present study is a representation of hospital record-based analysis, carried out at Hi-Tech Medical College and Hospital, Bhubaneswar, Odisha, India. The information like age, sex, side of involvement, bleeding from nose and other clinical features, nasal endoscopy findings, radiological, histopathological and laboratory findings was gathered by reviewing the stored case sheets of 197 patients of nasal masses who underwent surgery during a period of 2-year, ranging from July 2012 to June 2014.

In this study, solitary EMP was defined as a histopathologically proven single area of extramedullary tumor due to clonal plasma cells, normal bone marrow or less than 5% plasma cell infiltration in the bone marrow aspiration and a bone marrow biopsy specimen with no evidence of plasma cell nodules, normal skeletal survey, normal complete blood count, normal serum calcium level, the absence of related organ or tissue impairment such as renal dysfunction and the absence of M-protein in serum and/or urine.

OBSERVATION AND RESULTS

Among the 5 cases of solitary EMP of nasal tract, there were 4 male (80%) and 1 female (20%) patients with a mean age of 54.4 (range 43-75) years. Out of the 5 cases, 3 (60%) were new, while the remaining 2 had a history of nasal surgery for excision of some mass, within last 2 years. The main presenting symptoms were nasal obstruction (80%), nasal bleeding (60%), visible mass in nose (40%), and pain in nose (20%) (Table 1). The mean tumor size, as detected in the computed tomography scan was 4.7 (range 3.5-6) cm. The observation of the diagnostic nasal endoscopy of all these patients has been summarized in Table 2. Immunohistochemical staining was performed for kappa and lambda light chains in 3 cases. All the 5 patients (100%) were treated with gross surgical resection followed by radiotherapy. The median total radiation dose

was 46 (range 40-50) Gy. After a median follow-up period of 24 (range 18-40) months, 3 (60%) patients are alive and disease-free, 1 (20%) patient is alive with multiple myeloma and 1 (20%) patient died of multiple myeloma. There were no cases of loco-regional recurrence following radiotherapy until the documentation of this study.

DISCUSSION

Plasma cells are derived from B lymphocytes and by producing specific antibodies, play an important role in the non-cellular immune mechanisms. Malignant proliferation of these antibody producing plasma cells is known as plasmacytoma.⁸ There are three types of plasmacytoma described in literature - multiple myeloma, solitary plasmacytoma, and extramedullary plasmacytoma. In 1976, Wiltshaw described a staging system for EMP's.⁹

- Stage I disease is defined by the presence of a tumor at only one extramedullary site
- Stage II disease indicates involvement of regional lymph nodes
- Stage III disease involves multiple metastases – in which case, the patient by definition no longer has solitary plasmacytoma.

Schridde reported the 1st case of EMP in 1905.¹⁰ The inter-relationship between the different neoplastic disorders of plasma cells in head and neck was described by Batasakis in 1983. Approximately 80% of EMP occurs in head and neck.¹¹ The most frequently affected areas in the upper aerodigestive tract are the nasal cavity or paranasal sinuses (43.8%), followed by nasopharynx (18.3%), oropharynx (17.8%), and larynx (11.1%).³ Other sites in head and neck that have been reported include the tongue, minor salivary glands, thyroid, parotid, orbit, and temporal bone.¹² EMP is 3-4 times a more common in males than in females. It typically occurs in 6-7th decade with over 95% cases occurring in patients above 40 years of age.¹³

In the present study, the mean age of our patients was 54.4 (range 43-75) years. This finding is consistent with the observations of Miller *et al.*¹⁴ (50.4 years), Michalaki *et al.*⁶ (55 years) and Zhou *et al.*¹⁵ (57 years). The male:female ratio observed was 4:1. Male predominance in suffering from Solitary EMP of nasal cavity has also been noticed by Kapadia *et al.*¹³ (3.2:1) and Zhou *et al.*¹⁵ (5:1).

EMP is a destructive tumor and besides the tendency for local recurrence,¹³ has the ability to spread to regional lymph nodes and ability for distant metastasis with progression to multiple myeloma.⁹ In the present study, there were 2 cases with a history of surgery for excision of nasal mass within last 2 years of presentation. Details of the previous surgery

Table 1: Presenting symptoms

Age (years)	Sex	Chief complaints					Case type
		Nasal obstruction	Visible mass in nose	Side involved	Nasal bleeding	Pain in nose	
60	Male	+	+	Left	-	-	New
75	Female	+	+	Right	+	+	Recurrence
43	Male	+	-	Both	-	-	New
44	Male	-	-	Right	++	-	New
50	Male	+	-	Left	++	-	Recurrence

Table 2: Examination findings

Age (years)	Sex	Tumor size (cm) in CT scan	Diagnostic nasal endoscopy		
			Mass	Attached to	Bleeds on touch
60	Male	3.5	Dark red Subepithelial	Lateral wall above anterior end of inferior turbinate	-
75	Female	4	Grayish white with surface ulceration	Middle meatus	+
43	Male	4.5	Pink polypoidal mass with granular surface blocking choana	Nasal septum	-
44	Male	6	Dark red polypoidal	Posterior end of nasal septum	+
50	Male	5.5	Pinkish white polypoidal pushing septum to opposite side	Floor	+

CT: Computed tomography

and nature of excised mass were not available. But in the light of the present diagnosis of solitary EMP of the nasal cavity, these cases can be presumed as recurrence cases as per our knowledge about their potential for locoregional recurrence.

Galieni *et al.*,¹⁶ established five criteria for diagnosing EMP:

- Biopsy of the tissue must reveal monoclonal plasma cell histology
- Bone marrow plasma cell infiltration should not exceed 5% of all nucleated cells
- Osteolytic bone lesions and other tissue involvement must be absent
- Hypercalcemia and renal failure must be absent.
- A serum M protein concentration, if present, must be low.

Solitary EMP of nasal cavity usually has a long insidious course with the clinical features mainly being a very slow growing mass resulting in nasal obstruction and soft tissue swelling. Secondary infection and bone erosion result in pain. Uncommon features include – nasal discharge, epistaxis, and cervical lymphadenopathy.¹² The computed tomography scan and magnetic resonance imaging features of SEP of sinonasal tract are nonspecific⁷ and hence a biopsy is required to make a definite diagnosis. The main presenting symptoms in the present study were nasal obstruction (80%), nasal bleeding (60%), visible mass in nose (40%), and pain in nose (20%).

Macroscopically, EMP appears as fleshy, yellow-gray to dark-red, sessile or pedunculated, polypoid or lesion with a

smooth, non-ulcerated surface. On histologic examination, broadsheets of monomorphic plasma cells with variable degrees of cellular atypia and occasional areas of necrosis are seen replacing the native cellular background.¹⁷ In the present study, the macroscopic findings as noticed during diagnostic nasal endoscopy were highly variable, as depicted in Table 2.

Microscopically, the plasma cells are set in a sparse, delicate reticular stroma that is enriched with numerous blood vessels. A monoclonal pattern of immunoperoxidase staining for kappa and lambda immunoglobulin light chains helps confirm the diagnosis and differentiates SEP from reactive plasmacytosis. There are various immunohistochemical markers in use for typing of plasma cells, which include CD38, CD79a, CD138, monoclonal cIg, endothelial membrane antigen, CD45 (weak), and CD30.¹⁸ In the present study, immunohistochemical staining was performed for kappa and lambda light chains in 3 cases, and it yielded positive results.

The differential diagnosis includes other nasal tract malignancies, such as inverted papilloma, pleomorphic adenoma, squamous cell carcinoma, adenocarcinoma, adenocystic carcinoma, melanoma, esthesioneuroblastoma, rhabdomyosarcoma, lymphoma, sinonasal undifferentiated carcinoma, and Wegener granulomatosis.¹⁴

Treatment of localized EMP of head and neck is debatable. Some workers advocate radiation therapy while others advocate surgery alone. Since plasma cells are highly radiosensitive, localized primary radiotherapy has become

the treatment of choice for solitary EMP, especially for larger lesions. The British Society for Hematology recommends initial radiation treatment with 40 Gy in 20 fractions with a 2 cm margin for tumors smaller than 5 cm, and 50 Gy in 25 fractions for larger tumors.¹⁹ Radiotherapy does not always reduce the size of the tumor, perhaps because of an abundant deposition of amyloid within the mass.⁸

Surgery is indicated - in cases of small tumor masses, where clear margins can be obtained, to remove residual tissue after radiation therapy.¹⁸ Most clinicians recommend a combined approach (surgery + radiotherapy) for the management of sinonasal solitary EMP.^{8,9} Chemotherapeutic agents such as melphalan should be considered in the cases of recurrent and disseminated disease and in cases of transformation to multiple myeloma.¹⁹ In the present study, all the 5 patients (100%) were treated with gross surgical resection followed by radiotherapy. The median total radiation dose was 46 (range 40-50) Gy. Miller *et al.*¹⁴ (45-50 Gy) and Michalaki *et al.*⁶ (40-50 Gy) have also reported a similar radiation dose in their studies, respectively.

Acknowledging the tendency of EMP to progress into disseminated multiple myeloma, a life-long follow-up of these patients is recommended. The median survival of patients varies from 4 to 10 years. Local recurrence has been reported to occur in 8%-30% cases of EMP of upper aerodigestive tract.^{9,20} In the present study, after a median follow-up period of 24 (range 18-40) months, 3 (60%) patients are alive, and disease-free, 1 (20%) patient is alive with multiple myeloma and 1 (20%) patient died of multiple myeloma. There were no cases of loco-regional recurrence following radiotherapy until the documentation of this study.

CONCLUSION

Solitary EMP of the nasal cavity presents with nonspecific clinical and radiological features. It should be considered in the differential diagnosis of nasal masses. Surgery followed by radiotherapy gives promising results. Its awareness and multidisciplinary approach is a key to appropriate management. However, in lieu of its propensity for local recurrence and progression to multiple myeloma, a long-term follow-up is mandatory.

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How to cite this article: Maheshwari A, Panigrahi R, Mahajan S. Solitary Extramedullary Plasmacytoma of Nasal Cavity: An Emerging Differential Diagnosis of Nasal Masses. *Int J Sci Stud* 2016;3(11):178-181.

Source of Support: Nil, **Conflict of Interest:** None declared.

Routine Internal Sphincterotomy with Hemorrhoidectomy: A Prospective Study

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Abstract

Aim: The aim of this study is to compare open hemorrhoidectomy with/without internal sphincterotomy with regard to post-operative pain, post-operative complications and wound healing.

Materials and Methods: Patients admitted to JSS Hospital with second-degree hemorrhoids refractory to medical. A total of 100 patients were randomly divided into two groups: Group A - Control Group (50 patients): Patients undergoing open hemorrhoidectomy. Group B - Study group (50 patients): Patients undergoing open hemorrhoidectomy with internal sphincterotomy.

Results: On post-operative day-1 (POD-1), the group which underwent sphincterotomy had lesser complications with regard to pain ($P < 0.0001$), bleeding ($P = 0.1$), constipation ($P = 0.02$), urinary retention ($P = 0.02$). On POD-2, pain ($P < 0.001$), bleeding ($P = 0.05$), and constipation (0.2) were significantly lesser in with sphincterotomy group. At 2 weeks post-operative follow-up, the rate of complete wound healing was 100% in with sphincterotomy group, whereas in without sphincterotomy group it was 84%. The findings are statistically significant as indicated by the P value.

Conclusion: Addition of internal sphincterotomy to open hemorrhoidectomy is an effective method to reduce post open hemorrhoidectomy pain, complications as well as reduce the duration of complete wound healing without any significant morbidity.

Key words: Hemorrhoids, Internal sphincterotomy, Open hemorrhoidectomy, Post-hemorrhoidectomy pain

INTRODUCTION

Hemorrhoids are common clinical conditions. About half of the population has hemorrhoids by the age of 50 years. It is estimated that 58% of people aged over 40 years have the disease in the USA.¹⁻⁴ Almost one-third of these patients present to surgeons for treatment. Hemorrhoids can occur at any age, and they affect both men and women.

Exact incidence in developing countries is unknown, but the disease is being more frequently encountered, perhaps due to westernized lifestyle. Hemorrhoids have plagued humans since they attained the erect posture.⁵⁻⁸

The word “hemorrhoid” is derived from Greek word hemorrhoids, meaning flowing of blood (haem = blood, rhoos = flowing). The word “piles” comes from Latin word pila meaning a pill or ball. To be accurate, we should call the disease as piles when the patient complains of a swelling and “hemorrhoids” when he or she complains of bleeding.^{2,9-11} The most common method of treatment of hemorrhoids is by Hemorrhoidectomy which involves excision of pile mass, either by open hemorrhoidectomy (Milligan-Morgan) or closed hemorrhoidectomy (Ferguson) method.

MATERIALS AND METHODS

- Method of study: It is a prospective study of patients admitted in JSS Hospital Mysore
- Duration of study: November 2013-October 2015
- Sample size: 100 cases, (50 cases of Milligan-Morgan hemorrhoidectomy without sphincterotomy and 50 cases of open hemorrhoidectomy with sphincterotomy).
- The source of the data: All patients with Grade II, III and Grade IV hemorrhoids coming to the General

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Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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Surgery Department of JSSH, Mysore will be included for the study.

- A. Inclusion criteria
 1. Age 25-50 years
 2. Diagnosed to have second-degree hemorrhoids refractory to medical treatment
 3. Third-degree hemorrhoids
 4. Fourth-degree hemorrhoids.
- B. Exclusion criteria
 1. First- and second-degree hemorrhoids, managed by medical line of the treatment
 2. Patients with medical co-morbidities - Diabetes mellitus, hypertension, ischemic heart disease, asthma
 3. H/O anal fissures/anal fistula/perianal abscess
 4. Previous hemorrhoidal surgeries
 5. Fecal incontinence
 6. Previously treated with sclerotherapy and other modalities for hemorrhoids.

Methodology

A randomized case control trial with prospective data collection of 50 patients. Randomization process will be carried out by odd and even numbers. Patients admitted will undergo standard screening for anaesthetic fitness and will be operated under spinal block.

Patients will have to sign the informed consent before participating in the study. Standard antibiotic prophylaxis and bowel preparation will be carried out.

The severity of post-operative pain was assessed according to frequency of administration of analgesic, needed to control the pain for a patient which followed an “on the patient’s demand” protocol. Pain will be categorized as:

- Mild (Grade 1) - if analgesics were administered 0-2/48 hours to control pain
- Moderate (Grade 2) - if analgesics were administered 3-4/48 h, and
- Severe (Grade 3) - if analgesics were administered > 4/48 h.

All the patients will be given diclofenac as an analgesic intramuscularly. Details of the time and number of injections used will be recorded against each patient.

Visual Analogue Scale (VAS)

VAS is a single item vertical scale of 100 mm for pain intensity, categorized as:

- No pain (0-4 mm)
- Mild pain (5-44 mm)
- Moderate pain (45-74 mm)
- Severe pain (75-100 mm).

The patients will be followed up at pouch of douglas 1, 7 and at 2 weeks, 4 weeks, once a month for 3 months, under the following criteria:

1. Pain
2. Post-operative urinary retention
3. Constipation
4. Rectal bleeding
5. Wound hematoma
6. Submucosal abscess
7. Stenosis and
8. Wound healing.

Statistical methods used are:

1. Descriptive statistics
2. Chi-square test
3. Contingency co-efficient tests
4. “P” test independent

RESULTS

Age Distribution

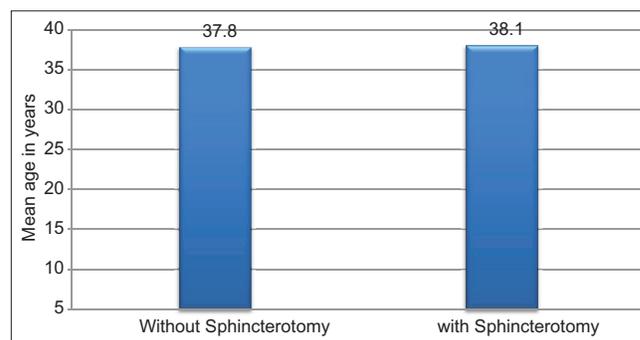
In my study, patients were of the mean age of 37.8 years in without sphincterotomy group, and 38.1 in with sphincterotomy group (Table 1 and Graph 1).

Sex Distribution

A number of females in the study group were 22 in without sphincterotomy group and 21 in with sphincterotomy group, i.e. 44% and 42%, respectively. Number of males in the study group were 28 in without sphincterotomy group and 29 in with sphincterotomy group, i.e. 56% and 58%, respectively (Table 2 and Graph 2).

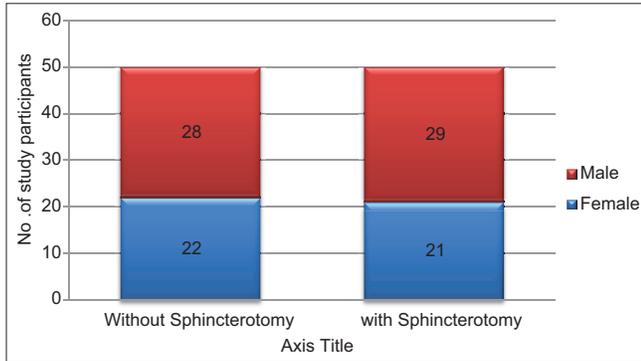
Distribution of grade of hemorrhoids without sphincterotomy group. Grade 2: 8%, Grade 3: 72%, Grade 4: 20%. With sphincterotomy group Grade 2: 10%, Grade 3: 70%, and Grade 4: 20% (Table 3).

Assessment of pain: Table 4 and Graph 3: Post-operative - day-1.

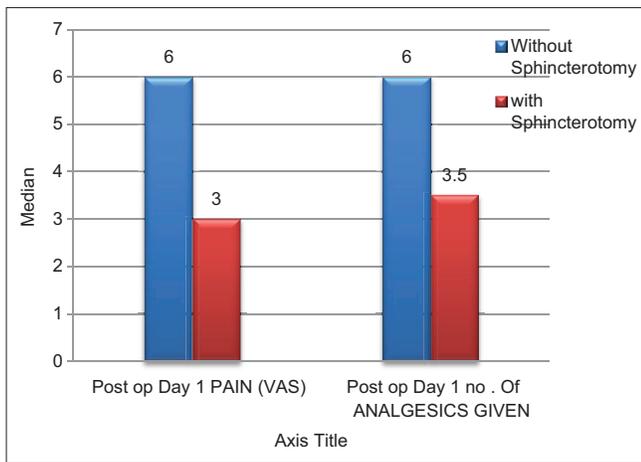


Graph 1: Age distribution

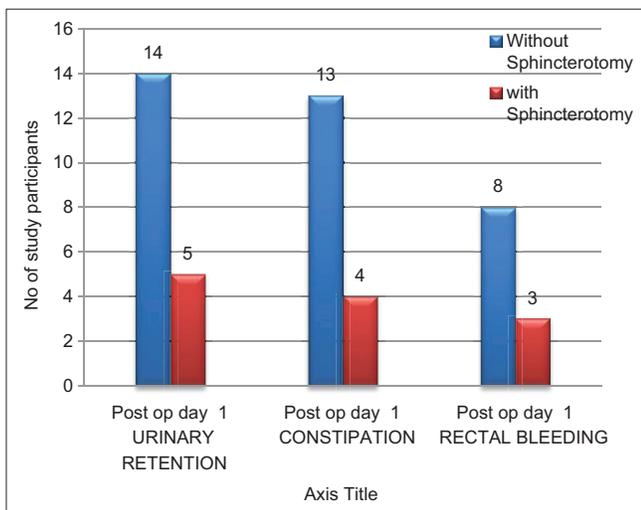
Assessment of pain - post-operative day-1 (POD-1) pain was assessed using two variables, i.e. VAS and numbered of analgesics given on day-1, patients who underwent hemorrhoidectomy without sphincterotomy had more pain ($P < 0.001$) when compared to patients who underwent sphincterotomy (Table 4 and Graph 3).



Graph 2: Sex distribution



Graph 3: Assessment of pain post-operative - day-1



Graph 4: Post-operative - day - 1: Assessment of complication

Table 5 and Graph 4: Post-operative - day - 1: Assessment of complication.

Assessment of complications: On POD-1, patients who did not undergo sphincterotomy had more

Table 1: Age distribution

	Group					
	Without sphincterotomy			With sphincterotomy		
	Mean	SD	Median	Mean	SD	Median
Age	37.8	7.7	38.5	38.1	8.3	39.5

$P=0.8$, Independent t test, SD: Standard deviation

Table 2: Sex distribution

Sex	Group (n (%))	
	Without sphincterotomy	With sphincterotomy
Female	22 (44.0)	21 (42.0)
Male	28 (56.0)	29 (58.0)

$P=0.8$, Chi-square test

Table 3: Distribution of grade of hemorrhoids

Grade of hemorrhoids	Group (n (%))	
	Without sphincterotomy	With sphincterotomy
Grade 2	4 (8.0)	5 (10.0)
Grade 3	36 (72.0)	35 (70.0)
Grade 4	10 (20.0)	10 (20.0)

$P=0.9$, Chi-square test

Table 4: Assessment of pain: Post-operative - day-1

Pain	Group						P
	Without sphincterotomy			With sphincterotomy			
	Mean	SD	Median	Mean	SD	Median	
POD-1 pain (VAS)	6.24	2.11	6.00	3.94	1.88	3.00	<0.0001
POD-1 (analgesics given)	6.24	1.90	6.00	3.72	1.16	3.50	<0.0001

VAS: Visual analogue scale, POD: Post-operative day-1, SD: Standard deviation

Table 5: Post-operative - day - 1: Assessment of complication

Complications	Group (n (%))		P
	Without sphincterotomy	With sphincterotomy	
POD-1 - Urinary retention			
No	36 (72.0)	45 (90.0)	0.02
Yes	14 (28.0)	5 (10.0)	
POD-1 - Constipation			
No	37 (74.0)	46 (92.0)	0.02
Yes	13 (26.0)	4 (8.0)	
POD-1 - Rectal bleeding			
No	42 (84.0)	47 (94.0)	0.1
Yes	8 (16.0)	3 (6.0)	

POD: Post-operative day

complication is regard to urinary retention ($P = 0.02$), constipation ($P = 0.02$), and bleeding ($P = 0.1$) (Table 5 and Graph 4).

Assessment of Pain

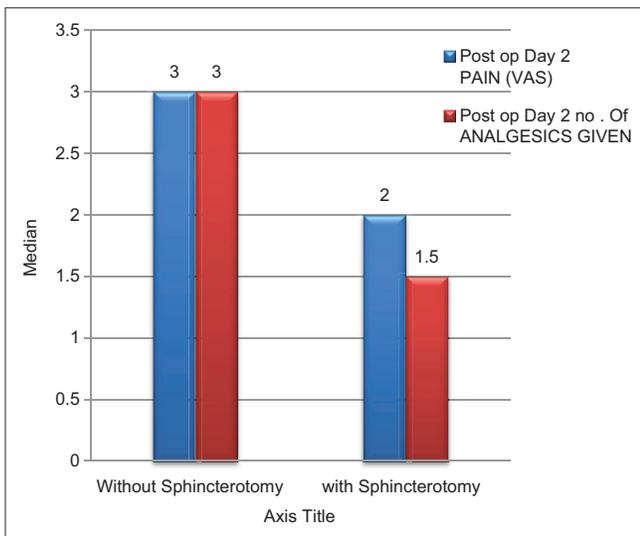
On POD-2, pain in without sphincterotomy group ($P < 0.001$) for VAS and number of Analgesics given was significantly more than with sphincterotomy group (Table 6 and Graph 5).

Assessment of Complications

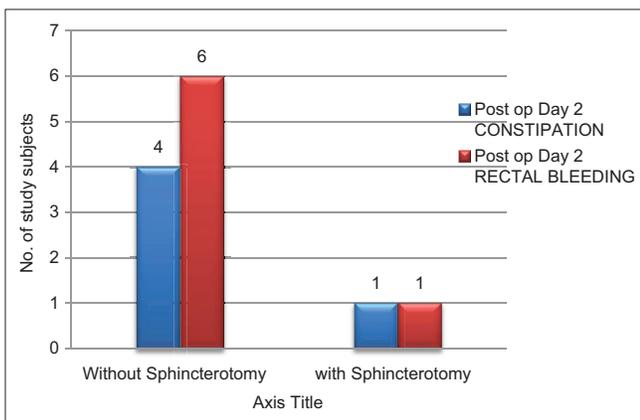
On POD-2, constipation ($P = 0.2$), rectal bleeding ($P = 0.05$) were significantly more in without sphincterotomy group when compared to with sphincterotomy group (Table 7 and Graph 6).

In our study, as mentioned, assessment of pain was carried out with two variables,

1. VAS
2. Number of analgesics administered.



Graph 5: Post-operative - day - 2 assessment of pain



Graph 6: Post-operative - day - 2 assessment of complications

On comparison, using both variables in patients of both groups, i.e. with sphincterotomy and without sphincterotomy in open hememorrhoidectomy, it was found that pain was significantly lesser in with sphincterotomy group ($P < 0.01$) on POD 1, 2, 7, 1 week and 2 weeks.

The patients undergoing open hemorrhoidectomy with sphincterotomy had early relief of pain when compared to patients undergoing open hemorrhoidectomy without sphincterotomy (Table 8 and Graph 7).

In our study, on comparing both the groups, i.e., with and without sphincterotomy post open hamemorrhoidectomy, it was found that post-operative rectal bleeding was significantly more in without sphincterotomy group (Table 9 and Graph 8).

Table 6: Post-operative - day - 2 assessment of pain

Pain	Group						P
	Without sphincterotomy			With sphincterotomy			
	Mean	SD	Median	Mean	SD	Median	
POD-2 - Pain (VAS)	3.66	1.30	3.00	1.96	1.23	2.00	<0.001
POD-2 - Pain (analgesics given)	2.68	0.68	3.00	1.58	0.73	1.50	<0.001

VAS: Visual analogue scale, POD: Post-operative day, SD: Standard deviation

Table 7: Post-operative - day - 2: Assessment of complications

Complications	Group (n (%))		P
	Without sphincterotomy	With sphincterotomy	
POD-2 - Constipation			
No	46 (92.0)	49 (98.0)	0.2
Yes	4 (8.0)	1 (2.0)	
POD-2 - Rectal bleeding			
No	44 (88.0)	49 (98.0)	0.05
Yes	6 (12.0)	1 (2.0)	

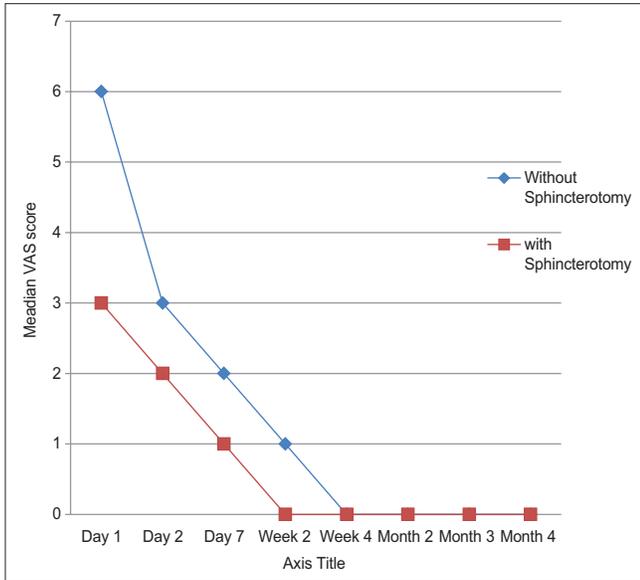
POD: Post-operative day

Table 8: Assessment of post-operative pain

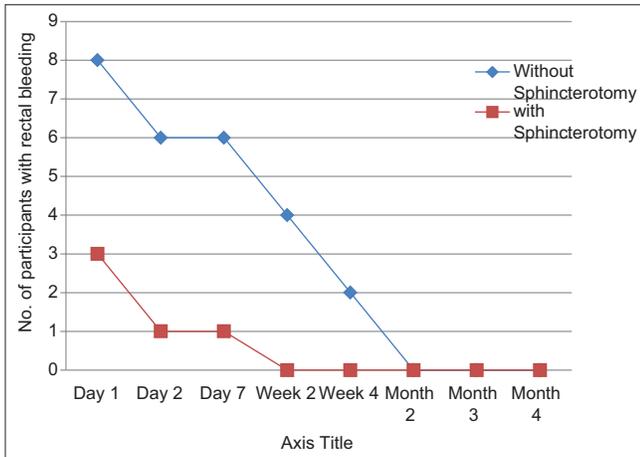
VAS	Group						P
	Without sphincterotomy			With sphincterotomy			
	Mean	SD	Median	Mean	SD	Median	
POD-1 - Pain	6.24	2.11	6.00	3.94	1.88	3.00	<0.001
POD-2 - Pain	3.66	1.30	3.00	1.96	1.23	2.00	<0.001
POD-7 - Pain	2.0	0.9	2.0	0.7	0.6	1.0	<0.001
2 weeks - Pain	1.18	0.87	1.00	0.18	0.44	0.00	<0.001
4 weeks - Pain	0.20	0.49	0.00	0.00	0.00	0.00	NS
2 months - Pain	0.10	0.36	0.00	0.00	0.00	0.00	NS
3 months - Pain	0.06	0.24	0.00	0.00	0.00	0.00	NS
4 months - Pain	0.00	0.00	0.00	0.00	0.00	0.00	NS

VAS: Visual analogue scale, POD: Post-operative day, SD: Standard deviation

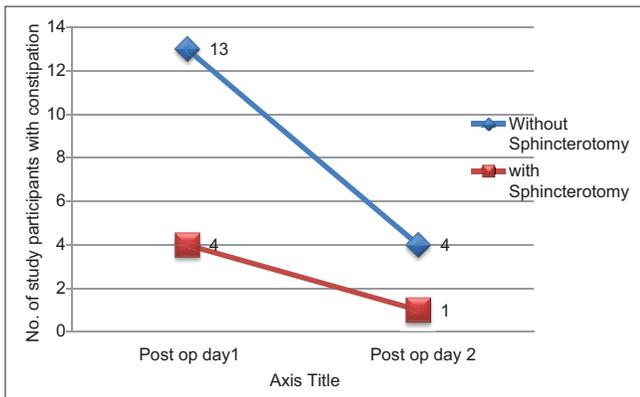
POD-1 ($P = 0.1$)
 POD-2 ($P = 0.05$)
 POD-7 ($P = 0.05$)
 Post-operative 2 weeks (0.02)
 Post-operative 4 weeks (0.2)



Graph 7: Assessment of post-operative pain



Graph 8: Assessment of post-operative rectal bleeding



Graph 9: Assessment of post-operative constipation

In our study, postoperatively, patients had constipation only in the early post-operative period, i.e. POD-1 and day 2.

On comparing both the groups, it was found that patients who underwent hemorrhoidectomy with sphincterotomy had significantly lesser episode of post-operative

Table 9: Assessment of post-operative rectal bleeding

Rectal bleeding	Group (n (%))		P
	Without sphincterotomy	With sphincterotomy	
POD-1			
No	42 (84.0)	47 (94.0)	0.1
Yes	8 (16.0)	3 (6.0)	
POD-2			
No	44 (88.0)	49 (98.0)	0.05
Yes	6 (12.0)	1 (2.0)	
POD-7			
No	44 (88.0)	49 (98.0)	0.05
Yes	6 (12.0)	1 (2.0)	
2 weeks			
No	46 (92.0)	50 (100.0)	0.02
Yes	4 (8.0)	0 (0)	
4 weeks			
No	48 (96.0)	50 (100.0)	0.2
Yes	2 (4.0)	0 (0)	
2 months			
No	50 (100.0)	50 (100.0)	NS
Yes	0 (0)	0 (0)	
3 months			
No	50 (100.0)	50 (100.0)	NS
Yes	0 (0)	0 (0)	
4 months			
No	50 (100.0)	50 (100.0)	NS
Yes	0 (0)	0 (0)	

POD: Post-operative day

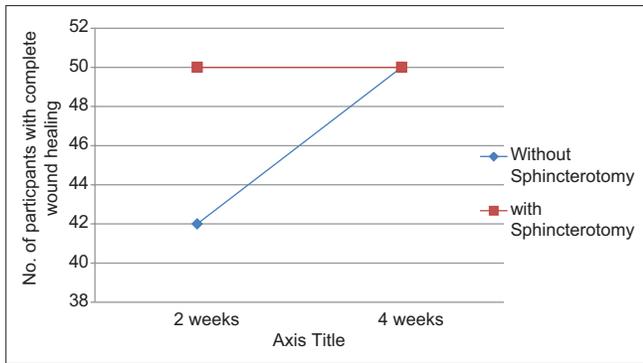
Table 10: Assessment of post-operative constipation

Constipation	Group (n (%))		P
	Without sphincterotomy	With sphincterotomy	
POD- 1- Constipation			
No	37 (74.0)	46 (92.0)	0.02
Yes	13 (26.0)	4 (8.0)	
POD-2 - Constipation			
No	46 (92.0)	49 (98.0)	0.2
Yes	4 (8.0)	1 (2.0)	

POD: Post-operative day

Table 11: Assessment of complete wound healing post-operative

Complete wound healing	Group (n (%))		P
	Without sphincterotomy	With sphincterotomy	
2 weeks			
No	8 (16.0)	0 (0)	0.003
Yes	42 (84.0)	50 (100.0)	
4 weeks			
No	42 (84.0)	50 (100.0)	0.003
Yes	8 (16.0)	0 (0)	



Graph 10: Assessment of complete wound healing post-operative

constipation (Table 10 and Graph 9). POD-1 ($P = 0.02$) and POD-2 ($P = 0.2$).

In our study, on comparing open hemorrhoidectomy with/without sphincterotomy for assessment of complete wound healing, it was found that the time taken for complete wound healing was significantly more ($P = 0.003$).

It also showed that in patients who underwent sphincterotomy, complete wound healing occurred by 2 weeks (Table 11 and Graph 10).

DISCUSSION

Age and sex distribution

	Without sphincterotomy		With sphincterotomy	
	Present study	Das et al. ¹²	Present study	Das et al. ¹²
Mean age	38.5	36	39.5	37.5
Male/female ratio	22/28	21/29	17/8	14/11

The age and sex distribution among the study group were compared with a study done by Das et al.¹² In my study, the mean age at presentation was about 2 years more than that of the compared study. The male: female ratio was almost similar in my study, whereas in the compared study males were more than females.

Post-operative pain

	Without sphincterotomy		With sphincterotomy	
	Present study	Das et al. ¹²	Present study	Das et al. ¹²
Number of patients	50	25	50	25
Mean pain score	2.0	2.32	1.23	1.60

In my study, the total number of patients in control and study group were more when compared to the study carried out by Das et al.¹² The mean pain score in my study was comparatively

lesser in the with sphincterotomy group. Furthermore, in my study, post-operative pain was statistically significant for the initial post-operative period in with sphincterotomy group, but in the later follow-up period, it was not significant. Therefore, hemorrhoidectomy with sphincterotomy post-operative pain was significantly lesser when compared to hemorrhoidectomy without sphincterotomy.

Complications

	Without sphincterotomy		With sphincterotomy	
	Present study	Das et al. ¹²	Present study	Das et al. ¹²
Urinary retention	14	8	5	1
Constipation	17	8	5	3
Rectal bleeding	10	Nil	5	Nil
Incontinence	Nil	2	Nil	Nil
Anal stenosis	Nil	Nil	Nil	1

In my study, on comparing the complications in the post-operative period, in both groups, it was found that patients undergoing hemorrhoidectomy without sphincterotomy had significantly more complications when compared to with sphincterotomy group.

Furthermore, in my study, no patients experienced any of the late complications such as incontinence or anal stenosis, whereas in the study conducted by Das et al.,¹² 2 patients in without sphincterotomy group had flatus incontinence and 1 patient in with sphincterotomy group had anal stenosis.

Complete wound healing (%)

	Without sphincterotomy		With sphincterotomy	
	Present study	Das et al. ¹²	Present study	Das et al. ¹²
Post-operative 2 weeks	84	80	100	100
Post-operative 4 weeks	16	20	-	-

Healing rates following with/without sphincterotomy after hemorrhoidectomy were compared between my study and the study conducted by Das et al.¹² In the follow-up period post-operative, it was found that Complete wound healing occurred by 2 weeks in with sphincterotomy group of both the studies. Thus, on comparison, healing rate was higher and early in hemorrhoidectomy with sphincterotomy group in my study as well as the study conducted by Das et al.¹²

CONCLUSION

Hemorrhoids is one of the oldest diseases known to mankind causing significant discomfort to the patient. The most common clinical presentations being bleeding and

mass per rectum. The most common surgical procedure for the treatment of hemorrhoids is Milligan Morgan or open hemorrhoidectomy.

Post-operative pain and delayed wound healing is of concern, post-open hemorrhoidectomy, and hence the study was done to compare the above procedure with the addition of internal sphincterotomy, with respect to post-operative pain, post-operative complications and wound healing.

The results of the study conclude that post-operative pain, post-operative complications were lesser in open hemorrhoidectomy with internal sphincterotomy, with early wound healing.

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How to cite this article: Harish S, Sringeri RR, Ajay G. Routine Internal Sphincterotomy with Hemorrhoidectomy: A Prospective Study. *Int J Sci Stud* 2016;3 (11):182-188.

Source of Support: Nil, **Conflict of Interest:** None declared.

Clinico-Etiological Profile and Outcome of Neonatal Respiratory Distress

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Abstract

Introduction: Respiratory distress (RD) syndrome is a common cause of admission in the neonatal unit. It poses a diagnostic dilemma. Early recognition of RD and initiation of appropriate treatment is important to ensure optimal outcomes. RD is one of the most common causes of morbidity in newborn.

Aims and Objectives: (i) To study clinical profile of neonatal RD (NRD), (ii) to find out most common etiology of RD in newborn, (iii) to assess the immediate clinical outcome of RD in our neonatal intensive care unit (NICU).

Materials and Methods: A prospective study was conducted at Kannur Medical College Kannur from January 2015 to July 2015 and study includes 102 cases. Term, pre-term and post-term babies both in-borns and out-borns cases were included in the study.

Results and Discussion: The study showed among the 300 newborns admitted in NICU, 102 (34 %) cases were admitted with RD. Of them, 61 babies (60%) were delivered vaginally and 41 (40%) by lower segment caesarean section. There were 44 (43%) pre-term babies, 56 (55%) term and 2 (2%) post-term neonates who were admitted with RD. The most common causes of NRD were transient tachypnea of newborn (TTN) 44%. The majority of cases clinically presented with tachypnea, flaring of alae nasi, and chest indrawing. The RD resolved on the 4th day in majority of cases.

Conclusion: Increased respiratory rate along with chest in drawing or grunt was the presentation of RD in the majority of cases. The survival rate was 98% among RD cases admitted to NICU. TTN was the most common cause and was observed maximally in babies delivered vaginally (70%).

Key words: Hyaline membrane disease, Neonatal respiratory distress, Transient tachypnea of newborn

INTRODUCTION

Respiratory distress (RD) is a challenging problem and is one of the most common causes of admission in neonatal intensive care unit (NICU).¹ The neonatal mortality rate varies by state but, overall, it is reported to be 39 a 1000 live births in India.² Neonatal period is a very vulnerable period of life due to many problems which can occur. Most of the causes of neonatal morbidity and mortality are preventable.³ The

common causes of RD in neonates includes transient tachypnea of the newborn (TTN), hyaline membrane disease (HMD), birth asphyxia, pneumonia, meconium aspiration syndrome (MAS), and other miscellaneous causes.^{4,5}

Since the millennium development goals (MDG) were formed, progress toward reducing child mortality has accelerated but remains insufficient to achieve MDG4. In particular, global progress toward reducing neonatal deaths that is deaths during the first 28 days of life has been slow and neonatal deaths now account for a greater proportion of child deaths than in 1990. India accounts for 27.3% of total neonatal deaths in the world. Distress NRD is ranging from 2.2% to 7.6% in developed countries and from 0.7% to 8.3% in India.⁶ It is caused by the delay in the absorption of fluid in the lungs after birth (i.e. excessive lung fluid).⁷

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Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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Aims and Objectives

The present study was planned to: (i) Find the commonest causes of RD in neonates brought to a referral NICU, (ii) evaluate clinical signs, and (iii) to find out immediate outcome of a neonate who were admitted in the NICU with RD.

MATERIALS AND METHODS

Study Design

A prospective study was conducted at Kannur Medical College Anjarakandy, and study included 102 cases of neonates who were admitted in NICU from January 2015 to June 2015. After obtaining permission from the head of the institute and taking informed consent from parents of the baby/guardian, they were enrolled in the study. Ethical clearance was obtained from Institutional Ethical Committee. Data were entered and analyzed using excel spreadsheet.

Inclusion Criteria

Both in-born and out-born neonate admitted to NICU with RD.

Exclusion Criteria

- Babies more than 28 days
- Babies <28 weeks of age.

Data Collection

Neonates were classified as term, pre- and post-term were enrolled as cases with RD on the basis of clinical profile. A detailed proforma including name, age, sex, and residence was obtained. Neonatal data recorded includes weight of the baby, gestational age, mode of delivery, APGAR score, if available, the need for resuscitation after birth, onset of RD and resolution of RD. Factors related to labor and deliveries were assessed including type of delivery normal vaginal or C-section. Elective or emergency, place of delivery, (any associated complications like; prolonged rupture of the membrane more than 24 h, prolonged labor, meconium stained liquor, antepartum hemorrhage and others). Maternal information was recorded including age, parity and any systemic diseases.

Other risk factors include delivery prior to 38 weeks of gestation, male sex, low birth weight and macrosomia^{8,9} and maternal diseases such gestational diabetes and asthma.^{8,9}

The cases were diagnosed clinically by the presence of at least 2 of the following criteria, namely RR of 60/min or more, subcostal in the drawing, and retraction, suprasternal in drawing, flaring of alae nasi, expiratory grunt and cyanosis. The diagnosis of clinical conditions producing RD was based mainly on careful scrutiny of the history, clinical and radiological findings. Continuous

monitoring of oxygen saturation was done using pulse oxymeter. The arterial blood gas (ABG) analysis was done frequently in unstable babies and with changes in ventilator settings. Blood glucose was monitored regularly using the dextrostix, sepsis workup was done when clinically indicated, endotracheal tube and blood culture sensitivity were ordered if septicemia or pneumonia was suspected as per guidelines baby was mechanically ventilated, and modified the settings according to ABG analysis.

RESULTS

Of the 102 (34%) cases admitted with RD, 61 babies (60%) were delivered vaginally and 41 (40%) by lower segment caesarean section (LSCS) (Table 1).

There were 67 (65%) males and 35 (34%) females in the study (Figure 1).

There were 44 (43%) pre-term babies, 56 (55%) term and 2 (2%) post-term neonates who were admitted with RD (Table 2).

DISCUSSION

The study shows that 67 cases (65%) were males and 35 (34%) were females. Present study observed that male sex is a risk factor for RD syndrome (RDS), another study done by Sarnakar *et al.* demonstrated that male sex is a risk factor for RD. It was also found that vaginally delivered babies (60%)

Table 1: Mode of delivery

Admissions	N (%)
Vaginal	61 (60)
C-section	41 (40)
Total	102 (100)

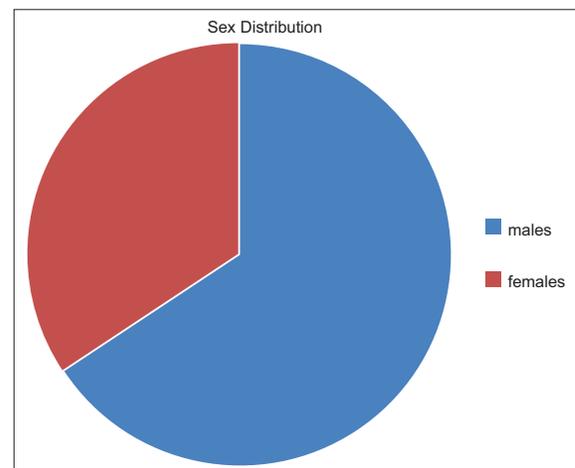


Figure 1: Gender-wise distribution

Table 2: Gestational wise distribution

Gestation	N (%)
Pre-term	44 (43)
Term	56 (55)
Post-term	2 (2)
Total	102 (100)

Table 3: Maternal risk factors of NRD

Maternal risk factors	N (%)
PROM	11 (11)
HT	5 (5)
MSAF	5 (5)
Maternal pyrexia	5 (5)
Foul smelling liquor	2 (2)
DM	1 (1)

NRD: Neonatal respiratory distress, PROM: Premature rupture of membranes, MSAF: Meconium-stained amniotic fluid, HT: Hypertension, DM: Diabetes mellitus

Table 4: Symptoms and signs of respiratory distress

Signs and symptoms	N (%)
Tachypnea	83 (81)
Flaring of alae nasi	82 (80)
Chest in drawing	83 (81)
Grunting	42 (41)
Cyanosis	42 (41)

Table 5: Onset of respiratory distress

Onset	N (%)
24 h	82 (80)
48 h	14 (14)
72 h	5 (5)
>72 h	1 (1)

Table 6: Etiology of RD

Diagnosis	N (%)
TTN	45 (44)
RDS	25 (24)
Sepsis	14 (13)
Birth asphyxia	10 (10)
MAS	5 (5)
CCHD (TGA)	1 (1)
Pneumothorax	1 (1)
Pneumonia	1 (1)
Total	102 (100)

RD: Respiratory distress, MAS: Meconium aspiration syndrome, RDS: Respiratory distress syndrome, CCHD: Critical congenital heart disease, TGA: Transposition of great artery, TTN: Transient tachypnoea of the newborn

Table 7: Distribution of outcome of RD

Outcome	N (%)
Survived	100 (98)
Deaths	2 (2)
Total	102 (100)

RD: Respiratory distress

had RD more when compared to LSCS babies (40%). 43% cases of RDS were pre-terms of 34-36 weeks of gestation, 55% term, and 2% post-term babies. The most common cause of NRD were TTN (44%) RDS (24%), sepsis (13%), birth asphyxia (10%), MAS (5%), and others (3%) similar study done Santhosh *et al.* in their study showed 39% term and 61% pre-term neonates who were developed RD in newborn. the incidence of MAS in developed countries is on the decline possibly due to improved obstetric care.¹⁰ Pneumothorax usually develops secondary to an underlying disease process but can occur spontaneously in 1% of newborns around the perinatal period, although only about 10% of these are symptomatic.¹¹ Similar study done by Sarnakar *et al.* the most common causes of RD in their study were TTN 40.7%, followed by RDS 17.2%, birth asphyxia 11.4% and MAS 9.3%.^{11,18} and present study observed that most of the cases developed RD at time of birth (80%) followed by 1st day (14%), 2nd day (5%), and 3rd day (1%). The RD resolved on the 2nd day (29%) and 3rd day (27%). However, it took more than 4 days to resolve in 41% of cases. There were 2 deaths (2%) and one case was referred to higher center. The majority of cases 83 (81%) presented with increased respiratory rate, chest in drawings. 82 (80%) babies had flaring of alae nasi. TTN babies develop an oxygen requirement that necessitates admission to the neonatal unit for a few days accounting for approximately 10% of all newborn term admissions.¹³ In a review of TTN, Yurdakok suggests a genetic link between TTN and later onset asthma.¹⁴ A similar study done by Keerti *et al.* showed that of all the symptoms, grunting, flaring of alae nasi had high specificity for RD in newborn while tachypnea, chest retractions and difficulty in feeding has high sensitivity.^{12,15} Every year a significant number of term-born infants are admitted to neonatal units for management of their respiratory distress.¹⁵ And that the most common clinical presentations were tachypnea, flaring of alae nasi and chest retraction.¹ It was also observed that there was a male preponderance with a ratio more than 1.5:1.^{1,7-9} And showed inversely proportional to gestational age and birth weight, and C section can favor the onset of RD in newborns.¹⁵ Study conducted by Ravindra *et al.* they observed that the most common causes for mortality were prematurity (42.1%) and RDS (Tables 3-7).¹⁶⁻¹⁸

CONCLUSION

Increased respiratory rate along with chest in drawing, flaring of alae nasi are the presentation of RD in majority of cases. Most common causes of RD were TTN, RDS, birth asphyxia and MAS. The survival rate was 98% among RD cases admitted to NICU. TTN was the commonest cause and observed maximally in babies delivered vaginally (70%) in all infants presenting with RD. The most common cause of death was pre-term with HMD.

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How to cite this article: Barkiya SM, Venugopal N, Kumari V. Clinico-Etiological Profile and Outcome of Neonatal Respiratory Distress. *Int J Sci Stud* 2016;3(11):189-192.

Source of Support: Nil, **Conflict of Interest:** None declared.

Membranoproliferative Glomerulo Nephritis Common Glomerular Disease - Changing Pattern of Biopsy Proven Renal Disease in a Tertiary Care Hospital

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Abstract

Introduction: Glomerular diseases are common causes of all renal syndromes including acute renal failure, chronic renal failure, and end-stage renal diseases, and thus they lead to increased morbidity and mortality worldwide. Hence making a definitive diagnosis in the initial stages of these glomerular disease helps in better management. Among glomerular diseases, there is a changing trend in the incidence worldwide and within India.

Materials and Methods: This is a retrospective analysis of kidney biopsies over a period of 1-year 3-month, from September 2014 to December 2015. A total of 60 kidney biopsies were included in the analysis.

Results: The most common indication of kidney biopsy was a nephritic syndrome. The most common histopathology was membranoproliferative glomerulonephritis (MPGN) which was seen in 21 biopsies that is the incidence of 35% among all kidney biopsy. Among the glomerular disease, MPGN was seen in 41%, the increased numbers can be due to varied etiologies including primary and secondary causes. Secondary causes include infections, connective tissue diseases, malignancies, hereditary and acquired complement factor and complement regulatory factor defects.

Conclusion: MPGN was commonest biopsy proven nephropathies in our study in contrast to other studies which have revealed it to be less. Study as concluded that immune complex mediated MPGN is common in study population which included adults.

Key words: Acute nephritic syndrome, Acute renal failure, Acute tubular necrosis, Chronic glomerulonephritis, C3 glomerulonephritis, Focal proliferative glomerular disease, Immunoglobulin A nephropathy, Lupus nephritis, Membranoproliferative glomerulonephritis, Membraneous nephropathy, Minimal change disease, Multiple myeloma, Nephrotic syndrome, Post-infectious glomerulonephritis, Rapidly progressive renal failure, and Rapidly progressive glomerulonephritis

INTRODUCTION

Membranoproliferative glomerulonephritis (MPGN) is third to fourth leading cause of chronic kidney disease (CKD) and end-stage renal disease (ESRD) worldwide.¹ Its presentation include from benign and slowly progressive to rapidly progressive glomerular

disease, it includes microscopic hematuria and non-nephrotic proteinuria (35%), nephrotic syndrome (NS) (35%), chronically progressive GN (20%), and rapidly progressive glomerulonephritis (RPGN) (10%).² We have analyzed the clinical presentations, clinical syndromes, clinicopathological correlation, and prognosis in these subjects and this analysis is very important since MPGN is one of the common cause of ESRD all over the world and the recurrence rate is very high following renal transplantation, especially for Type 11 MPGN.³ Hence, early renal biopsy, and optimal treatment would decrease the burden of ESRD in these subjects. MPGN is traditionally classified into three subtypes on the basis of pathological features identified by light, immune fluorescence, and

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Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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electron microscopy (EM). Type I MPGN is characterized by subendothelial deposits in the capillary wall. In Type II MPGN, elongated electron dense densities are seen within the glomerular, tubular and Bowman's capsular basement membrane. It is also referred to as "linear dense deposit disease." In Type III MPGN, there are many subepithelial as well as subendothelial deposits.^{4,5} New classification is according to type of deposits - immune complex associated MPGN and complement associated MPGN.⁶

MATERIALS AND METHODS

Kidney biopsies performed in our institute from September 2014 to December 2015 were retrospectively analyzed.

Inclusion Criteria

All adult patients with an indication to do a renal biopsy.

Exclusion Criteria

Biopsies of the native kidney with other diagnosis other than MPGN, transplant kidney, tumor, and inconclusive results.

Details for each patient: Name, age, sex, indication for renal biopsy, histopathological diagnosis, various type of MPGN like immunoglobulin or complemented mediated, primary or secondary form of MPGN and laboratory investigations such as serum creatinine, 24-h urinary protein, urine microscopy, virology (hepatitis B surface antigen [HBsAg], anti-hepatitis C virus [HCV], HIV), and serology (anti-dsDNA antibody, antinuclear antibody), C3, C4 were recorded. Renal biopsy specimens were analyzed by pathologist. Analysis included light microscopy and immunofluorescence (IF). EM was done whenever it was indicated. Indications for renal biopsy were: NS, acute nephritic syndrome, asymptomatic urinary abnormalities, hematuria, non-recovering acute renal failure (ARF), chronic renal failure (if biopsy was feasible), and rapidly progressive renal failure, RPGN. Automated biopsy guns were used to do biopsy. Data were analyzed and compared with studies published from India and different regions of the world.

Statistical Analysis

Simple descriptive statistics such as median and mean \pm standard deviation were used for variables such as age, clinical, and laboratory features. Percentage was used for categorical data.

RESULTS

Among all renal pathologies in 60 patients primary glomerulonephritis (PGN) is the most predominant renal disease as analyzed in our study, followed by secondary

glomerulonephritis (SGN) and tubulointerstitial nephritis. The vascular diseases are less frequent. MPGN was the common manifestation of both PGN and SGN.

Of the 21 patients with MPGN, 18 (86%) patients had immune complex associated MPGN, and 3 (14%) had complement associated MPGN. 15 (71%) patients had primary MPGN, and 6 (25%) had secondary MPGN. Mean age (years) at presentation was 41 ± 6.4 for immune complex associated MPGN and 32 ± 5.6 for complement associated MPGN. Since our center does not include pediatric patients we did not have pediatric patients. Male to female ratio in an immune complex associated MPGN was 1:1.5 and for complement associated MPGN it was 1:0. Of 21 cases 6 patients had secondary MPGN, three had lupus nephritis (LN), one had multiple myeloma (MM), one had HBsAg positive and one patient had chronic osteomyelitis (Table 1).

The most common clinical syndrome was a nephritic syndrome, in an immune complex associated MPGN it was 50% and in complement associated MPGN it was 33.3% similarly in this category ARF, CKD were also equally seen. However, in an immune complex associated MPGN ARF incidence was 16.6%, CKD incidence was 16.6%, NS was 33.3%, and RPGN 22%. Hypertension was very common in these patients it was seen in 89% of immune complex associated MPGN and 66.6% in complement associated MPGN. All patients who presented with RPGN had crescentic glomerulonephritis. All patients with CKD had significant glomerular sclerosis and interstitial fibrosis and tubular atrophy. Other than CKD only 2 patients had interstitial fibrosis and tubular atrophy of 5-10% only (Table 2).

Most common histopathology finding was hypercellularity and lobularity of the glomeruli (85%), followed by a double contoured basement membrane (73%). Based on immunofluorescence MPGN are classified, immune complex associated MPGN (86%)

Table 1: Clinical characteristics of the patients at presentation according to MPGN type

Characteristics	Immune complex associated MPGN	Complement associated MPGN
Age (years) (mean)	41 \pm 6.4	32 \pm 5.6
Male/female (ratio) (%)	1:1.5 (38/62%)	1:0 (100/0%)
Hypertension <i>n</i> (%)	16 (89)	2 (66.6)
Nephritic <i>n</i> (%)	9 (50)	1 (33.3)
Nephrotic <i>n</i> (%)	6 (33.3)	0 (0)
ARF <i>n</i> (%)	3 (16.6)	1 (33.3)
CKD <i>n</i> (%)	3 (16.6)	1 (33.3)
RPGN <i>n</i> (%)	4 (22)	0 (0)

MPGN: Membranoproliferative glomerulonephritis, ARF: Acute renal failure, CKD: Chronic kidney disease, RPGN: Rapidly progressive glomerulonephritis

and complement associated MPGN (14%). 100% biopsy specimen had C3 positivity; that is C3 deposit in glomeruli capillary and mesangium was the most common deposit. Immunoglobulin G (IgG) was positive in 85%, IgM was positive in 76%, C1q deposits in 60%, least common deposits were IgA in 18%.

Though it is seen that full house pattern (IgG, IgM, IgA, C3, C1q) is common in LN, in our study, it is seen in 100% of LN but two primary MPGN cases also had full house pattern.

Figure 1 shows the histopathology in MPGN, hematoxylin and eosin stain showing hypercellular and lobulated glomeruli with fibrocellular crescent, atrophied tubules are also seen.

After definitive diagnosis by renal biopsy, treatment was started. Among 15 primary MPGN, 4 CKD patients were not on any immunosuppression, three of these CKD patients are not on dialysis and one is dialysis dependent. In remaining 11 patients, crescentic glomerulonephritis

Table 2: Histopathological and IF characteristics at presentation seen in MPGN patients

Hypercellularity and lobularity of glomeruli	85%
Double contoured basement membrane	73%
Crescents in glomeruli	19%
Interstitial fibrosis and tubular atrophy	28%
Obsolescent glomeruli	33%
Full house pattern	24% (100% in 3 LN case and 2 case among primary MPGN)
IgG deposits	85%
IgM deposits	76%
IgA deposits	18%
C3 deposits	100%
C1q deposits	60%

IF: Immunofluorescence, IgG: Immunoglobulin G, MPGN: Membranoproliferative glomerulonephritis, LN: Lupus nephritis

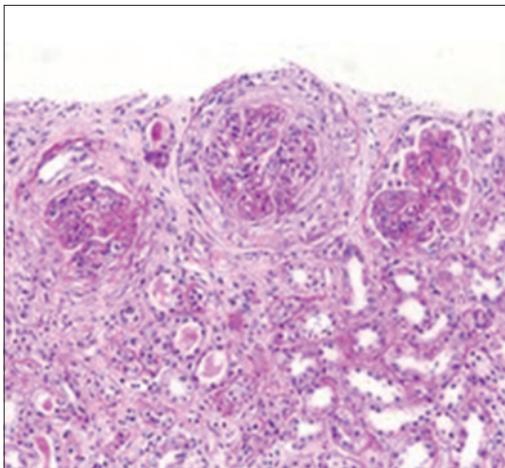


Figure 1: Histopathology in membranoproliferative glomerulonephritis

patients were started treatment with cyclophosphamide followed by steroids. All other cases are on treatment with steroids and mycophenolate. Among secondary causes of MPGN, MM case referred to an oncologist for further management. Chronic osteomyelitis with MPGN case is dialysis dependent, HBsAg case is on antiviral and steroids, among the LN cases one patient died, and other two are on immunosuppression treatment.

DISCUSSION

MPGN is also called mesangiocapillary GN. MPGN may be idiopathic or secondary. Secondary causes include: (1) Immune complex mediated, and (2) complement-mediated causes.⁶

1. Immune complex associated condition include:
 - a. Infection
 - b. Autoimmune or rheumatological diseases
 - c. Malignancy.
 - Infections: HCV (70-90% of patients), bacterial endocarditis, chronic hepatitis B viral infection, abscess, infected ventriculoatrial shunt, human immunodeficiency virus; hantavirus malarial (*Plasmodium malariae*), schistosomal infections, chronic fungal infection can cause MPGN
 - Collagen vascular disease: Systemic lupus erythematosus, Sjögren's syndrome
 - Malignancy: Chronic lymphocytic leukemia, non-Hodgkin's lymphoma, light chain deposition diseases like MM.⁶⁻⁸
2. Complement-mediated MPGN includes hereditary complement deficiency (C1q, C2, C4, or C3), acquired complement deficiency (presence of C4 nephritic factor), associated with factor H defect or autoantibodies to factor H. This type MPGN can be associated with or without partial lipodystrophy and retinal abnormalities.⁶⁻⁸

In immune-complex-mediated MPGN. Deposition of immune complexes in the glomeruli occurs due to persistent antigenemia. This leads to antigen-antibody immune complexes formation. Elevated levels of circulating immune complexes occur in chronic infections, autoimmune diseases, and paraproteinemias due to monoclonal gammopathies. These immune complexes trigger the activation of the classical pathway of complement and cause deposition of complement factors of the classical pathway and terminal complement pathway in the mesangium and along the capillary walls. A kidney biopsy specimen typically shows both immunoglobulin and complement on IF microscopy.⁶⁻⁸

Complement-mediated MPGN. The complement cascade plays an important role in innate immunity. Complement

factors can induce a potent inflammatory response that results in phagocyte chemotaxis, with opsonization and lysis of cells, including microorganisms. Complement activation occurs through the classical, lectin, or alternative pathways, all of which converge to form C3 convertase, which cleaves C3 into C3a and C3b. C3b, in the presence of factor B and factor D, associates with C3 convertase, generating even more C3 convertase and results in a potent amplification of the inflammatory loop. Thus, C3 convertase is a nodal point in the complement cascade. The association of C3b and C3 convertase also results in the formation of C5 convertase, which activates the terminal complement complex pathway and the formation of the membrane attack complex (C5b-C9) on cell surfaces, thereby resulting in lysis including damage to cell membranes such as the glomerular basement membrane as well as membranes of pathogenic microorganisms. To prevent self-damage, activation of the alternative pathway occurs in a tightly regulated, sequential manner. Multiple complement-regulating and complement-inhibiting proteins operate at different levels of the cascade, particularly at the C3 and C5 convertase level. Such regulators include factors H and I and factor B, decay-accelerating factor (CD55), membrane cofactor protein. Hence, either defect in these complement regulator proteins or autoantibodies to these regulatory proteins causes unregulated complement activation and damage to glomeruli.⁶

In our study the most common type of MPGN was immune complex mediated. Hence, the incidence of the complement mediated condition is rare, only three out of 21 case had this type of MPGN. This may be due to the study population in our study include only adults and complement-mediated MPGN are common in children and adolescents. We can conclude that inherited defect, mutations and autoantibodies to complement regulatory proteins are rare in the adult population. In contrast, to this entity the overall MPGN was very high in contrast to most studies which reveal it to be 7-10%^{1,2} in our study, it is 35%. Compared to complement-mediated MPGN immune complex MPGN was the predominant category, 85% of the MPGN in the study population. Again the secondary causes were seen in only 6 out of 21 patients, three cases of LN, one case of MM, one case associated with chronic osteomyelitis and one case with HBsAg positive.

Hence, there is an increased number of idiopathic MPGN. The high incidence in our study may be our institute is a tertiary care hospital which provides medical service to low

socioeconomic class of people. These patients are prone for persistent subclinical and clinical chronic infections which may lead to chronic antigenemia and immune complex activation and predispose them to develop MPGN. This emphasize that overall control and prevention of infection at this level of low socioeconomic class of people would decrease the incidence of MPGN in these people.

The main drawback of the study is it included a small group of people since it as analyzed over a period of 1-year 3-month, more longer duration of the study with more number of study group would give a better understanding of these cases of MPGN.

CONCLUSION

The study has highlighted the changing trend in the glomerular disease, MPGN being the most common disease. Since it appears to be related to chronic subclinical infection, most of these can be decreased by prevention of infection.

ACKNOWLEDGMENT

I acknowledge our deep sense of gratitude to Dr. Suchitra, Consultant Pathologist, JSS Medical College, Mysuru and all patients who underwent biopsy.

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How to cite this article: Himamani S. Membranoproliferative Glomerulo Nephritis Common Glomerular Disease - Changing Pattern of Biopsy Proven Renal Disease in a Tertiary Care Hospital. *Int J Sci Stud* 2016;3(11):193-196.

Source of Support: Nil, **Conflict of Interest:** None declared.

Clinico-Epidemiological Profile of Esophageal Cancer in Kashmir

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Abstract

Background: Esophageal cancer (EC) is a highly virulent disease with an aggressive clinical course. It is an endemic in many parts of the world, particularly in the developing nations. EC shows one of the widest geographical variations among all malignancies and is the eighth most common cancer worldwide. "Kashmir valley" has a high incidence of EC, which almost parallels the infamous "EC belt" of Central Asia. Squamous cell carcinoma remains the predominant histology of the developing world but over the years, western data suggests an increase in the incidence of adenocarcinoma.

Aim and Objective: To analyze the clinico-epidemiological profile of EC in Kashmir.

Materials and Methods: Profile of 345 patients, who presented to our outpatient department between July 2011 and July 2015, was analyzed, in a cross-sectional study with regards to their demographic and clinical profile.

Results: EC is still a predominant disease of developing nations, affecting mostly the elderly and rural population. Advanced disease is seen mostly in the population of low socio-economic status and males outnumber females at every stage of the disease. Various demographic parameters seem to affect the presenting stage of the disease.

Conclusion: Old age, male sex, and low socio-economic status coupled with peculiar dietary habits within an endemic geographical region seem to be the prime determinants affecting EC prevalence in a given population.

Key words: Epidemiology, Esophageal cancer, Incidence, Kashmir valley

INTRODUCTION

Esophageal cancer (EC) is the eighth most common cancer worldwide with a case fatality rate of 90%.¹ It is one of the malignancies with highest geographic, ethnic, and gender variations.² The high incidence areas of Linxian, China, Russia, and the Caspian region of Iran report incidences as high as 100/100,000 persons, whereas it is relatively

uncommon in the United States, where the lifetime risk of being diagnosed with the disease is reported to be <1%.³ In India, in states such as Karnataka, Tamil Nadu, Kerala, and Assam, EC is the most common gastrointestinal (GI) malignancy.⁴ EC has a high prevalence in Kashmir valley, but there are no population-based data available on its incidence.⁵

Esophageal carcinoma accounts for approximately 6% of all GI malignancies worldwide with most cases occurring in males, at a rate of 4:1 relative to females.⁶ It is the most common malignancy in Kashmir valley.⁷ Overall squamous cell carcinoma (SCC) is the most prevalent histology of EC worldwide^{8,9} but the last 20 years have witnessed an increase in the incidence of adenocarcinoma (ADC). This increase is more rapid than that for any other cancer.¹⁰

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Month of Submission : 11-2015
Month of Peer Review : 12-2015
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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There has been no consensus on the exact role of risk factors as causative agents in EC. Various factors, including tobacco consumption, unhealthy diet and diet deficient in trace elements, alkalinity of soil, genetic aberrations, and socio-economic status, have been implicated in the etiology of EC.^{11,12} SCC is predominantly seen in upper two-thirds of esophagus unlike ADC, which is seen in lower one-third. The outcome of EC has been dismal even with the advent of modern surgical and radiotherapy techniques, targeted molecules and newer chemotherapeutic agents, owing primarily to the late presentation of the disease. This study has been undertaken for a better understanding of the association between risk factors, clinical profile, and disease parameters in patients with cancer esophagus.

MATERIALS AND METHODS

This study was conducted in the Department of Radiation Oncology, Government Medical College Srinagar, from July 2011 to July 2015. A total of 345 patients who had histological documentation of EC were enrolled in the study. Data were then analyzed for clinico-demographic information such as age, sex, residence, dietary habits, tobacco or alcohol consumption, performance score, presenting symptoms and signs, and their correlation with disease parameters such as tumor location, histology, endoscopic morphology, grade, and stage of the disease. Patients were staged clinically or pathologically depending on the surgical status. Staging investigations included endoscopy, endoscopic ultrasound, and contrast-enhanced computed tomography scans including appropriate metastatic evaluation wherever indicated. TNM American Joint Committee on Cancer 2010 classification system was used for staging. Endoscopic morphology of the tumors was classified according to the “Guidelines for Clinical and Pathologic Studies on Carcinoma of the Esophagus.”¹³

RESULTS

345 patients with histological documentation of EC were enrolled over a period of 4-year from July 2011 to July 2015. The study included 212 males (61%) and 133 females (39%) in the ratio of 1.5:1. Median age of the patients was 62, and mean age was 58 years. The majority of the patients (51%) in both the sexes were above 60 years of age; with males and females constituting 52% and 50% of patients in their respective groups. 268 (77%) patients were from a rural background, of these 156 (58%) were males and 112 (42%) females. Around 45% patients belonged to “Kuppuswamy Socio-economic Class” scale (KSS) IV and V,¹⁴ which was statistically significant (0.002). Non-vegetarian diet was consumed by 339 (98%) patients of whom 208 (61%) were males and 131 (39%) females, and

the association was statistically significant ($P = 0.003$). 60 patients (18%) consumed smoked meat. 288 (83%) patients consumed tobacco of which 194 (67%) were males and 94 (33%) females; 235 (81%) belonged to rural areas while rest 53 (19%) to urban areas. 36 (12%) patients consumed more than one form of tobacco. In all the forms of tobacco consumption, males outnumbered females except “hookah” smoking which was prime mode of tobacco consumption in 57% females which was significant statistically ($P = 0.0002$). Only six (0.01%) patients consumed alcohol of which none was female. The majority of the patients in both the genders; 98 (46%) males and 70 (52%) females had “Eastern Cooperative Oncology Group” performance score (PS) of “I” at presentation (Table 1).

Overall dysphagia was the most common presenting symptom in both the sexes (78%), with 162 (76%) males and 109 (81%) females but patients with tumors located <20 cm had odynophagia as the prominent symptom (57%) (Table 2). Weight loss was the most common finding in males 129 (60%) as well as females 75 (56%) (Table 3).

Overall lower one-third (30-40 cm) was the most common site of disease location in both the sexes accounting for 161 (46%) of the total patients (which included 97/212 [45%] males and 64/133 [48%] females).

Table 1: Patient characteristics

Patient parameters	Male	Female
Gender	212	133
Age		
<40	7	2
40-60	94	65
>60	111	66
Residence		
Rural	156	112
Urban	56	21
Dietary habits		
Smoked non-veg	47	13
Cooked non-veg	161	118
Dried veg	1	1
Cooked veg	3	1
Tobacco consumption		
Cigarette	54	0
Hookah	79	77
Snuff	30	12
Combination	31	5
No consumption	18	39
Alcohol consumption		
Yes	6	0
No	206	133
Performance score		
0	60	33
I	98	70
II	52	26
III	2	4

Endoscopic morphology as classified by “JSED” revealed 5 males and 4 females in superficial carcinoma (tumor limited to mucosa, submucosa, and *in-situ* carcinoma) and 336 patients (207 males and 129 females) in advanced carcinoma. Of the advanced carcinomas, majority (171) (50%) patients had “ulcerated and localized” morphology. Ulcerative localized was the predominant morphology in all the stages (44%, 58%, 49%, and 48% in Stages I, II, III, and IV, respectively).

SCC was the most common histology with 340 patients, and only 5 patients had ADC. In both males 110 (61%) and

females 70 (39%), G2 was the most common histological grade.

Overall Stage III was the most common presenting stage with a total of 156 (45%) patients, comprising of 114 (53%) males and 42 (31%) females. 136 patients (87%) of the Stage III patients were from a rural background and over half 136 (51%) of patients from rural background had Stage III disease while as, majority 33 (43%) of urban patients had Stage II disease.

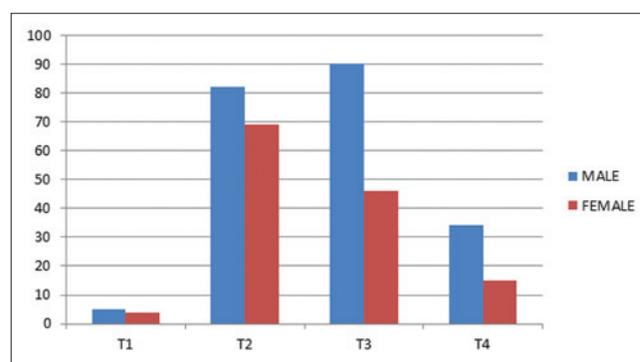
Males predominantly presented with T3 disease (42%) while females with T2 disease (51%) (Bar diagram 1). N1 was the predominant nodal stage in males (46%) as well as

Table 2: Patient symptomatology

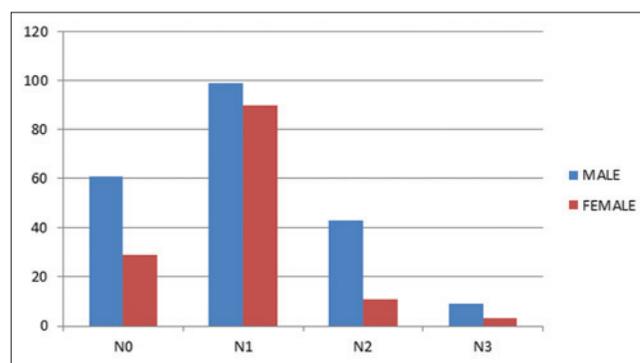
Presenting symptom	<20	20-25	25-30	30-40
Odynophagia	19	8	1	0
Vomiting	2	4	8	3
Dysphagia	11	15	100	145
Hematemesis	0	5	8	1
Melena	0	1	2	6
Loss of appetite	1	3	1	1

Table 3: Correlation of clinico-demographic profile with stage

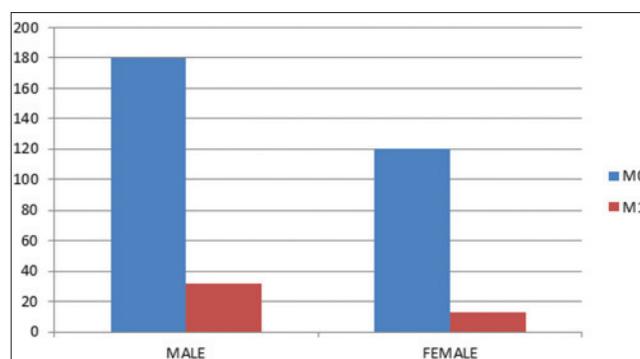
Patient parameters	Stage I	Stage II	Stage III	Stage IV
Gender				
Male	25	41	114	32
Female	18	60	42	13
Residence				
Rural	28	68	136	36
Urban	15	33	20	9
Socio-economic class				
I	11	11	7	8
II	14	31	28	5
III	9	27	43	6
IV	5	26	55	19
V	4	6	23	14
Presenting sign				
Anemia	14	27	53	9
Clinical lap	0	0	13	9
Weight loss	29	74	90	11
Abdominal lump	0	0	0	16
Endoscopic level				
<20	4	11	15	3
20-25	7	12	13	4
25-30	12	46	47	15
30-40	20	32	81	23
Histological grading				
G1	27	29	20	2
G2	6	55	104	15
G3	10	17	31	26
G4	0	0	1	2
Endoscopic appearance				
0-I	4			
0-II	2	1		
0-III	1	1		
Protruding	9	12	40	5
Ulcerative and localized	16	58	77	21
Ulcerative and infiltrating	7	15	22	8
Diffusely infiltrating	4	14	17	11



Bar diagram 1: T stage



Bar diagram 2: N stage



Bar diagram 3: M stage

females (67%) (Bar diagram 2). Stage IV was more common in, males (15%) (Bar diagram 3), rural population (13%), and patients with “KSS” scale of IV and V (Table 3).

On the whole, liver was the most common presenting site for distant metastasis with 22 (49%) patients, followed by lung 16 (38%), bone 5 (11%), and brain metastasis 1 (0.02%) patients. 19 (87%) of the patients with liver metastasis had a primary site located at 30-40 cm (Table 4).

DISCUSSION

The incidence of EC is rapidly increasing worldwide.¹⁵ Nearly two third of ECs in the United States are ADCs,¹⁶ whereas in Asian nations squamous cell cancer continues to be the major histological type.¹⁷ Esophageal cancer is predominantly a disease of the elderly, where nearly one third of the diagnosed patients are more than 75 years of age.¹⁸ The lifetime risk of EC is reported to be 0.8 for males and 0.3 for females and mean age of diagnosis is 67 years.¹⁹ The majority of the patients in our study were above 60 years age in both the sexes, with males outnumbering females in all age groups. About 90% of ECs worldwide occur in defined high incidence areas of low and middle-resource countries and economically deprived communities.²⁰ Most of the patients in our study were males, from a rural background with a low socio-economic status. Dysphagia is one of the earliest and predominant presenting symptoms of EC.²¹ Nearly 80% of the patients in our study has dysphagia as the most common presenting symptom though patients with tumor located <20 cm presented predominantly with odynophagia. Cancer esophagus is invariably associated with weight loss in nearly two-thirds of patients.²² 60% of our patients had associated weight loss.

Nearly three-fourths of all ADCs are found in the distal third of esophagus, whereas SCCs are more evenly distributed throughout the distal two-thirds;²³ however, in our study, distal one-third (30-40 cm) was the most common site in both the sexes. Higher incidence of distal EC in west may primarily be attributed to a higher incidence of ADCs. SCC still is the predominant histological subtype in Asian nations where most of the cases occur in middle or lower third.²³ Only five cases of ADCs were registered in our study population.

Table 4: Correlation of endoscopic level and metastatic site

Endoscopic level	Liver	Lung	Bone	Brain
<20	0	1	1	1
20-25	0	2	2	0
25-30	3	10	2	0
30-40	19	4	0	0

In a study conducted on nearly 400 EC patients in Japan, two most frequent morphological types were “ulcerative localized” and “ulcerated infiltrative” type (JSED Types 2 and 3).²⁴ Association of macroscopic appearance with histological types and subtypes was drawn, with polypoid types of “protruding superficial” and “advanced malignant” tumors reported to be “carcinosarcomas,” “SCC” or “malignant melanomas.” Plateau types of protruding tumors were usually “basaloid squamous” cell carcinomas, “adenoid cystic” carcinomas, “poorly differentiated” SCCs or ADCs. Predominantly, subepithelial types of protruding tumors were found to be small cell type undifferentiated carcinomas, basaloid SCCs or adenoid cystic carcinomas.²⁴ The appearance of lesions during endoscopy has been reported to be helpful in assessing the likelihood of lymph node metastasis. In particular, flat lesions are said to metastasize less likely to a lymph node than a depressed or elevated lesion.²⁵ In our analysis, ulcerative localized was the most common morphology and SCC was the most common histology in all the stages implying no correlation between endoscopic morphology and stage. Histological grade is known to affect lymph node metastasis. In a study by Bollschweiler *et al.*,²⁶ it was reported that G1/G2 histology was associated with a lower rate of lymph node metastasis compared with G3 in early EC. Our analysis revealed G2 to be the most common tumor grade overall, with the majority of G2 patients in Stage III.

Low socio-economic status and general deprivation have been proposed to be one of the many factors for high incidence of EC in Asian nations.²⁰ Close to half of the patients (44%) in our study had KS of IV and V and 88% of these (KS IV and V) patients were from rural background.

Approximately one-third of EC patients are loco-regionally advanced at presentation.¹⁶ Stage III was the most common presenting stage in our study with around 45% patients. Close analysis revealed that 85% of the total advanced Stage (III and IV) patients came from rural areas.

Lymph node metastasis in the range of 0-3%²⁷ and 26-50%^{28,29} have been seen in esophageal SCC invading the mucosal (T1a) and submucosal (T1b), respectively, whereas the rate of nodal involvement is 0-2% in cases of esophageal ADC invading the mucosa (T1a) and 27-41% in ADC with submucosal invasion (T1b).^{30,31} Lymph node metastasis is the single most important prognostic factor in EC.³²

Evaluation of the lymph node metastasis risk in association with the invasion depth was previously deemed necessary to predict prognosis and decide on the therapeutic modality.^{28,30} The prevalence of nodal metastasis has been

seen to correlate with T status and as per one data >50% nodal metastasis was seen with T2 invasion and all patients had lymph node metastasis with T4 invasion.^{33,34} In our study also, nodal stage was seen to increase with increasing T stage (T1 = 22%, T2 = 65%, T3 = 82%, and T4 = 100%). In the absence of nodal metastasis, the prognosis of EC has been seen to be related to T stage, histology, grade, and location of the tumor.²⁵ Relevant to our data, most of the Stage IV patients were men with distal esophagus being the most common site and liver being the most common site of metastasis. Patients having T3 and T4 disease were the most common among Stage IV cases.

We could not elucidate correlation between genetic factors and premalignant conditions with disease parameters of our patients due to lack of proper evidence for the same.^{35,36}

CONCLUSION

Old age, male sex, and low socio-economic status coupled with peculiar dietary habits within an endemic geographical region seem to be the prime determinants affecting EC prevalence in a given population. The fact that improvised treatment modalities have not changed the outcome of EC necessitates focusing on primordial prevention and early detection at a genetic level as the majority of patients still present with a locally advanced or advanced stage. The role of clinical and demographic parameters depicts mixed results when compared with data elsewhere. Old age, male sex, low socio-economic status, smoking and non-vegetarian diet, positive correlation of T stage with N and M stage, proclivity of distal EC for distant metastasis were the variables consistent with other literatures, whereas increasing incidence of ADC, higher stage with increasing grade of tumor, association of endoscopic morphology with disease stage, prevalence of premalignant pathologies were non-corroborative with world literature.

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How to cite this article: Mustafa SA, Banday SZ, Bhat MA, Patigaroo AR, Mir AW, Bhau KS. Clinico-Epidemiological Profile of Esophageal Cancer in Kashmir. *Int J Sci Stud* 2016;3(11):197-202.

Source of Support: Nil, **Conflict of Interest:** None declared.

Efficacy of Oral Vitamin K Compared to Injectable Vitamin K in Neonates

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Abstract

Introduction: According to guidelines of American Association of Pediatrics and Indian Association of Pediatrics, Vitamin K is routinely given immediately after delivery.

Aim of Study: This is a comparative study to evaluate the efficacy of oral Vitamin K and parenteral Vitamin K.

Materials and Methods: 150 breastfed infants weighing more than 2.5 kg were evaluated to find out the efficacy of different routes of administration of Vitamin K to prevent hemorrhagic disease of newborn. The babies were grouped into three. Group A was given 1 mg of Vitamin K intramuscular; Group B, 2 mg of Vitamin K orally; and Group C no Vitamin K. The prothrombin index was estimated in all babies.

Results: The prothrombin index was $94.98 \pm 7.64\%$, $95.08 \pm 9.91\%$, and $80.39 \pm 15.9\%$, respectively, among the three groups. The difference between Group A and B were insignificant ($P < 0.01$). However, in Group C, prothrombin index was reduced significantly as compared with other two groups ($P < 0.001$).

Conclusion: Oral Vitamin K is as effective as intramuscular Vitamin K and its usage can be recommended in our country to reduce complications and cost of parenteral therapy.

Key words: Hemorrhagic disease of newborn, Prothrombin index, Prothrombin time, Vitamin K

INTRODUCTION

Exclusive breastfeeding is recommended for all newborns and breast milk is a poor source of Vitamin K. Vitamin K is necessary for the modification and activation of coagulation factors namely II, VII, IX, and X. A newborn baby has poor bacterial flora which can synthesize Vitamin K.^{1,2} So, universally Vitamin K prophylaxis is recommended. Hemorrhagic disease of newborn (HDN) may be markedly reduced in the future since more and more mothers accept the recommendation of exclusive breastfeeding.

Unfortunately, there are not many studies regarding the efficacy of oral Vitamin K in our country to recommend

oral Vitamin K as prophylaxis for HDN. The American Academy of Pediatrics has recommended that Vitamin K is given as a single parenteral dose of 0.5 mg to 1 mg or an oral dose of 2 mg for the newborn infant.³

Mallik *et al.* done a study on the comparative efficacy of oral and injection Vitamin K and showed that oral Vitamin K is equally effective in preventing HDN.⁴ The present study was undertaken to evaluate the efficacy of oral Vitamin K preparation (menadione sodium bisulfite vs. injectable Vitamin K in preventing HDN in neonates.

MATERIALS AND METHODS

This prospective study was done in the post-natal wards of Kannur Medical College, Anjarakkandi, Kannur district, Kerala. It included 150 exclusively breastfed term neonates without any complications of delivery including birth asphyxia. Pre-term babies, small for gestational age babies, and babies with asphyxia and immediate neonatal problems were excluded from the study. After taking the informed

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www.ijss-sn.com

Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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consent from the parents, the neonates were randomly grouped into three categories. Group A included those babies who received 1 mg of intramuscular Vitamin K, Group B received 2 mg of oral Vitamin K, and Group C received no Vitamin K. The Vitamin K preparation used was menadione sodium bisulfite. Oral or injectable Vitamin K was given immediately after birth. Blood samples for prothrombin time by quicks one stage method⁵ were collected, and relevant data were recorded in pre-structured proforma.

Statistical Analysis

Statistical analysis is with the help of SPSS version 11. Data are analyzed by unpaired Student's *t*-test. *P* < 0.05 is considered significant.

RESULTS

The number of neonates studied was 150. The neonates were divided into three groups of 50 each. The mean weight of all neonates was 2.96 ± 0.35 kg. The birth weight of the babies in all groups ranged between 2.6 and 3.5 kg which was comparable and the sex distribution (M: F) in Group A, B, and C was 28:22, 26:24, and 25:25, respectively, i.e. the prothrombin index was nearly identical in Group A and B but was significantly lowered in Group C (at 5.5 level of significance).

Prothrombin index difference was not statistically significant among injectable Vitamin K and oral Vitamin K (*P* < 0.01), but the difference was significant between injectable Vitamin K and control group (*P* < 0.0001) and between oral Vitamin K and control group (*P* < 0.0001). Even though there was statistical significance between the control group and Vitamin K group but none of the babies in all the three groups have not developed any HDN clinically (Tables 1-3).

DISCUSSION

HDN is a potentially serious condition in the neonate resulting from transient deficiency of Vitamin K-dependent factors.⁶⁻⁸ The normal full term neonate is born with levels of Vitamin K dependent clotting factors that are low by adult standards (up to 50%). The levels further decrease rapidly reaching at a peak at 48-72 h especially in breastfed infants. This physiological post-natal decrease in a few infants results in HDN.⁹⁻¹¹ Various studies have shown normal prothrombin time ranging from 14.5 ± 1 s⁹ to 17.5 ± 3.2 s¹² in the newborn infant.

Many reports in the literature have shown that oral Vitamin K is as effective as injectable Vitamin K in

Table 1: Gender distribution of the study population

Group	Male	Female	Total
A	28	22	50
B	26	24	50
C	25	25	50

Table 2: Mean weight distribution of the study population

Group	Weight (mean)	SD
A	2.91	0.25
B	3.12	0.40
C	2.85	0.20

SD: Standard deviation

Table 3: Distribution of prothrombin index in study group and control group

Group	Prothrombin index (mean)	SD
A	94.98	7.64
B	95.08	9.91
C	80.39	15.9

SD: Standard deviation

preventing HDN.¹³⁻¹⁵ O'Connor and Addiego showed in their study that oral Vitamin K caused a significant fall in the prothrombin time.⁴ Furthermore, Ishii and Uedo showed the same using thrombo test.¹⁶ Similarly, Dunn¹⁷ documented only one case of HDN when 31,000 infants were given oral Vitamin K. Earlier Indian studies also proved efficacy of oral Vitamin K.^{11,17,18}

The present study revealed that prothrombin index was almost identical in Group A and B but not in Group C. Thus, 1 mg of intramuscular Vitamin K is as effective as 2 mg of oral Vitamin K. Further analysis has showed that prothrombin index was significantly decreased and prothrombin time was markedly prolonged in Group C (where no Vitamin K was given) as comparable to other groups but not enough to increase the risk of bleeding.^{19,20}

CONCLUSION

Oral Vitamin K is as effective as injectable Vitamin K. Oral Vitamin K is cheap and affordable. This can be practiced in resource-poor setup.

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How to cite this article: Venugopalan N, Vanaja T. Efficacy of Oral Vitamin K Compared to Injectable Vitamin K in Neonates. *Int J Sci Stud* 2016;3(11):203-205.

Source of Support: Nil, **Conflict of Interest:** None declared.

Maternal and Perinatal Mortality and Morbidity in Hypertensive Disorder Complicating Pregnancy

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Abstract

Introduction: Hypertensive disorders complicating pregnancy is one of the extensively researched subjects in obstetrics. The pathology should be understood, and the involvement of multi-organ dysfunction should be taken into account.

Objectives: To analyze the cases of hypertensive disorder complicating pregnancy and its maternal and perinatal outcome in patients admitted in the Kannur Medical College in Anjarakandy.

Methods: A total number of 233 cases of hypertensive disorder complicating pregnancy (gestational hypertension, pre-eclampsia, and eclampsia) admitted to KMCH from 2009 July 1st to 2010 June 30th.

Selection of Cases: Both booked and referred and all patients who were diagnosed hypertension complicating pregnancy.

Results: Hypertensive cases complicating pregnancy accounted for 9.1% of the total deliveries, out of which gestational hypertension accounted for 3 %, pre-eclampsia 5.5%, and eclampsia 0.7%. In this study, a maximum case where seen in the age groups 20-30 in primigravida belonging to low socio-economic strata. The majority of patients detected to have high blood pressure at 32-36 weeks of gestation, and a mean gestational age of 35 weeks. Hemolysis, elevated liver enzymes, and low platelets syndrome was the most common maternal complication and intrauterine growth restriction, the most common fetal complication. 21 cases followed by abruptio placentae, acute renal failure, postpartum hemorrhage, and postpartum eclampsia. Maternal mortality occurred in one case. Prematurity/preterm was the most common cause of perinatal death.

Conclusion: Training and continuing medical education of the attending staff and the structuring management protocols relevant to local needs are also an important part in case of hypertension complicating pregnancy.

Key words: Eclampsia, Hemolysis, elevated liver enzymes and low platelets, Hypertension, Pre-eclampsia, Pregnancy

INTRODUCTION

Hypertensive disorders complicating pregnancy are common and form one of the deadly triads, along with hemorrhage and infection resulting in maternal mortality and morbidity.

In Kerala, gestational hypertension continues to be responsible for the largest proportion of perinatal mortality.

Hypertensive disorders in pregnancy are classified as:

- Gestational hypertension
- Pre-eclampsia and eclampsia
- Pre-eclampsia superimposed on chronic hypertension
- Chronic hypertension.

Approximately 70% of hypertensive disorders are due to gestational hypertension - Pre-eclampsia, whereas the other 30% are due to pre-existing and/or undiagnosed hypertension of renal disease.

Incidence ranges from 5 to 15%, 16% in primigravida, and 7% in multigravida. Increases perinatal morbidity and mortality by 10-15% and it still remains high due to pre-eclampsia to the extent of 20-50% and due to eclampsia 30-50% in developing countries. Maternal mortality ranges from 2 to 30%.

Access this article online



www.ijss-sn.com

Month of Submission : 12-2015

Month of Peer Review : 01-2016

Month of Acceptance : 01-2016

Month of Publishing : 02-2016

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Maternal complication includes abruptio placentae, hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome, acute left ventricular failure with pulmonary edema, acute renal failure (ARF), postpartum hemorrhage (PPH), disseminated intravascular coagulation (DIC), and fetal complication includes intrauterine device (IUD), intrauterine growth restriction (IUGR), prematurity, antepartum, and intrapartum asphyxia.

Objectives

To analyze the cases of hypertensive disorder complicating pregnancy and its maternal and perinatal outcome in patients admitted in Kannur Medical College in Anjarakandy.

MATERIALS AND METHODS

A total number of 233 cases of hypertensive disorder complicating pregnancy (gestational hypertension, pre-eclampsia, and eclampsia) admitted to KMCH from 2009 July to 2010 June.

All patients with hypertension, proteinuria, and convulsion beyond 20 weeks were included, and all chronic hypertension cases were excluded.

Both booked and referred and all patients who were diagnosed to have hypertension complicating pregnancy were selected for this study.

RESULTS

In this study, 73.4% were in the age group of 20-30 years with mean age of 26 years with standard deviation of 4.6 years. The maximum cases were primigravida, 140 cases (60.08%). The majority of the cases had regular antenatal check-up (81.05%). In this study, maximum cases were referred, i.e., 123 (52.8%), these patients were booked outside and referred to KMCH Anjarakandy for further management. In this study, the majority of patients were from low socio-economic status, i.e., blood pressure (BP) load 206 cases 88.4%. This indicates that socio-economic status has a close relationship with pre-eclampsia and eclampsia (Table 1).

The majority of patients detected to have high BP at 32-36 weeks of gestation, mean gestational age at which high BP detected was 35 weeks. Number of cases where systolic BP (SBP) >160 mmHg were 107 (45.9%) and diastolic BP (DBP) >110 mmHg were 44 (18.9%).

In this study, maximum perinatal mortality was found when the BP was above 160/110 mmHg and proteinuria

3+ and above. Liver function test was abnormal in 19 cases (8.2%), and renal function test was abnormal in 51 cases (21.9%) (Table 2).

Gestational age at delivery divided into 3 groups - 59.7% patients delivered after 36 weeks and 30% between 32 and 36 weeks and 10.3% before 32 weeks. In this study, vaginal deliveries (53.7%) were more than cesarean deliveries (46.3%). In this, 137 cases were induced for termination of pregnancy (Graph 1).

HELLP syndrome was the most common maternal complications. 21 cases followed by abruptio placentae, ARF, PPH, and postpartum eclampsia. Maternal mortality occurred in one case.

Among the neonatal complications preterm labor occurred in 110 cases (46.05%) and the remaining delivered at term (Table 3).

DISCUSSION

There were 348 patients admitted with hypertensive disorders in pregnancy during this period. Out of this,

Table 1: Different types of hypertensive disorder complicating pregnancy

Type of hypertension	Number of cases	Percentage
Gestational hypertension	76	32.6
Mild pre-eclampsia	38	16.3
Severe pre-eclampsia	101	43.3
Eclampsia	18	7.7
Total	233	100

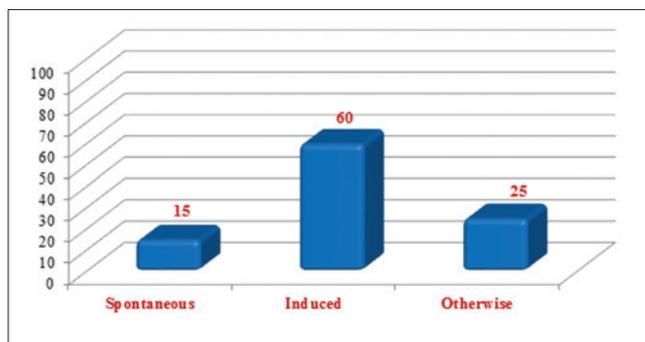
Table 2: Mode of treatment

Treatment given	Number of cases	Percentage
Methyldopa	42	18.0
Nifedipine	3	1.3
Methyldopa	70	30.1
Methyldopa, nifedipine, MgSO ₄	61	26.2
No treatment	57	24.4
Total	233	100

Table 3: Neonatal complications

Complications	Number of cases	Percentage
IUGR	47	19.6
Birth asphyxia	29	12.1
Intraventricular hemorrhage	4	1.7
Pulmonary hemorrhage	1	0.4
Neonatal jaundice	7	2.9
Sepsis	6	2.5
Metabolic complications	5	2.1
Neonatal death	23	9.5

IUGR: Intrauterine growth restriction



Graph 1: Onset of labor

233 who satisfy the inclusion criteria were included in the study. The overall incidence of hypertensive disorders in pregnancy in this study was 9.1%. According to Alokendu and Geetha,¹ NRS Medical College, Calcutta, hypertension in pregnancy in western population is also almost similar to.

In this study, 73.4% were in the age group of 20-30 years with mean age of 26 years. There was more primigravida consisting of 60.8% compared to multigravida 39.2%. This is comparable to Mac Gillivray² study which shows that primigravida has 15 times greater risk compared to multigravida for developing pre-eclampsia. Incidence of pre-eclampsia in nulliparous population is 3-10%.³

In the present study, 88.4% of patients belonged to below poverty line. According to Majhi *et al.*,⁴ the majority of patients (82%) belonged to low socio-economic status, which indicates that socio-economic status, poor nutrition, and inadequate antenatal care have a close relationship with pre-eclampsia and eclampsia. 81.5% had a regular antenatal check-up. Among patients diagnosed as eclampsia 88% cases were referred. According to Majhi *et al.*, 2001,⁴ 82.3% of patients did not have a regular antenatal check-up.

The mean gestational age at which high BP detected was 35 weeks. Gestational age is the variable that is the strongest predictor fetal morbidity and mortality, Shear *et al.*⁵ High-risk factors identified in this study were gestational diabetes in 17 cases (7%), twins in 7 cases (3%), anemia in 9 cases (3.9%), thyroid disease 8 cases (3.4%), bronchial asthma 7 cases (3%), and heart diseases 4 cases (1.7%). A Canadian study by Garner *et al.*⁶ confirmed that the risk of pre-eclampsia doubled in diabetes. In the about 7% cases was hypertensive disorder associated with gestational diabetes.

History of hypertension in previous pregnancy was observed in 15.5% of cases. This is comparable to study by Shaheen and Tahir⁷ where previous of hypertension was found in 10% patients. If women had severe pre-eclampsia, she has 20% risk of developing pre-eclampsia in her subsequent pregnancy.^{8,9} If pre-eclampsia presents clinically

before 30 weeks of gestation, the recurrence rate may be as high as 40% by Sibai *et al.*¹⁰ The group of women with DBP more than 110 mmHg was associated with a maximum number of low birth weight (LBW) babies compared to DBP <110 mmHg.¹¹ The failed to show this association.

In this study, severe proteinuria $\geq 3+$ were found in 62 cases (26.6%). In this study, maximum perinatal mortality was found when BP was above 160/110 mmHg and proteinuria 3+ and above. In this study, hypertensive cases complicated by HELLP syndrome had overall abnormal liver and renal function tests and 33 among HELLP syndrome had overt thrombocytopenia.

In this study, all cases with gestational hypertension (excluding severe cases) were not given any treatment, 57 out of 76 cases of gestational hypertension. A total number of babies born in this group (no treatment) without any complications were 45. A total number of babies born with IUGR were 3 cases, and a total number of neonatal deaths in this group were 2.

The mild cases of pre-eclampsia usually do not require any antihypertensive.¹² In this study, methyldopa was given when DBP was more than 100 mmHg, methyldopa, and nifedipine combination was started only when DBP was >105 mmHg and SBP more than 160 mmHg. As recommended by the working group - National High Blood Pressure Education Program 2000¹³ indication of antihypertensive agents is when SBP more than 160 mmHg and DBP more than 105 mmHg. Methyldopa was the predominantly used drug in this study when BP was not controlled nifedipine was added. MgSO₄ as an anticonvulsant was used in all cases of impending eclampsia and eclampsia - MgSO₄ regime (according to our protocol was followed for 61 cases - total babies born without any complication were only 16, IUGR babies were 13.

The overall perinatal mortality was 27 cases, out of which, number of IUDs were 12, and early neonatal death were 15. Out of the 61 cases were MgSO₄ was used, 18 cases were eclampsia.

In this study, 137 cases (57.9%) of patients were induced for termination of pregnancy. The overall cesarean rate was 46.3%, most common indication was fetal distress (9.4%), followed by failed induction (8.5%) success rate was 66%. Coppage and Polzin¹⁴ concluded that immediate abdominal delivery did not improve maternal and perinatal outcome in severe pre-eclampsia and induction of labor did not lead to increased morbidity and mortality. The most common complication in this study was HELLP syndrome 21 cases, Pal *et al.*,¹⁵ had reported an incidence of 4% for

HELLP syndrome. The other complications were abruptio placentae in 10 cases, postpartum eclampsia 6 cases, DIC in 3 cases, PPH in 4 cases, and ARF in 6 cases. There was only 1 maternal death due to severe pre-eclampsia.

Perinatal Outcome

The total preterm deliveries were 110 (46.05%). Severe pre-eclampsia was responsible for a maximum number of preterm deliveries (30.4%). The study performed by Buchbinder *et al.*,¹⁶ showed preterm deliveries associated with severe hypertension. In the birth weight of most of the babies were in the group more than 1.5-2.5 kg. Mean birth weight 2.1 kg. Lydakis *et al.* in 2001¹⁷ demonstrated that LBW is associated with pre-eclampsia. The cause may be prematurity or IUGR. 48 (20%) out of 213 babies in this study had (27 out of 240 were IUD's) the APGAR <5 at 1 min and 24 out of 213 babies had APGAR <7 at 5 min. In this study, 98 babies (40.8%) needed neonatal intensive care unit admission, out of which 23 needed ventilator support. IUGR was the most common complication totally up to 47 cases followed by birth asphyxia, neonatal jaundice, and neonatal death. Total number of IUD in this study was 27, and a total number of early neonatal deaths were 23. So that, perinatal mortality in this study was 50 (20.8%), perinatal mortality due to pre-eclampsia (mild and severe) in this study was 36 cases. Perinatal mortality in eclampsia is 8 cases (3.3%). The incidence in the perinatal mortality in this study by Gregg¹⁸ was 5%. A poor perinatal outcome in this study is due to the high contribution of prematurity.

CONCLUSION

Hypertensive disorders complicating pregnancy is one of the extensively researched subjects in obstetrics. The pathology should be understood, and involvement of multi-organ dysfunction should be taken into account.

The early use of antihypertensive drugs, optimum timing of delivery and strict fluid balance, anticonvulsants in cases of eclampsia will help to achieve a successful outcome.

Early transfer to the specialist center is important, and the referral centers should be equipped to treat such critically ill patients.

Training and continuing medical education of the attending staff and the structuring management protocols relevant to local needs are also an important part in case of hypertension complicating pregnancy.

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How to cite this article: Rajamma CK, Sridevi P. Maternal and Perinatal Mortality and Morbidity in Hypertensive Disorder Complicating Pregnancy. *Int J Sci Stud* 2016;3(11):206-209.

Source of Support: Nil, **Conflict of Interest:** None declared.

Panorama of Pleomorphic Adenoma in a Series of Patients Presented over a Period of 5-year

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Abstract

Introduction: Salivary gland tumors are one of the most heterogeneous groups of human tumors with over 40 subtypes of neoplasms reported. Pleomorphic adenoma is the most common salivary gland tumor accounting for nearly 60% of all the salivary gland neoplasms. As there has been very little study, if any, carried out on salivary gland pathology in our region, hence we conducted this study on histological diversity and variability among cell types within pleomorphic adenoma. This study can help us determine the various characteristics of pleomorphic adenoma.

Purpose: To study the panorama of pleomorphic adenoma including its histopathological patterns and cell types.

Materials and Methods: A retrospective study, over a period of 5-year, was carried out on the material, which included the histopathological slides and tissue blocks and relevant clinical data were obtained from the Department of Pathology.

Results: Parotid gland was the most common salivary gland affected by a pleomorphic adenoma (66.3%). Stroma-rich pleomorphic adenomas were the most common histopathological type (45.65%) with plasmacytoid cells being the most common single cell types seen (85.87%).

Conclusion: In our study, parotid gland came out to be the most common site for the development of pleomorphic adenoma with stroma-rich pleomorphic adenoma being the most common histopathological type. Among minor salivary glands, the palate was most commonly affected.

Key words: Histopathological diversity, Pleomorphic adenoma, Salivary gland neoplasms

INTRODUCTION

The salivary glands in the body are classified into the major salivary glands and the minor salivary glands. The major salivary glands include the paired parotid glands, the submandibular glands, and the sublingual glands. The minor salivary glands are smaller in size, more numerous and are present throughout the upper aerodigestive tract such as the floor of mouth, palate, lips, tongue, cheeks, and oropharynx. There is a whole range of lesions, both reactive and neoplastic that can be encountered in more than 500 salivary glands present in the human body. Histologically,

salivary gland tumors have been described as one of the most heterogeneous group of human tumors and over 40 subtypes of neoplasms have been reported.¹ Salivary gland tumors are rare neoplasms comprising <3% of all neoplasms of head and neck region and are known by their diverse histological features.² Pleomorphic adenoma is the most common salivary gland tumor and accounts for about 60% of all salivary gland neoplasms. The mean age at presentation is 46 years, but the age ranges from the first to the tenth decade with a slight female predominance. About 80% of pleomorphic adenomas arise in the parotid, 10% in the submandibular gland and 10% in the minor salivary glands.³ Pleomorphic adenoma is characterized by histological diversity and shows variable cell types, hence also known as a mixed tumor or polymorphic adenoma. The aim of the current study was to describe the various characteristic features of pleomorphic adenoma including clinical features and special reference to the various histopathological patterns and cell types seen in this tumor type.

Access this article online



www.ijss-sn.com

Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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MATERIALS AND METHODS

This was a hospital-based retrospective study carried out in the Department of Pathology, Vir Chander Singh Garhwali Government Medical Science and Research Institute, Srinagar, Garhwal, Uttarakhand. The material for the study included histopathology slides, and tissue blocks, of all salivary gland tumor specimens received between August 2010 and August 2015. All cases of benign salivary gland tumors including pleomorphic adenomas diagnosed on histopathology were taken for study. The hematoxylin and eosin (H and E) stained histopathology slides were retrieved and were reviewed using light microscopy under various magnifications. Various cytological and histopathological findings were noted. Fresh sections were taken from tissue blocks in some cases, wherever required, and were stained with H and E stain. The various histopathological features of all cases were noted down. Data were analyzed using tables, figures, and percentages.

OBSERVATIONS

A total of 116 cases of benign salivary gland neoplasms were reported in the mentioned study period, extending from August 2010 to August 2015, of which 92 cases were diagnosed as pleomorphic adenoma. All the relevant data including the age of patients, site of tumors, side or laterality, size of the tumors, and gender distribution were recorded. Parotid glands were found to be the most commonly affected salivary glands followed by submandibular glands and sublingual glands. Predominant cell types in sections and

stromal tissue percentages were studied and are represented in tabulated form as in Tables 1-4.

Site

81 cases of pleomorphic adenoma were seen affecting major salivary glands while the rest 11 cases were seen affecting minor salivary glands. The most common site was a parotid gland, which was affected in 61 cases (66.3%) followed by submandibular gland with 11 cases (11.9%), sublingual with 9 cases (9.8%), and all minor salivary glands included together amounting to 11 cases (11.9%). Out of all the minor salivary glands, the palate was seen to be the most common site of pleomorphic adenoma with 6.5% of total cases. One case of pleomorphic adenoma affecting lacrimal gland in orbit was also seen. The detailed description is given in Table 1.

Age and Sex Distribution

In our study, we found out pleomorphic adenoma affecting patients in all age groups. The youngest case affected was a 14-year-old male and the eldest was a 72-year-old female. The most common age group affected was of 21-30 years and more than 50% cases were found in third and fourth decades of life. Pleomorphic adenoma was found to be more commonly affecting the females than males. Out of a total of 92 cases, 52 (56.52%) were found in females, and 40 (43.48%) were seen in males. The descriptive analysis is given in Table 2.

Laterality and Size

Out of 72 cases of pleomorphic adenoma affecting parotid and submandibular glands, left sided salivary glands were seen to be affected in 40 (55.56%) cases, and right sided were seen to be affected in 32 (44.44%) cases. 50 cases were seen to be presenting with tumors having size between 3 and 6 cm, while 28 cases were seen presenting with tumor size <3 cm and only 4 cases were seen to be presenting with tumor size more than 6 cm.

Table 1: Anatomic distribution of pleomorphic adenoma

Site of tumor	Number of cases	Percentage
Parotid	61	66.3
Submandibular gland	11	11.9
Sublingual	09	9.8
Palate	06	6.5
Cheek	02	2.2
Lip	02	2.2
Lacrimal gland	01	1.1
Total	92	100

Table 2: Age distribution & sex distribution of pleomorphic adenoma

Age (years)	N (%)	Female	Male
11-20	04 (04.35)	2	2
21-30	26 (28.26)	14	12
31-40	24 (26.09)	14	10
41-50	16 (17.39)	10	06
51-60	14 (15.22)	07	07
61-70	08 (08.69)	05	03
Total	92 (100)	52 (56.52)	40 (43.48)

Table 3: Laterality of pleomorphic adenoma

Site	Side	
	Left	Right
Parotid	34	27
Submandibular	6	5
Total (%)	40 (55.56)	32 (44.44)

Table 4: Distribution of histological types of pleomorphic adenoma

Histological pattern	N (%)
Stroma-rich	42 (45.65)
Classical type	32 (34.78)
Cell-rich	18 (19.57)
Total	92 (100)

Predominant Histological Type and Predominant Cell Type

Pleomorphic adenoma was classified into stroma-rich or myxoid, cell-rich or cellular and classical types as described by Seifert *et al.*⁴ Stroma-rich pleomorphic adenomas (Figure 1) were the most common accounting for 42 cases (45.65%), followed by classical type with 32 cases (34.78%) and cell-rich type (Figure 2) with 18 (19.57%) cases and are depicted in Table 4. Plasmacytoid cells and spindle cells (Figure 3) were the most common cell types seen, and all the 100 % cases had the presence of either of the two. Plasmacytoid cells were the most common single type of cells seen in 79 (85.87%) cases while spindle cells, basaloid cells, and squamous cells were seen in 72cases (78.26%), 34 cases (36.95%), and 15 cases (16.30%), respectively. Islands of cartilage, foci of mature bone, and microcystic pattern were seen in few cases (Figures 4-6).

affecting the minor salivary glands. Parotid gland was seen to be the most commonly affected gland, and it accounted for 61cases (66.3%). These findings are similar to the findings from the studies done by Ito *et al.*,⁵ Waldron,⁶ and Eveson and Cawson⁷ whose studies found 70%, 63%, and 71% cases of pleomorphic adenoma affecting parotid glands, respectively. Pleomorphic adenomas were seen affecting 11 minor salivary glands in our study and out of those, 4 cases were found in the palatal area. Palate was seen to be the most common site of pleomorphic adenoma among the

DISCUSSION

Pleomorphic adenoma also known as a benign mixed tumor or polymorphic adenoma is a slow growing benign salivary gland neoplasm, most commonly affecting the parotid gland. In the present study of 92 cases of pleomorphic adenomas, the majority of cases were seen to be affecting the major salivary glands, while only 11 cases (11.6%) were seen to be

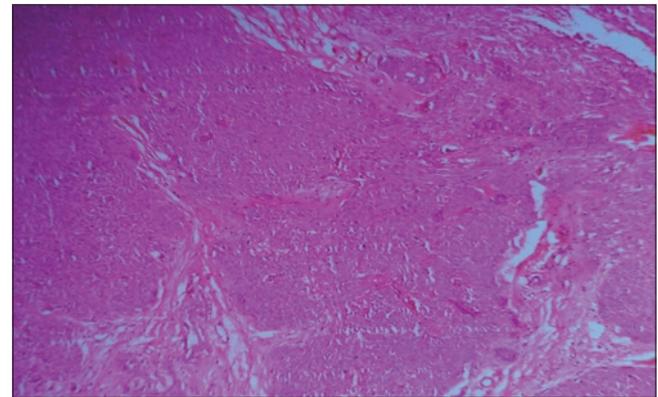


Figure 3: Cellular pleomorphic adenoma showing spindle cells and plasmacytoid cells (H and E stain, x100)

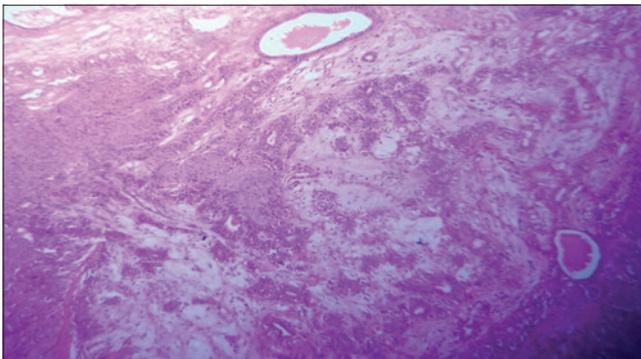


Figure 1: Pleomorphic adenoma showing myxoid areas (H and E stain, x100)

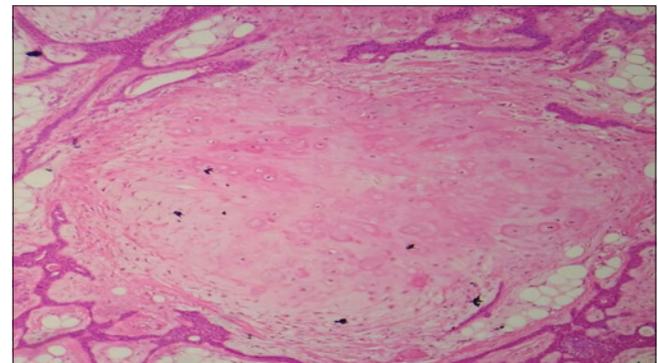


Figure 4: Pleomorphic adenoma showing cartilaginous differentiation (H and E stain, x100)

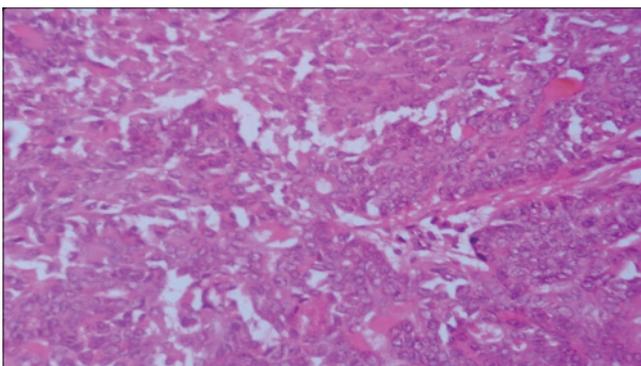


Figure 2: Pleomorphic adenoma with hypercellular appearance (H and E stain, x100)

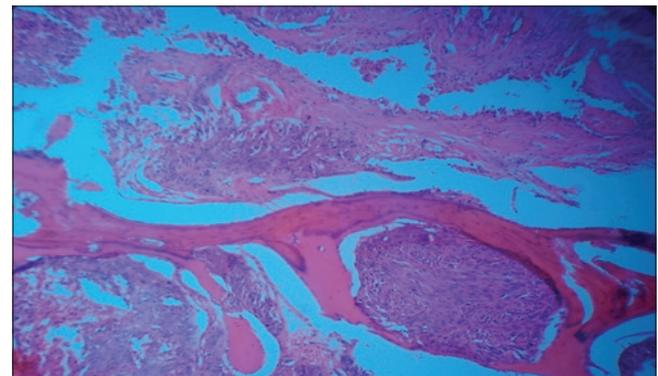


Figure 5: Pleomorphic adenoma with osseous differentiation (H and E stain, x100)

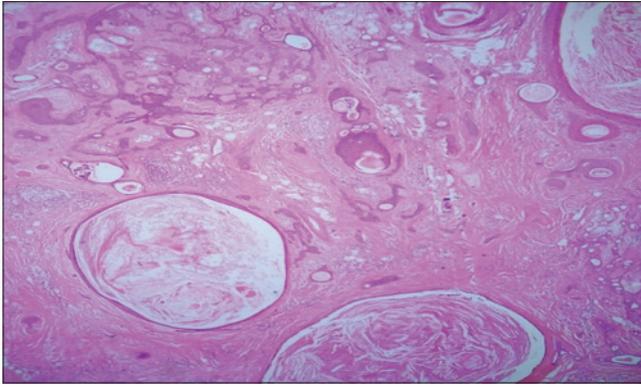


Figure 6: Pleomorphic adenoma showing keratinized epithelial plugs in the lumen (H and E stain, x100)

minor salivary glands which is in close concordance with the study of Vaidya *et al.*⁸ In our study, the most common age group affected was seen to be of 21-30 years and more than 50% cases of pleomorphic adenomas were found in patients in their third and fourth decades of life. Nearly 56% of all patients were females. However, studies of Al-Khtoum *et al.*⁹ found it marginally more common in males. Our study findings were very similar to the study done by Chidzonga *et al.*,¹⁰ who in a study of a series of more than 200 cases of pleomorphic adenomas, found 58% of tumors occurred in females, and the tumor was most common in the 3rd, 4th, and 5th decades of life. However, quite a few studies including the studies of Eveson and Cawson⁷ and Chidzonga *et al.*¹⁰ showed this neoplasm affecting patients in the 4th and 5th decades. In studies done by Al-Khtoum *et al.*⁹ and Friedrich *et al.*,¹¹ laterality of tumors was more obvious, and the two studies showed the involvement of right side in 72.5% and 65.8% cases, respectively. However, in our study, we found left sided major salivary glands (56%) marginally more commonly involved than the right sided (44%), which was in concordance with the study of Ito *et al.*⁵ We also came to the conclusion from our study that most of these tumors were smaller in size and only 4 (4.34%) were larger than 6 cm at the time of presentation. All the minor salivary gland pleomorphic adenomas were <6 cm in size. In our study, stromal rich type corresponded with 45.6% cases while classical subtype and cell-rich subtype were lesser common with 34.7% and 19.5% cases, respectively. Most of other studies, such as the studies of Stennert *et al.*¹² and Paris *et al.*,¹³ were having a similar distribution of the subtypes with stromal subtype being the most common. Plasmacytoid cells were the most common cell type in almost all the studies such as the studies of Ellis and Auclair¹⁴ and Ito *et al.*,⁵ which found spindle cells the second most common type of cell after plasmacytoid cells.

CONCLUSION

In our series of patients, pleomorphic adenoma of the salivary glands was found to have similar characteristic features clinically as well as histopathologically to many of the studies done and published worldwide. However, a paradox to many studies on pleomorphic adenoma in literature, we found the neoplasm affecting predominantly younger patients and also sublingual glands were involved in quite a few cases, in our study. Furthermore, from our study, we concluded that while diagnosing pleomorphic adenoma, various histopathological patterns should be thoroughly kept in mind, the knowledge of which is essential for correct diagnosis.

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How to cite this article: Bhat P, Bhat S, Hatwal D, Chaudhri S. Panorama of Pleomorphic Adenoma in a Series of Patients Presented over a Period of 5-year. Int J Sci Stud 2016;3(11):210-213.

Source of Support: Nil, **Conflict of Interest:** None declared.

Effect of Intrathecal Fentanyl with Bupivacaine on Maternal Hemodynamics and Fetal Outcome during Cesarean Section: A Comparative Study with Two Different Doses

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Abstract

Introduction: Intrathecal opioids to increase analgesic effect of bupivacaine during cesarean section are being used worldwide. Fentanyl a short-acting synthetic opioid is particularly suited for this purpose in doses from 10 to 30 µg.

Materials and Methods: Total of 120 parturients of American Society of Anaesthesiologists Grades I and II scheduled for cesarean section were randomly allocated to receive either 10 mg of 0.5% injection bupivacaine (Group B, $n = 40$) or 0.25 ml (12.5 µg) fentanyl with 10 mg of 0.5% injection bupivacaine (Group BF1, $n = 40$) or 0.50 ml (25 µg) fentanyl with 10 mg of 0.5% injection bupivacaine (Group BF2, $n = 40$). The total volume of drug was made 2.5 ml in every group by adding distilled water, and maternal hemodynamic parameter was assessed every 5 min for first 15 min, then at 15 min interval for remainder of operation, thereafter at 30 min interval for 2 h postoperatively.

Results: Four patients (10%) in Group B had intraoperative discomfort and required ketamine supplementation while none in the fentanyl groups complained of pain. About 19 patients (47.50%) in Group BF2, 11 patients (27.50%) in Group BF1 and eight patients (20%) in Group B required vasopressors ($P < 0.05$ between Group B and Group BF2 and BF1 and BF2 group and $P > 0.05$ between Group B and Group BF1).

Conclusion: There was no significant difference in neonatal Apgar and neurological and adaptive capacity scores score among any of the group. There was no significant difference in adverse effects among the three study groups. 25 µg fentanyl intrathecally causes significantly more hypotension as compared to 12.5 µg fentanyl.

Key words: Fentanyl, Maternal hypotension, Neonate

INTRODUCTION

The subarachnoid blockade is the most frequent anesthetic technique for caesarian section. However, local anesthetics alone are usually insufficient to provide uniform block despite the high sensory level of anesthesia.^{1,2}

The epidural or subarachnoid administration of opioids to increase analgesic effect of bupivacaine during caesarean section is being used widely. The use of hydrophilic agents such as morphine was associated with prolonged duration of action and delayed respiratory depression.³ To overcome these drawbacks newer agents, such as fentanyl were introduced. Fentanyl has a rapid onset of action and does not tend to migrate to fourth ventricle in sufficient concentration to cause delayed respiratory depression when administered intrathecally.⁴

It has been used in doses ranging from 10 to 30 µg for supplementing subarachnoid block during caesarean delivery.^{5,6}

Access this article online



www.ijss-sn.com

Month of Submission : 12-2015

Month of Peer Review : 01-2016

Month of Acceptance : 01-2016

Month of Publishing : 02-2016

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This study was designed to evaluate the effect of 2 different doses of fentanyl (12.5 µg and 25 µg) on the maternal hemodynamic status and neonatal outcome.

MATERIALS AND METHODS

The study was conducted on 120 primigravida as well as multigravida patients belonging to American Society of Anaesthesiologists Grades I and II, between the ages of 18-30 years. After obtaining approval from the Institutional Ethical Committee, written informed consent was obtained from all the patients. Beside general contraindications to regional anesthesia during cesarean section, patients with fetal heart rate (FHR) >160 or <100 were excluded from the study.

Patients were randomly allocated to receive either 10 mg of 0.5% injection bupivacaine (hyperbaric) (Group B, $n = 40$) or 10 mg of 0.5% injection bupivacaine and 12.5 µg fentanyl (Group BF1, $n = 40$) or 10 mg of 0.5% injection bupivacaine and 25 µg fentanyl (Group BF2, $n = 40$). All the study agents were introduced intrathecally and the total volume of agents administered was made equal (2.5 ml) by adding distilled water.

In the operating room, after establishing an intravenous (IV) line, patients were premedicated with injection metoclopramide and injection ranitidine IV and were preloaded with 15 ml/kg ringer lactate solution. Pulse rate, blood pressure, respiratory rate (RR), SpO₂, and FHR were recorded before giving spinal anesthesia.

Under all aseptic precautions, lumbar puncture was performed with 25 gauge Quincke needle in L₃L₄ space in left lateral position and study drug were injected as per group of patients according to random assignment. The patient was turned in supine position, table was tilted to 15° head down position, and a wedge was placed under the right hip of the patient. All patients received oxygen supplementation (3-4 L/min) via ventimask immediately after administration of spinal anesthesia. FHR were noted for any bradycardia. Pulse rate, blood pressure, rate of respiration, tidal volume, SpO₂, and side effects such as pruritus, nausea, vomiting and shivering were recorded every 5 min for first 15 min and then at 15 min interval for remainder operation and thereafter at 30 min interval for 2 h postoperatively.

The decrease in systolic blood pressure (more than 20% from baseline values and/or <90 mmHg) after spinal injection was treated by increasing the rate of IV fluid administration, by exaggerating the uterine shift and by injecting ephedrine 5-10 mg IV.

10 U of oxytocin was given intravenously after delivery of baby. Neonatal Apgar score was recorded at 1 and 5 min after delivery of baby and neurological and adaptive capacity scores (NACS) scoring (Table 1) was performed at 15 min and 2 h interval.

Data were analyzed by using one-way analysis of variance test.

RESULTS

The study groups were comparable with respect to age, weight, height, parity and gestational age (Table 2) and operative management (Table 3).

The level of anesthesia was considered sufficient for the surgical procedure because no patient had a sensory level below T₆. None of the patient in the study experienced respiratory depression, (RR <9 breaths/min), desaturation (SpO₂ <90%), or significant decrease in tidal volume. 8 patients (20%) in bupivacaine group, 11 patients (27.50%) in 12.5 µg fentanyl group and 19 patients (47.50%) in 25 µg fentanyl group had hypotension and required ephedrine administration. The difference was statistically significant between bupivacaine group and 25 µg fentanyl group and 12.5 µg and 25 µg fentanyl group ($P < 0.05$) while it was insignificant between BF1 and B group. Maximum fall from baseline in mean blood pressure was seen 10 min after block in Group B, 20 min after block in Group BF1 and 5 min after block in Group BF2 (Table 4). 4 patients in Group B had intraoperative pain and were given ketamine 30 mg. No patient in fentanyl groups had pain. 5 patients in bupivacaine group (12.5%), 3 patients in 12.5 µg fentanyl group (7.5%) and 1 (2.5%) patient in 25 µg fentanyl group had intraoperative nausea ($P < 0.05$). No patient in either of the group had bradycardia, hypoxia or pruritis. 5 (12.50%) patients in bupivacaine group, 2 patients (5.0%) in 12.5 µg fentanyl group and 3 patients (7.50%) in 25 µg fentanyl group had shivering ($P > 0.05$). There was no significant difference in neonatal Apgar or NACS score among the three groups.

DISCUSSION

Opioids added to local anesthetics for spinal anesthesia was the first introduced into clinical practice in 1979. Morphine was the first opioid used intrathecally⁷ but problem with morphine was its slow onset of action and delayed respiratory depression. To overcome these drawbacks, newer agents such as fentanyl and sufentanil were

Table 1: Neurological and adaptive capacity scores

NACS scoring	0	1	2
Adaptive capacity			
Respond to sound	Absent	Mild	Vigorous
Habituation of sound	Absent	7-12 stimuli	<6 stimuli
Response to light	Absent	Mild	Brisk blink
Habituation to light	Absent	7-12 stimuli	<6 stimuli
Consolability	Absent	Difficult	Easy
Passive tone			
Scarf sign	Encircles the neck	Elbow slightly passes midline	Elbow does not reach midline
Recoil of elbow	Absent	Slow, weak	Brisk
Popliteal angle	>100	100-110	<90°
Recoil of lower limbs	Absent	Slow, weak	Brisk
Active tone			
Active contraction of neck flexors	Absent	Difficult	Good
Active contraction of neck extensors	Absent	Difficult	Good
Palmar grasp	Absent	Weak	Good
Response to traction	Absent	Lifts part of body weight	Lifts all body weight
Supporting reaction	Absent	Incomplete	Strong
Primary reflexes			
Automatic walking	Absent	Difficult to obtain	Perfect
Moro reflex	Absent	Weak	Perfect
Sucking	Absent	Weak	Perfect
General assessment			
Alertness	Coma	Lethargy	Normal
Crying	Absent	Weak, excessive	Normal
Motor activity	Absent	Diminished	Normal

Table 2: Patients demographics

Demographics	Group B	Group BF1	Group BF2	P value
Age (years)	23.19±5.62	24.22±5.96	24.36±3.56	>0.05
Height (cm)	152.3±4.81	152.5±6.44	150.63±11.22	>0.05
Weight (kg)	60.96±6.20	62.06±6.79	62.43±7.62	>0.05
Multiparous (n)	15	16	17	>0.05

Table 3: Operative management

Parameters	Group B	Group BF1	Group BF2	P value
Induction-delivery interval (min)	11±5.6	12±3.2	11±4.2	>0.05
Skin incision-delivery interval (min)	6.4±2.3	6.6±3.1	6.5±3.6	>0.05
Uterine incision-delivery interval (s)	40±15	37±20	39±22	>0.05
Duration of surgery (min)	45±6.8	47±7.2	44±6.4	>0.05

Table 4: Changes in mean arterial blood pressure

Mean arterial blood pressure (mmHg)	Group B	Group BF1	Group BF2
Pre-operative	80.03±12.60	83.13±15.61	85.89±16.20
Just after block	79.46±12.04	81.54±13.60	78.65±12.20
At 5 min	74.17±11.18	76.78±12.56	70.32±10.42
At 10 min	70.19±11.34	74.68±12.40	72.39±11.56
At 20 min	73.66±8.40	73.08±13.45	74.16±12.50
At 30 min	77.18±8.34	74.60±10.72	78.79±9.86

introduced. Because of high lipid solubility of fentanyl, only a small proportion of the administered dose tends to

migrate cephalad to the cervical region or 4th ventricle⁸ so there is no respiratory depression. An additional advantage is rapid onset of action, analgesia occurs within 5-10 min following intrathecal administration.

A wide range of doses of fentanyl is being used as adjuvant to bupivacaine for intrathecal administration during cesarean section, ranging from 10 to 30 µg.^{5,9} This study was conducted to find most appropriate fentanyl dose which has minimum hemodynamic side effects and is sufficient to provide good analgesia during cesarean delivery.

The result of this study showed that fentanyl 25 µg causes significantly higher incidence of hypotension (47.50%) as compared to 12.5 µg fentanyl (27.50%) when used as adjuvant to bupivacaine for LSCS.

Incidence of nausea did not differ significantly among the study groups and no patient had vomiting in any of the group (Table 5). This may be because of the use of injection metoclopramide and injection ranitidine as premedication to all patients.

10% patient in bupivacaine group complained of intraoperative discomfort while non in the fentanyl groups had intraoperative discomfort. The site of action of intrathecal fentanyl is substantia gelatinosa in spinal cord. Neuraxial opioids act by inhibiting release of substance P in this region of spinal cord.¹⁰

No significant difference was there in incidence of shivering among the 3 groups. No patient in either of the group had hypoxia or respiratory depression. This may be due to highly lipophilic nature of the drug limiting its rostral spread.

Neonatal condition was assessed by both Apgar score and NACS score. We used NACS score also because it was designed specifically to study effects of maternal drug administration on fetus.¹¹ Results of study revealed that fentanyl in doses of 12.5 µg and 25 µg have no adverse effect on neonatal Apgar score or NACS scoring (Table 6) which is in agreement with other studies.¹²

Table 5: Maternal side effects (n=40)

Side effects	n (%)		
	Group B	Group BF1	Group BF2
Nausea	5 (12.5)	3 (7.5)	1 (2.5)
Vomiting	0 (0)	0 (0)	0 (0)
Hypotension	8 (20.0)	11 (27.50)	19 (47.50)
Bradycardia	0 (0)	0 (0)	0 (0)
Hypoxia	0 (0)	0 (0)	0 (0)
Shivering	5 (12.50)	2 (5.00)	3 (7.50)
Pruritis	0 (0)	0 (0)	0 (0)
Complaint of discomfort by patient	4 (0.0)	0 (0)	0 (0)

Table 6: Neonatal outcome

Parameters	Group B	Group BF1	Group BF2	P value
Apgar score				
1 min	8.00±0.77	7.83±0.74	8.06±0.77	P>0.05
5 min	9.26±0.73	8.86±0.99	9.23±0.80	P>0.05
NACS				
15 min	37.93±1.80	37.73±1.96	37.56±2.01	P>0.05
2 h	35.92±1.40	39.16±1.20	38.96±1.67	P>0.05

NACS: Neurological and adaptive capacity scores

CONCLUSION

We conclude that fentanyl in doses of 12.5 and 25 µg although equally safe from neonatal prospective but, 25 µg fentanyl added to 10 mg bupivacaine for SA during cesarean section causes significantly higher incidence of hypotension in mother as compared to 12.5 µg fentanyl without any additional benefit, so ideal dose of fentanyl as adjuvant to bupivacaine during SA for cesarean section should be 12.5 µg.

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How to cite this article: Kumar R, Sahi P, Jain A, Shobhne H. Effect of Intrathecal Fentanyl with Bupivacaine on Maternal Hemodynamics and Fetal Outcome during Cesarean Section: A Comparative Study with Two Different Doses. *Int J Sci Stud* 2016;3(11):214-217.

Source of Support: Nil, **Conflict of Interest:** None declared.

Distal Polyneuropathy in Type 2 Diabetes Mellitus in and Around Jabalpur, Madhya Pradesh, India

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Abstract

Background: Diabetes is a systemic disorder characterized by metabolic abnormalities and angiopathy. Small vessel disease in the form of polyneuropathy contributes the major cause of disability. The relationship between the degree of glycemic control and development of long complication poses an intriguing though vital problem. The magnitude of morbidity calls for a reassessment of the situation and hence this study.

Aims and Objectives: To study the pattern of distal polyneuropathy (DPN) in Type 2 diabetes mellitus (T2DM) and its correlation with duration of disease and degree of glycemic control.

Materials and Methods: Pattern of peripheral neuropathy in 838 cases of T2DM (478 males and 360 females) varying from 25 years to 65 years has been analyzed. The study was conducted over 1 year December 2014 to December 2015. Subjects were put to detailed clinical workup including body mass index, hypertension labeled as per the WHO criteria. A thorough neurological assessment was made.

Results: DPN was encountered in 64% ($P < 0.05$) being more frequent in advancing age ($P < 0.001$) of the long duration (16-20 years) ($P < 0.05$). Autonomic neuropathy was a common accompaniment (43%). The presence of polyneuropathy in patients on the low caloric diet had a higher incidence of polyneuropathy while the blood sugar level has no direct retinopathy. Elevated serum triglycerides and low high-density lipoprotein cholesterol were associated with higher incidence of polyneuropathy. The presence of DPN even after glycemic control (180 out of 296 cases impaired glucose tolerance 60.8%) make us feel that polyneuropathy is regarded as a component rather than a complication of diabetes.

Conclusion: Metabolic decompensation of diabetes has a detrimental effect. No single mechanism appears to explain polyneuropathy, a combination of factors appear to be responsible. Mode of therapy and glycemic control can only lessen the severity. Diabetic polyneuropathy is regarded as a component of and not a complication of diabetes.

Key words: Body mass index, Distal polyneuropathy, High-density lipoprotein, Impaired glucose tolerance, Small vessel disease

INTRODUCTION

There is the global rise of diabetes mellitus (DM) and it has reached epidemic proportions worldwide. Recent estimates suggest that the prevalence of diabetes is rising globally, particularly in developing countries, an estimated 80-85% of the global population with diabetes lives in

developing countries.¹ DM has become an important health concern in the South Asian region with a projected rise in the prevalence of diabetes of over 150-160% between 2000 and 2035.¹ Diabetes is a systemic disorder characterized by metabolic abnormalities and angiopathy.²⁻⁶ Neuropathy is considered the most common microvascular complications DM.^{7,8} Neuropathies in diabetes can impair the normal functioning of the peripheral central and autonomic nervous systems.⁹ Diabetic polyneuropathy also called distal peripheral neuropathy and affected the peripheral nervous system and is by far the most common type of neuropathy seen in DM.¹⁰ Distal polyneuropathy (DPN) is considered the major risk factor for amputation, and hence a significant cause of morbidity in DM.¹¹ The relationship between the degree of blood sugar control

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Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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and development of long-term complication poses an intriguing though vital problem. Of these, the neurological complication contributes to the main cause of disability,¹²⁻¹⁴ and some of the theories have been proposed for its pathogenesis.⁴ The magnitude of morbidity calls for the reassessment of the situation and hence this study.

MATERIALS AND METHODS

838 cases of Type 2 DM attending the OPD of Department of Medicine, Sukh Sagar Medical College and Hospital, Jabalpur between December 2014 to December 2015 contributed a sample of this study. Subjects were put to detailed clinical workup including base metabolic index; the later was calculated as = kg/m², hypertension labeled as per the WHO Criteria.⁶ A thorough neurological assessment was done of samples. Polyneuropathy was regarded as the bilateral loss of ankle jerks or gross sensory deficit in both feet as per who criteria multinational study. A 75 g oral glucose tolerance test was carried out, and the WHO criteria were adopted.⁶ Blood glucose was estimated by the ortho-toluidine, while glycosylated hemoglobin by the modified chemical method of Flickinger and Winterhalter.^{15,16} Lipid profile and serum creatinine were determined in the fasting state of patients.

OBSERVATIONS

Observations are shown in Tables 1-14.

The Table 1 shows highly significant increase ($P < 0.001$) in the frequency of DPN with advancing age.

The Table 2 reveals that BMI has no bearing to the incidence of peripheral neuropathy.

The Table 3 shows that duration has no linear correlation though the highest incidence was encountered in disease of 16-20 years duration. However, this rising trend of incidence was not maintained in disease of more than two decades.

It is revealed from the Table 4 that low caloric intake has a significant bearing ($P < 0.05$) in the frequency of polyneuropathy.

Table 5 shows that fasting blood sugar has no linear relationship with incidence of peripheral neuropathy.

It is evident from Table 6 that post-prandial hyperglycemia too does not have a linear relationship.

Thus, no consistent correlation was observed (Table 7).

Table 1: Age versus peripheral neuropathy in T2DM

Age (years)	Cases	Peripheral neuropathy	%
25	10	2	20
26-35	52	25	47.70
36-45	204	83	40.60
46-55	310	159	51.20
56-60	128	112	87.50
61 and above	134	128	95.50
Total	838	509	

T2DM: Type 2 diabetes mellitus

Table 2: Peripheral neuropathy and BMI

BMI	T2DM	Peripheral neuropathy	%
19	250	100	66.60
19-23	294	200	68.02
Above 23	294	209	71.06

BMI: Body mass index, T2DM: Type 2 diabetes mellitus

Table 3: Peripheral neuropathy and duration of diabetes

Duration (years)	Cases	Peripheral neuropathy	%
0-5	612	403	66.17
6-10	70	50	71.42
11-15	52	30	57.69
16-20	24	20	83.33
Above 20	10	6	60

Table 4: Peripheral neuropathy versus caloric intake

Calories	T2DM	Peripheral neuropathy	%
1500	298	285	90.63
1501-2000	500	204	40.80
2001-2500	38	20	52.63
2500 and above	2	0	-

T2DM: Type 2 diabetes mellitus

Table 5: Peripheral neuropathy versus fasting blood sugar level

Fasting blood sugar (mg%)	Number of cases	T2DM with peripheral neuropathy	%
120	312	169	45.16
120-140	168	100	59.52
141-160	76	70	92.10
161-180	60	60	100
181-200	64	60	93.75
Above 200	158	150	94.93

T2DM: Type 2 diabetes mellitus

Table 8 shows a close and significant correlation between serum triglyceride and peripheral neuropathy.

Table 9 shows that values of high-density lipoprotein (HDL) cholesterol have a significant correlation with frequency of peripheral neuropathy. It is inversely proportional to the incidence of peripheral neuropathy. Probably lower HDL

Table 6: Peripheral neuropathy with post-prandial blood sugar

Post-prandial blood sugar (mg%)	T2DM	T2DM peripheral neuropathy	%
150	86	20	23.25
151-200	230	80	34.78
201-240	194	100	51.54
241-280	108	104	96.29
281-320	92	85	92.39
231 and above	128	120	93.75

T2DM: Type 2 diabetes mellitus

Table 7: Peripheral neuropathy versus serum cholesterol

Serum cholesterol (mg%)	T2DM	Peripheral neuropathy	%
150-200	176	109	61.93
201-250	316	208	65.32
251-300	260	130	50.00
301-350	58	52	89.65
350 and above	28	10	37.51

T2DM: Type 2 diabetes mellitus

Table 8: Peripheral neuropathy and serum triglyceride level

Serum triglyceride (mg%)	T2DM	Peripheral neuropathy	%
100	318	109	34.27
101-150	402	300	74.62
151-200	92	81	88.04
201-250	18	15	83.33
251-300	3	3	100
301 and above	1	1	100

T2DM: Type 2 diabetes mellitus

Table 9: Peripheral neuropathy and HDL cholesterol

HDL (mg%)	T2DM	Peripheral neuropathy	%
36-45	318	139	43.71
46-55	402	310	77.11
56-64	102	56	54.60
65 and above	12	4	33.33

T2DM: Type 2 diabetes mellitus, HDL: High-density lipoprotein

values enhance the micro-angiopathy and thereby lead to increase in the incidence of peripheral neuropathy.

The Table 10 shows that DPN frequently presents as pain syndrome and paresthesic. Vibration sense was more diminished in lower extremities than in the upper limbs. Motor disorders were found in only 2% cases. In 95% of patients with DPN, the tendon reflexes were diminished. Abnormal ankle jerk was encountered most frequently, and diminution was often asymmetric. Symmetric polyneuropathy was encountered in 488 out of 509.

Table 10: Symptomatology of distal polyneuropathy in 509 cases

Symptoms	Literature	Present series %
Subjective disturbances	86.2	82
Pain	76.1	70.3
Paresthesia	47.70	60
Cramps	47.70	60
Sensation of weakness and heaviness in lower extremities	37.70	10
Objective disturbances	85	78
Sensory disorders	83.80	62
Tactile hypoesthesia	35.40	18
Diminished sense of vibration	80	76
Impaired musculo-articular sense	9.20	1.80
Impaired discriminative sensation	35	1.20
Motor disorders		
Atrophy of muscles of extremities	16.10	2.00
Fasciculations	00	00
Paresis	00	00
Diminished reflexes	85.30	97
Biceps	11.50	10
Triceps	10	6
Radial	10	6
Knee jerk	50.80	48.00
Ankle jerk	98	95
Trophic disorders	51.60	21.20
Ulcer	0.80	1.20
Osteoarthropathy	1.80	6.20

Table 11: Asymmetric neuropathy

Asymmetric polyneuropathy	Cases (%)
Total	21 (4.01)
Acute/sub-acute motor	2 (0.40)
Cranial mono-neuropathy	7 (1.10)
Truncal neuropathy	12 (2.11)
Entrapment neuropathy	0

Table 12: Features of autonomic neuropathy

Symptoms	%
Diabetic impotence	60.00
Cardiac neuropathy	19.10
Neurogenic bladder	11.00
Seating disturbance	9.00
Neuropathic ulcer	0.60
Nocturnal diarrhea	0.30

The Table 11 reveals that asymmetric polyneuropathy is less common among the diabetics.

Impotence is probably the most frequent manifestation of autonomic neuropathy (Table 12).

It includes cases of impaired glucose tolerance and T2DM with mild hyperglycemia. It appears from the Table 13 that the incidence of peripheral neuropathy is lowest in the insulin-treated group as compared to those on oral hypoglycemic agents/or combinations. The

Table 13: Correlation of peripheral neuropathy with management

Group	Cases	Peripheral neuropathy	%
Diet	296	180	60.80
OHA+diet	480	350	72.90
Insulin	40	04	10
OHA+insulin	22	20	90

Table 14: Correlation of peripheral neuropathy with glycaemic control

HbA1C%	T2DM cases	Peripheral neuropathy	%
Less than 8%	202	109	53.90
8% and above	638	400	62.89

Z=2.55. (P<0.01). T2DM: Type 2 diabetes mellitus, HbA1C: Glycosylated hemoglobin

oral hypoglycemic agent might probably contribute to peripheral neuropathy.

The Table 14 shows that in uncontrolled diabetes frequency of polyneuropathy is higher, which is statistically significant ($P < 0.01$). It seems to be an important exacerbating factor of subclinical polyneuropathy.

DISCUSSION

Analysis of our material reveals a significant increase in the frequency of DPN with an increase in patient age (Table 11) ($P = 0.001$). This is corroborated by the finding of Jordan (1936), Rundles (1945), Martin (1953), and Gelman (1967).^{17,18} The factor of age in the development of DPN could be:

1. The increase in duration of diabetes as the age advanced.
2. Higher incidence of concomitant atherosclerosis leading to DPN.
3. Wittingham *et al.* (1971) have postulated that diabetics may acquire senile neuropathy at middle age.¹⁹

We observed that incidence of polyneuropathy in the obese diabetic was by about the same as in normal weight (Table 2). This is corroborated by the finding of Richardson (1953). Higher incidence of peripheral neuropathy in diabetes and its decompensation leading to a development of angiopathy in the middle-aged patient. Table 3 shows no linear correlation though highest incidence was noted in disease of 16-20 years. However, this rising trend of incidence was not maintained in disease of more than two decades.

We found that low caloric intake (Table 4) correlated favorably with the frequency of polyneuropathy. Martin (1953), Gelman (1967),^{17,18} believe that long-term hyperglycemia is direct or an indirect cause of peripheral

neuropathy. We found that the incidence of DPN shows no linear correlation with the fasting or post-prandial hyperglycemia (Tables 5 and 6). Moreover, DPN was also encountered in IGI group. This too shows that glycemia is probably not intimately related to polyneuropathy.

Jorden *et al.* 1935^{19,20} showed that in diabetes content of cholesterol, phospholipid in peripheral nerve was reduced, Adams (1954)²¹ found that activity of acetic-thiokinase in peripheral nerve of alloxan-diabetic animals was sharply reduced. And considered it as manifestation of the syndrome of abnormal fat metabolism which may lead to earlier development atherosclerosis in vessels of the extremities. However, Table 7 shows no consistent correlation though Table 8 shows significant correlation with serum triglycerides. Table 9 shows that HDL cholesterol is inversely proportional to the incidence of polyneuropathy. Probably lower HDL values enhance the micro-angiopathy and thereby lead to increase the incidence of peripheral neuropathy.

Vibration sense was more diminished in lower extremities than in upper limbs. The disparity between manifestations in upper and lower limb can be explained on the anatomical basis. The cranial mono-neuropathy involving the 7th and 3rd cranial nerves may be due to compression of the nerve in a bony canal.¹²

The prolonged administration of large doses of sulfonamides may produce polyneuritis Govseev and Mints (1948), Stepin (1956),^{3,14,19} have reported DPN in diabetes due to sulfonylurea. Our observation contained in Table 13 corroborates these reports.

There are several theories have been postulated for pathogenesis of polyneuropathy viz:⁵

1. Accumulation of sugar, alcohol, leading to swelling and tissue damage.
2. Deficiency of intracellular inositol leading to impairment of membrane phospholipid function.
3. Deficiency of myelin synthesis due to hypoinsulinemia, leading to the segmental myelin loss.
4. Glycosylation of neural membrane proteins with impairment of neural function.
5. Accelerated death and turnover of Schwann cell either secondary to cell injury from of the above or directly due to diabetes independent of metabolic abnormality leading to thickening and accumulation of abnormal basal lamina and impaired nerve function.
6. Immunoreactive mechanism with lipid acting as haptens and glycolipid as antigens.

Locke and Tarsy¹⁹ have defined complication as "Any pathological process occur in antecedent but not

compulsory to the main disease, and the causes for that not connected with the cause of principal disease.” Thus contrary to the consensus regarding polyneuropathy as a complication of diabetes, we believe that it is an accompaniment.

CONCLUSION

1. Mode of therapy and glycemic control can only lessen the severity.
2. Metabolic decompensation of diabetes has a detrimental effect.
3. No single mechanism appears to explain polyneuropathy, a combination of factors appear to be responsible.
4. Diabetic polyneuropathy is a component rather than a complication of diabetes.

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How to cite this article: Patel HS, Jain SK. Distal Polyneuropathy in Type 2 Diabetes Mellitus in and Around Jabalpur, Madhya Pradesh, India. *Int J Sci Stud* 2016;3(11):218-222.

Source of Support: Nil, **Conflict of Interest:** None declared.

Effects of Aerosolized Levosalbutamol Verses Salbutamol on Serum Potassium Level and Heart Rate in Children with Acute Exacerbation of Asthma

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Abstract

Background: Aerosolized levosalbutamol (LEV) and Salbutamol are used commonly today in the management of acute exacerbation of childhood asthma and the complications and side effects with salbutamol and LEV therapy needs to be carefully studied. Published data shows that LEV will not cause much change in the serum potassium levels compared to salbutamol.

Materials and Methods: This prospective study conducted in a teaching hospital catering to the lower socioeconomic class. The study period was from December 2014 to May 2015. It included 60 known asthmatic children aged between 5 and 15 years who presented with acute exacerbation of childhood asthma were studied. Baseline clinical parameters were recorded before and after giving 3 back to back nebulization at 20 min apart in the 1st h of presentation. Respiratory rate (RR) heart rate (HR), oxygen saturation in room air SpO₂, forced expiratory volume in 1 s (FEV1) measured, asthma score and serum potassium level asthma score were monitored post nebulization.

Results: The present study Group-1 LEV cases were showing clinical improvement in terms of FEV1 asthma score and SpO₂ with reduced RR and there was not much statistically significant fall in the serum potassium level and HR at 60 min after nebulization as compared to the baseline. $P = 0.0001$. In Group 2 - Salbutamol cases were showing significant clinical improvement in SpO₂, FEV1, RR, and asthma score, but there were significant tachycardia and fall on serum potassium level after nebulization $P = 0.0001$. Among them 70% of children showing a drop of potassium level 0.5-0.8 mEq/L from the baseline values. The results were all found to be independent of extraneous factors like pH, prior use of inhaled steroids or bronchodilators and nutritional status.

Conclusion: The aerosolized LEV is superior medicine in the management of acute exacerbation of asthma in children and no side effects like increase in HR and hypokalemia.

Key words: Childhood asthma, Hypokalemia, Levosalbutamol, Salbutamol

INTRODUCTION

Asthma is a common disease worldwide. It is the most common chronic disease in children.¹ The prevalence of asthma in childhood is 10-30%.^{2,3} It is the leading cause of hospitalizations in children <15 years of age, and the leading cause of school absence.⁴ In India, the estimated

burden of asthma is believed to be more than 15 million.⁵ Most children admitted to the hospital because of acute asthma do not require intensive care treatment.

The salbutamol and levosalbutamol (LEV) inhalation therapy are effective way of management of acute exacerbation of childhood asthma, but their uses are associated with undesirable side effects such as tachycardia and hypokalemia. Salbutamol, the most commonly used bronchodilator, is a chiral drug with R and S isomers. The commonly used formulation is a racemic mixture that contains equal amount of both R and S isomer. β_2 -agonist Racemic Salbutamol has been the mainstay of treatment for bronchial smooth muscle contraction since 1982.⁶ β_2 -agonist are a racemic mixture that is composed

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Month of Submission : 11-2015
 Month of Peer Review : 12-2015
 Month of Acceptance : 01-2016
 Month of Publishing : 02-2016

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of a 50:50 ratio of (R) and (S) isomers. "LEV" was approved by Food and Drug Administration in 1999 as a purified single isomer for clinical use in asthma patients.^{1,7} The bronchodilator effects of salbutamol are attributed entirely to (R)-salbutamol (LEV), while (S)-salbutamol has been shown to possess bronchospastic and pro-inflammatory effects both *in vitro* and *in vivo* studies. LEV, the (R) enantiomer of salbutamol is currently available only in a liquid formulation for use via a nebulizer. LEV has approximately 2-fold greater affinity than the racemic salbutamol for the β_2 adrenergic receptor and approximately 100 fold greater binding affinity than S-salbutamol. LEV elevates intracellular concentration of cyclic adenosine monophosphate (cAMP) by activating adenylyl cyclase. In the airways, increased concentration of cAMP relaxes bronchial smooth muscle by reducing intracellular calcium and prevents contraction of hyperresponsive airways. Increased concentration of cAMP also inhibits the release of inflammatory mediators from mast cells and eosinophil.⁸⁻¹² There are several studies which demonstrate a significant decrease in serum potassium level after aerosol therapy.^{13,14}

In studies of outpatient asthma patients who were treated with LEV they experienced a significantly greater increase in forced expiratory volume in 1 s (FEV1), a longer duration of action and fewer side effects.¹⁵⁻¹⁹ Though salbutamol is an effective treatment of acute exacerbation, its use is associated with undesirable side effects like tachycardia.²⁰ The purpose of the present study is to evaluate the effects of LEV versus Salbutamol on serum potassium level and heart rate (HR).

Objective

To study the effects of LEV versus salbutamol nebulization on serum potassium level and HR in children with acute exacerbation of asthma aged between 5 and 15 years.

MATERIALS AND METHODS

This is a prospective study done on 60 children aged 5-15 years attending the pediatric emergency Department of Kannur Medical College, Anjarakkandy, and were grouped into children receiving LEV (Group I-30 cases) and those receiving salbutamol (Group II, 30 cases). The studied medicines nebulized salbutamol (2.5 mg) or LEV (0.63 mg) was diluted in 2.5 ml NS and was nebulized over a period of 7-10 min, 3 times in an hour. After 60 min, HR and serum potassium levels were measured.

Inclusion Criteria

Patient aged between 5 and 15 years presenting with acute exacerbation of asthma.

Exclusion Criteria

Age >15 and <5 years, severe asthma, children already on preventive therapy (inhaled steroids or long-acting bronchodilator), patients on treatment diuretics, aminoglycosides, bicarbonates, acute gastroenteritis, the presence of baseline hypokalemia, congenital heart diseases and patients with hepatic, pre-existing renal disease.

Data Collection and Evaluation

Parents were given a detailed briefing about the purpose of the study. After obtaining permission from the head of the Institute and taking informed consent from parents of the children/guardian, they were enrolled in the study. Ethical clearance was obtained from Institutional Ethical Committee. Data were entered and analyzed using excel spread sheet. Nebulized salbutamol (2.5 mg) diluted in 2.5 ml NS was administered 3 times during the 1st h in Group I and LEV (6.3 mg) diluted in 2.5 ml NS to Group II. The following parameters were recorded initially and after giving 3 nebulizations at 20 min interval in the 1st h of presentation-respiratory rate (RR), HR, oxygen saturation in room air SPO₂, FEV₁, asthma score and serum K⁺ level. Clinical asthma severity score includes 5 parameters (tachypnea, hypoxia, retractions, wheeze and dyspnea) (Table 1).⁶ Each parameter was scored from 0 to 3 (maximum total score was 15). A score of more than 7 was considered as severe. All the values were expressed as mean \pm standard deviation (SD) for pre- and post-treatment effects. Comparative analysis of baseline parameters of two groups and within the groups and percentage of improvement between these two groups before and after treatment was done using unpaired "Z" test. All the statistical analysis was performed using SPSS package 21 version.

Complete blood count, serum creatinine, serum electrolytes, ABG and X-ray of chest were studied when it was required. All the patients were monitored by continuous electrocardiography, and arterial oxygen saturation by pulse oximetry with a finger oximeter. The baseline peak expiratory flow rate was measured. An intravenous (IV) line for repeated blood sampling was established. After the third administration of back to back LEV or salbutamol nebulization in 20 min apart total three doses (60 min), RR and serum potassium levels were assessed. The mean and SD were calculated for baseline and subsequent measure of potassium. Serum potassium level was monitored at 0 h and 60 min post nebulization.

RESULTS

To study the effects of medicines following parameters were recorded pre and post nebulizations that there was

a statistically significant fall in the serum potassium level at 60 min as compared to the baseline level of potassium in the group - Salbutamol after back to back nebulization.

. After (Group 1) LEV nebulization, there was a significant increment in FEV1 and SPO2 with a decrease in tachypnea and asthma score ($P = 0.0001$) while no significant difference was found in pre- and post-treatment HR and serum K⁺ levels (Table 4). In the salbutamol (Group 2), there was a clinical improvement in terms of FEV, oxygen saturation and asthma score, but a significant tachycardia and decrease in potassium levels ($P = 0.0001$) (Table 5). Of 70% of children and showed a fall of 0.2-0.6 mEq/L from the baseline values. Serum potassium concentration decreased significantly (3 mEq/L) in one patient in the continuous salbutamol nebulization; however, this patient had inadvertently been given IV maintenance fluids without potassium chloride. Supplemental potassium chloride (20 mEq/L) was added to her IV fluids and the hypokalemia resolved without any adverse consequences. The results were all found to be independent of extraneous factors like pH, Prior use of inhaled steroids or bronchodilators and nutritional status.

The majority of cases were aged between 9 and 11 years, 25 cases (42%) followed by 21 (35%) cases age between 12 and 15 years and 14 (23%) children belong to 5-8 years (Table 2). Among them 28 (58%) males and 32 (42%) cases were females who presented with acute exacerbation of childhood asthma (Table 3).

All the values for pre- and post-treatment parameters are expressed as mean \pm SD. Comparison done using unpaired t test at 5% level of significance. All the statistical analysis was performed by SPSS 21 version (Tables 4 and 5).

Mean baseline FEV1 52.2 ± 0.53 /min (range 80-120%). Serum potassium levels decreased significantly from 4.46 ± 0.61 (baseline) to 3.643 ± 0.35 mEq/L (60 min) ($P = 0.0001$) and HR increased from 101.80 ± 8.2 (baseline) to 124.6 ± 6.8 beats/min post salbutamol nebulization ($P = 0.0001$) (Tables 6 and 7).

In Group 1 patients, the effects of LEV nebulization will not cause the hypokalemia and tachycardia. $P = 0.0001$.

DISCUSSION

Asthma is the most common chronic disease of children.¹⁻³ It contributes significantly to the number of cases in pediatric emergency. Acute exacerbation of asthma was the 3rd most common diagnosis most common diagnosis (5.2%) after acute diarrhea and seizures.⁴⁻⁸ No clinical study data available and all study done with comparative effects of LEV verses salbutamol on potassium and HR in acute exacerbation of asthma only one data available that Singhi et al.,¹² study was done two decade ago and they observed that after salbutamol nebulization the serum potassium level decreased marginally from 3.9 ± 0.5 mEq/L to 3.7 ± 0.5 mEq/L ($P < 0.05$). A decrease in serum potassium concentration was noted in 26 (56.5%) and hypokalemia (serum potassium < 0.005). Recently, a randomized, double-blind clinical study comprising 84 asthmatic children admitted at 11 different centers over 3 years was conducted in Bangladesh.^{1,10}

Another study done by Punj et al.,² in India among children aged 5-18 years presenting in the ED with acute exacerbation of asthma. The patients had initial mean PEFR < 0.01) and better tolerability, less tachycardia and less hypokalemia compared to salbutamol ($P < 0.01$).^{2,14} Our study result shows that both have same therapeutic effect with less significantly less side effects like tachycardia and hypokalemia in the Levosalbutamol Group 1 ($P - 0.0001 < 0.05$). The study conducted by Punj et al.,^{2,15} they observed that LEV has equally good effect with salbutamol in improving FEV1, SpO2 and asthma score in the treatment of acute exacerbation of asthma in children but better tolerability in terms of tachycardia and hypokalemia compared to salbutamol. A similar study done by Rahman et al.,^{1,16} concluded that LEV has similar therapeutic effects with salbutamol in acute exacerbation of asthma but has no side effects such as tachycardia and hypokalemia. Ralston et al.,^{14,16,17} compared LEV with a combination of salbutamol and ipratropium bromide in children between 6 and 18 years presenting with acute asthma and reported that LEV was associated with less tachycardia but showed no other advantage of associating RAC with ipratropium bromide. Our study underlines the fact that while having similar effects with Sabutamol group 2 alone, levosalbutamol Group 1 does not cause either tachycardia or hypokalemia.^{9,10,20}

Table 1: CASS (6)

Score	RR	Room air saturation*	Auscultation (wheeze)	Retractions	Dyspnea
0	<30	97-100	None	None	None
1	31-45	94-96	End expiration	\pm	Full sentences
2	46-60	91-93	All expiration	++	Partial sentences
3	>60	<91	Inspiration and expiration without stethoscope	+++	Single word/grunt

*Off oxygen for 5 min or until saturation drops $< 91\%$. CASS: Clinical asthma severity score, RR: Respiratory rate

Severity assessment			
	Mild	Moderate	Severe
Asthma score	5-7	8-11	12-15
% FEV1	<80	50-65	<50

FEV1: Forced expiratory volume in 1 s

Table 2: Age distribution

Age in years	Group 1 LEV	Group 2 Salbutamol	Percentage
5-8	06	08	23
9-11	13	12	42
12-15	11	10	35
Total	30	30	100

LEV: Levosalbutamol

Table 3: Gender wise distribution

Index	Male	Female	Total
Number of cases	28	32	60
Percentage	58	42	100

Table 4: Pre-treatment observations

Parameters	Pre-treatment LEV	Pre-treatment salbutamol
RR	29.79±0.73	28.20±0.61
HR	100.6±7.1	101.8±8.2
SPO2	94.76±0.59	94.76±0.59
FEV1	52.20±0.53	56.4±0.73
Serum potassium level mEq/L	4.46±0.79	4.26±0.36
Asthma score	6.60±0.55	6.6±0.75

RR: Respiratory rate, HR: Heart rate, FEV1: Forced expiratory volume in 1 s, LEV: Levosalbutamol

Table 5: Post-treatment observations

Parameters	Post treatment LEV	Post treatment salbutamol
RR	21.7±1.6	22.6±1.25
HR	106.2±8.1	124.6±6.8
SpO ₂	98.33±2.99	97.93±1.95
FEV1	68.98±12.21	67.13±1.77
Serum potassium level MEq/L	4.43±0.60	3.64±0.35
Asthma score	5.0±1.31	5.2±0.82

RR: Respiratory rate, HR: Heart rate, FEV1: Forced expiratory volume in 1 s, LEV: Levosalbutamol

Table 6: Pre-treatment observations of LEV versus salbutamol

Parameters	LEV	Salbutamol	P value
HR	100.6±7.1	101.8±8.2	0.5469 (>0.05)
Serum potassium	4.46±0.66	4.26±0.36	0.1505 (>0.05)

HR: Heart rate, LEV: Levosalbutamol

Table 7: Post-treatment observations of LEV and salbutamol

Parameters	LEV	Salbutamol	P value
HR	106±8.1	124.6±6.8	0.0001 (<0.05)
Serum potassium	4.43±0.60	3.64±0.35	0.0001 (<0.05)

HR: Heart rate, LEV: Levosalbutamol

CONCLUSIONS

All previous study was assessed the efficacy of levosalbutamol versus salbutamol in the management of acute exacerbation of asthma. Present study shows that the effects of aerosolized LEV (Group 1) is the superior and safer drug in the treatment of acute exacerbation of asthma and no effect on Serum potassium level in 30 children who were admitted in the Paediatric Emergency department. It was concluded that there was not much significant fall in serum potassium and heart rate in children with acute exacerbation of asthma after using aerosolized LEV. when compared to aerosolized salbutamol there was a change in serum potassium level from 0.5 to 0.8 mEq/L and heart rate increased from 25 to 30 beats per minute post nebulisation the most significant fall occurring at 60 minutes.

A significant hypokalemia occurred only 3.3% but extra caution needs to be taken when subjecting patients with gastroenteritis, on oral steroids, diuretics, underlying renal or hepatic disease, cardiac cases etc. who are more prone for to develop the electrolyte imbalances to nebulized salbutamol.

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How to cite this article: Barkiya SM, Kumari V, Venugopal, Aseez A. Effects of Aerosolized Levosalbutamol Verses Salbutamol on Serum Potassium Level and Heart Rate in Children with Acute Exacerbation of Asthma. *Int J Sci Stud* 2016;3(11):223-227.

Source of Support: Nil, **Conflict of Interest:** None declared.

Prevalence of Smoking and Smokeless Forms of Tobacco Use In Adults More Than 18 Years in an Urban Area

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Abstract

Introduction: A prevalence of tobacco use has increased over the past decades. Over one-third of tobacco consumed regionally is smokeless. Traditional forms like betel quid, tobacco with lime and tobacco tooth powder are commonly used, and the use of new products is increasing, not only among men but also among children, teenagers, women of reproductive age.

Objective: To study the prevalence of both smoking and smokeless forms tobacco use among men above the age of 18 years in an urban area.

Methodology: The study design was community-based cross-sectional study. The study participants were adults aged above 18 years. The calculated sample size was 725. After obtaining informed consent, the interview was done separately for each participant using pre-structured and pretested questionnaire which was prepared based on Global Youth Tobacco Survey. Categorical outcomes were summarized by rates. Numerical outcomes were summarized by mean and standard deviation.

Results: The prevalence of both smoking and smokeless forms of tobacco together was 55.7%. Out of 725 study participants, 25.9% were using only smoking form of tobacco, 10.3% only smokeless form and 19.4% of the subjects were using both forms of tobacco. 44.3% subjects were not using any form of tobacco. 29.76% smoked on all days of the month and 21.96% smoked for 20-29 days of the month. 25.14% men smoked for 10-19 days of the month and 23.1% smoked for 6-9 days/month.

Conclusions: The present community-based study, reported a higher prevalence of tobacco use among men above the age of 18 years. The tobacco use varied with age and type of tobacco. Most of the smokers used both cigarettes and beedis.

Key words: Prevalence, Smokeless, Smoking, Tobacco, Urban area

INTRODUCTION

The tobacco epidemic kills nearly 6 million people a year. Over 80% of tobacco deaths take place in the developing countries. In 2004, about 5 million adults aged 30 years and above died from direct tobacco use around the world.¹ If these trends persist, tobacco will kill more than 8 million people worldwide each year by the year 2030, with 80% of these premature deaths in low and middle-income

countries. By the end of 21st century, tobacco may kill more than a billion people unless urgent action is taken.²

The six most effective policies that can curb the tobacco epidemic are outlined in the WHO MPOWER strategy:

Monitoring tobacco use and prevention protecting people from tobacco smoke offering help to give up tobacco use warning people about the hazards of tobacco enforcing bans on tobacco advertising, promotion and sponsorship raising taxes on tobacco.²

Based on age and sex-specific rates for tobacco use in urban and rural areas, as reported in the second national level survey, it is estimated that in 1996, 184 million persons (150 million males and 34 million females) in India used tobacco.³

Access this article online



www.ijss-sn.com

Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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Prevalence of tobacco use has increased over the past decades. Hence, the present study was undertaken to know the prevalence of tobacco use in adult men.

Objective

The objective of the study was to study the prevalence of tobacco use among men above the age of 18 years in an urban area.

REVIEW OF LITERATURE

What we commonly describe “tobacco” comprises cigarettes, cigars, loose pipe tobacco, chewing tobacco, and snuff. These products are the dried, processed leaves of the tobacco plant *Nicotiana rustica* or *Nicotiana tabacum*. All tobacco contains nicotine, an addictive drug. Nowadays, tobacco contains thousands of other chemical ingredients added to make the products more user-friendly and addictive.

Within a short period after Christopher Columbus first observed this strange behavior of smoking among the natives of America in 1492, tobacco use increased worldwide and assumed major social, political, industrial, economic and medical significance. It is known that tobacco use compensates the body, causes diseases, compromises users' health, shortens lifespan and leads to early death. One cigar has as much nicotine as almost three packs of cigarettes. A cigar can contain up to 444 mg of nicotine while a cigarette can contain up to 11 mg of nicotine. A pocket-size packet of smokeless tobacco contains as much nicotine as three packs of cigarettes. The moister the tobacco, higher is the nicotine content.

Tobacco contains a variety of toxic chemicals. Smokeless tobacco contains formaldehyde, which is embalming fluid, nitrosamine and benzopyrene, which are known carcinogens, and uranium 235 and polonium 210, both of which are nuclear products. In all, chewing tobacco contains at least 28 cancer-causing chemicals. The nitrosamine content of smokeless tobacco is over 1,000 times greater than the amount allowed by the FDA.⁴

National Household Survey of Drug and Alcohol Abuse in India (NHSDAA), conducted in 2002, among males which covered over 40,000 individuals aged 12.60 years in nearly 20,000 households in 25 states showed that the overall prevalence of current tobacco use was 55.8%. There is an increase in tobacco use with age, leveling off after 50 years of age.⁵

According to NFHS-3, the prevalence of any tobacco use in 15-49 years age group was 57% in males and 10.8% in females. The prevalence of smoking alone was 32.7% in

both urban and rural area. Prevalence of pan and Gutkha chewers was 36.5% in males.³

A survey conducted in South Arcot district, Tamil Nadu showed that, among men aged 35-69 years, showed that nearly 47% were ever-smokers. During the same period, a survey in Chennai city found that 38% men were ever-smokers.⁶

METHODOLOGY

The present study was conducted at the Urban Health Centre, Ramnagar, Belagavi, Karnataka, India which is an urban field practice area of Department of Community Medicine, Jawaharlal Nehru Medical College, Belagavi, Karnataka, India. The UHC is situated at about 2.5 km from J. N. Medical College and caters to a total population of 29,521. The study design was community-based cross-sectional study.

The study subjects were adults aged above 18 years residing in areas under Urban Health Centre Ramnagar, Belagavi, Karnataka, India which is an urban field practice area of Department of Community Medicine, Jawaharlal Nehru Medical College, Belagavi, Karnataka, India. Adult men above the age of 18 years who were permanent residents and who gave informed consent were included.

Based on Global Adult Tobacco Survey (GATS) India 2009-2010, the prevalence of tobacco use in any form among men in urban area was 48%. The sample size was calculated to be 721. Therefore, 725 adult men above the age of 18 years were included in the study. The sampling frame of all the adults of the areas was made, and simple random sampling method was used to select 725 adult men who were included in the study using random number table. The study was approved from Institutional Ethics Committee. Based on the selection criteria, the study participants were selected and written informed consent was obtained from all the participants, before collecting the data.

A questionnaire was prepared based on Global Youth Tobacco Survey. A pilot study was conducted using the predesigned questionnaire and required modifications were made.

Data were collected from the participants through interview. Data regarding socio-demographic variables such as age, sex, address, educational status, occupation, marital status, and socio-economic status (SES) were collected. All the subjects in the sample were informed about the purpose of the study and after obtaining informed consent,

they were interviewed separately using pre-structured and pretested proforma. The data collection was done using predesigned and pretested questionnaire. A pilot study was conducted to know the feasibility. Categorical outcomes were summarized by rates. Numerical outcomes were summarized by mean and standard deviation.

RESULTS

The present study was conducted in Urban Health Centre, Ramnagar, Belagavi, which is a field practice area of Department of Community Medicine, Jawaharlal Nehru Medical College, Belagavi, Karnataka, India.

Of the 725 persons who participated in the study, 29 (4%) were in the age group of 18-25 years, 185 (5.5%) were in 26-35 age group, 236 (32.6%) were in 36-45 years, 167 (23%) were in 46-55 years, 75 (10.3%) were in 56-65 years, and 33 (4.6%) were in the age group of 65 years. Mean age group of the study participants was 43.5 ± 12.11 years. Range was 18-86 years. In the present study, 130 (17.9%) were found to be illiterate, 195 (26.9%) had primary school education, 139 (19.2%) had middle school education, 119 (16.4%) had high school education, and 142 (19.6%) were educated up to college level. Unemployed or student group comprised 126 (17.4%) of study participants. In the present study, 270 (37.2%) belonged to Class II SES as per modified B.G. Prasad's classification; 202 (27.9%) to Class V; 134 (18.5%) to Class IV, 88 (12.1%) to Class III and only 31 (4.3%) belonged to Class I.

In present study, the prevalence of both smoking and smokeless forms of tobacco together was 55.7%. Out of 725 study participants, 188 (25.9%) were using only smoking form of tobacco, 75 (10.3%) only smokeless form and 141 (19.4%) of the subjects were using both forms of tobacco. 321 (44.3%) subjects were not using any form of tobacco (Table 1 and Figure 1).

Out of 725 study participants, 329 (45.69%) were current smokers and 396 (54.31%) were not smoking tobacco currently (Table 2).

In the present study, 216 (29.79%) study participants were using smokeless form of tobacco and 509 (70.21%) were not using smokeless form of tobacco (Table 3).

Table 1: Distribution of study subjects according to current smoking status

Smoking status	N (%)
Smoker	329 (45.69)
Non-smoker	396 (54.31)
Total	725 (100)

In the present study, 103 (29.76%) smoked on all days of the month and 76 (21.96%) smoked for 20 to 29 days of the month. 87 (25.14%) men smoked for 10-19 days of the month and 80 (23.1%) smoked for 6-9 days/month.

Distribution of Smokers According to Cigarettes/Beedis Smoked per Day

In present study, 137 (39.6%) smoked 6-10 cigarettes or beedis per day, 104 (30%) smoked 2-5/day, 59 (17%) smoked 11-20/day, 26 (7.5%) men smoked more than 20/day, and 20 (5.7%) smoked less than or equal to 1 cigarette or beedi per day (Table 4 and Figure 2).

In the present study, among 346 smokers, 36 (10.4%) were using filtered form (cigarette) and 17 (4.91%) men were using only beedis. However, most of them were using both

Table 2: Distribution of study subjects according to current status of use of smokeless form of tobacco

Usage of smokeless form of tobacco	N (%)
Currently using smokeless form	216 (29.79)
Currently not using smokeless form	509 (70.21)
Total	725 (100)

Table 3: Distribution of smokers according to number of days smoked in past 30 days

Smoking in past 30 days	Number of days smoked (%)
3-9	80 (23.1)
10-19	87 (25.14)
20-29	76 (21.96)
All 30	103 (29.76)
Total	346 (100)

Table 4: Distribution of study subjects according to type of cigarettes/beedis smoked in past 30 days (N=346)

Type of smoking form of tobacco	N (%)
Filters	36 (10.4)
Beedis	17 (4.91)
Both	291 (84.1)
Others (cigars etc.)	2 (0.57)
Total	346 (100)

Table 5: Distribution of study subjects according to usage of different smokeless forms of tobacco products in past 30 days (N=216)

Smokeless form of tobacco products	N (%)
Chewing tobacco	158 (21.8)
Snuff	3 (0.4)
Pan masala	20 (2.8)
Gutkha	35 (4.8)
Total	216 (100)

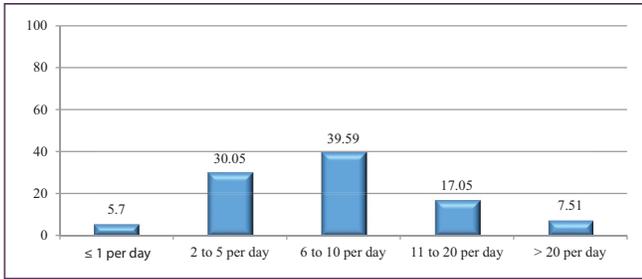


Figure 1: Distribution of study subjects according to use of different forms of tobacco

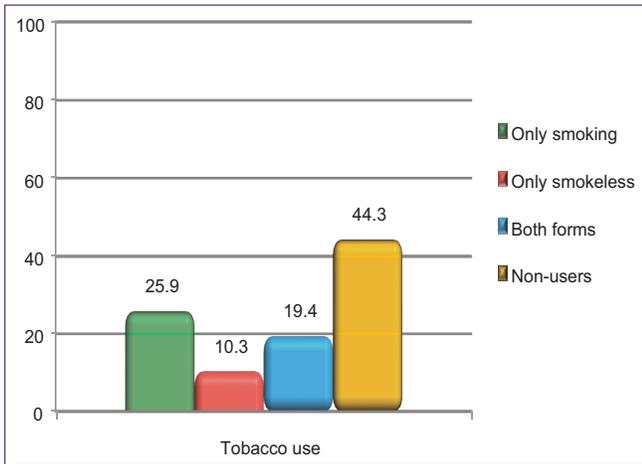


Figure 2: Cigarettes/beedis smoked per day

forms of tobacco 291 (84.1%) and only 2 (0.57%) of them were using cigars (Table 5).

In the present study out of 725 men, 216 (28.8%) were users of smokeless forms of tobacco. 158 (21.8%) subjects used chewable tobacco, 3 (0.4%) used it in snuff form, 20 (2.8%) used pan masala and 35 (4.8%) were Gutkha users.

DISCUSSION

In the present study, the prevalence of both smoking and smokeless forms of tobacco together was 55.7%. This finding was similar to the NFHS-3⁷ and NHSDAA in India, conducted in 2002. Whereas, the overall prevalence of tobacco use in the present study is higher than in GATS India (47.9%). In another study the prevalence of tobacco use was 61.89%.⁸

The prevalence of smoking was 45.7% and prevalence of smokeless form was 29.8% in the present study. The prevalence of use of both forms of tobacco by same user was 19.6%. In GATS survey, the prevalence of smoking was 24.3% which was lesser than present study. The prevalence of use of smokeless form of tobacco was

32.9% in GATS India which is higher than present study. In another study, where the prevalence of smokers in slum was 30.7% and in non-slums it was 26.9% and that of smokeless form of tobacco was 35.1% in slums and 25.9% in non-slums.⁹ According to NFHS-3 data, one-third of men in 15-49 years age group smoke cigarettes or beedis.⁴ In a study, the prevalence of smoking in men was 81.1%.⁸ In another study, the prevalence was 30.7%.⁹ A high use of tobacco in present study subjects was due to social acceptance as the majority of the areas covered by Urban Health Centre Ramnagar are urban slums and faith regarding minor ailments like toothache.

In the current study, the majority of the smokers were regular smokers (29.76%), who smoked on all days of the month followed by 21.96% smoked on 20-29 days of the month. 25.14% men smoked on 10-19 days of the month, 17.9% smoked on 6-9 days and least (5.2%) were in the group who smoked on 3-5 days. In GATS India, regular smokers were 19.4%¹¹ (both cigarette and beedi) which is lesser than present study. According to NFHS-3 data, 91% of the smokers were regular smokers which are much higher than present study.³

In present study, majority of the smokers (39.6%) smoked 6-10 cigarettes or beedis per day, 30% smoked 2-5/day, 17% smoked 11-20/day, 7.5% men smoked more than 20/day and least were 5.7% who smoked less than or equal to 1 cigarette or beedi a day.

In the present study, the mode of acquiring the smoking forms of tobacco for 71.38% men was buying in a store or a shop, 14.45% gave money to someone else to buy for them, 3.75% of them borrowed from someone else and least (2.58%) of them got by stealing from an older person and some other ways. According to GATS India report, about half of all cigarette (51%) and beedi (49%) smokers and users of smokeless tobacco products (55%) purchased tobacco products from stores.¹¹

In the present study, most of them were using both cigarettes and beedis (84.1%), 10.4% were using only filtered form (cigarette), 4.91% men were using only beedis and 0.57% of them were using cigars. According to GATS India report, 34.42% of the smokers were using cigarettes and 65.58% were using beedis.¹⁰

In the present study out of 216 users of smokeless forms of tobacco, most of the subjects (73.14%) used chewable tobacco since most of the users are construction workers, 1.4% used snuff, 9.25% used pan masala and 16.2% used Gutkha. In GATS India report, 32.9% of the male population above 15 years were using smokeless tobacco product. Among them 7.5% were using betel quid with tobacco, 18%

were using Khaini or tobacco-lime mixture, 13.1% were using Gutkha, tobacco lime, areca-nut mixture, 3.3% were using oral tobacco as snuff, mishri, gul, gudakhu and 3.5% were using other smokeless forms of tobacco. 27.4% men were regular users of smokeless form of tobacco.¹⁰

CONCLUSION

The present community-based study, reported a higher prevalence of tobacco use among men above the age of 18 years. The tobacco use varied with age and type of tobacco. Most of the smokers used both cigarettes and beedis. There was a significant association with socio-demographic factors like age group, education, occupation, marital status, type of family and socio-economic class.

LIMITATIONS

1. Some people may not disclose about their habits at home since tobacco use is considered as a bad habit
2. There are chances of recall bias, particularly, in the case of long-term tobacco users.

RECOMMENDATIONS

Behavioral and lifestyle change can be brought through education of people. Since age of initiation of tobacco use was high in the adolescent age group, education regarding ill effects of tobacco use should be made compulsory in schools and colleges. School curriculum should include health consequences of tobacco use. There should be a

separate allocation of funds, personnel and other resources by the government to perform educational activities to prevent tobacco use.

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How to cite this article: Neelopant SA, Ashtagi GS. Prevalence of Smoking and Smokeless Forms of Tobacco Use In Adults More Than 18 Years in an Urban Area. *Int J Sci Stud* 2016;3(11):228-232.

Source of Support: Nil, **Conflict of Interest:** None declared.

Recurrence Rate in Post Irradiated T1 and T2 Supraglottic and Glottic Carcinoma of the Larynx

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Abstract

Background: T1 and T2 carcinoma of the supraglottis and glottis can be treated by radiation or conservative surgery. Our aim was to study the recurrence rate following treatment with radiation alone, the sites of involvement, the risk factors involved and to assess the hemoglobin (Hb) levels in relation to the prognosis and treatment outcome.

Materials and Methods: A total of 61 patients with T1 and T2 laryngeal carcinoma were enrolled for this purpose. One succumbed to death due to unrelated cause. All the patients were given external beam radiation and followed up for 3 years. Association of risk factors like smoking and alcohol were recorded and the pretreatment Hb levels were checked.

Results: Local control rate at the end of 3 years was as follows: 53.57% for T1 and T2 supraglottic cancer and 87.5% for T1 and T2 glottic cancer. A maximum number of recurrence was found to be with infrahyoid supraglottic cancer. Parameters such as tumor extent and TNM staging, pretreatment Hb levels, histological differentiation, and continuance of risk factors significantly influenced the recurrence rate on univariate analysis, but by logistic regression table, significant *p* value was obtained only in the higher recurrence rate for infrahyoid supraglottic carcinoma, when compared to the other sites of the larynx.

Conclusion: Early T1 and T2 laryngeal cancers can be treated by radiotherapy or surgery. The choice of therapy is dependent on both patient and treatment institution related factors. While T1 and T2 glottic cancers had a control rate by radiotherapy comparable to that by surgery, infrahyoid supraglottic cancers had a higher rate of recurrence by radiotherapy. Conservative partial laryngectomy, transoral laser surgery or other alternative techniques in radiotherapy may be considered in treating these tumors.

Key words: Carcinoma, Glottis, Radiotherapy, Recurrence, Supraglottis

INTRODUCTION

Laryngeal cancers are considered to be the 11th most common malignancy of the head and neck cancers¹ and constitute about 25% of all head and neck malignancies. Adult males are more commonly affected, but the male to female ratio has come down significantly, over the recent past from 15:1 to less than 5:1.² More than 90% of these cancers are squamous cell carcinomas (SCC). Tobacco smoking and alcohol consumption are important risk factors for SCC of the larynx.³

The larynx is divided into the following three anatomical regions.⁴

- The supraglottic larynx includes the epiglottis, false vocal cords, ventricles, aryepiglottic folds, and arytenoids.
- The glottis includes the true vocal cords and the anterior and posterior commissures.
- The subglottic region begins 5 mm below the free margin of the true vocal cords or 10 mm below the apex of the ventricle and extends to the lower border of the cricoid cartilage.

The incidence and the preferential involvement of the site varies geographically. Glottic tumors predominate in the Anglo-Saxons, while the glottic cancers and supraglottic tumors equal in number approximately among the Indians and French populations.¹

Early laryngeal cancers are treated with either radiation or transoral laser surgery or conservative partial laryngectomy

Access this article online



www.ijss-sn.com

Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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procedures, while advanced tumors require combined modalities of treatment.⁴

In the present study, patients who had undergone radiation alone were selected to determine the recurrence rate in the post irradiated cases of T1 and T2 supraglottic and glottic laryngeal cancer lesions. The influence of risk factors, the hemoglobin (Hb) levels, and the surgical options in the treatment of early laryngeal carcinoma are discussed.

OBJECTIVES

1. To study the incidence of recurrence in early supraglottic and glottic carcinoma of larynx following treatment with radiation
2. To assess the effectiveness of radiation therapy in early laryngeal carcinomas.
3. To study the risk factors and to assess the Hb levels in relation to the prognosis and treatment outcome.
4. To study the treatment modalities that are presently used in the management of early supraglottic and glottic carcinoma of the larynx.

Inclusion Criteria

1. T1 and T2 N0 supraglottic and glottis carcinoma of the larynx.
2. Patients in the age group between 30 and 80 years were included in this study. Below 30 years incidence of laryngeal malignancy is less. Above 80 years, the treatment options may differ due to associated comorbidities. Both sexes were included.

Exclusion criteria

1. Suspected cases of benign lesions and tumors are excluded after tissue diagnosis.
2. Those presenting with neck lymph node metastasis as the staging of cancer becomes advanced.
3. Patients who developed a second primary during the study period to be excluded.
4. Subglottic cancer patients due to the rarity in presentation in early stages.

MATERIALS AND METHODS

The present study was approved by the Ethical Research Committee of the institution.

A prospective study of 3 years, between April 2010 and March 2014, patients with T1 and T2 N0 supraglottic and glottis laryngeal cancers, who attended the ENT and Radiology Departments, at MCH, Vandanam, Alappuzha, Kerala, India were enrolled after getting the informed consent to participate in this study. The patients were

divided into subgroups according to the TNM classification and to the site of involvement.

Staging of laryngeal cancer was according to the TNM classification designated by the American Joint Committee of Cancer.⁴

Supraglottis T1 - Tumor limited to one adjacent subsite of the supraglottis without fixation of the larynx.

Supraglottis T2 - Tumor invades mucosa of more than one subsite of supraglottis or glottis or region outside the supraglottis (e.g. mucosa of the base of tongue, vallecula, medial wall of pyriform sinus) without fixation of the larynx.

Supraglottic lesions were further classified into T1 and T2 suprahypoid and T1 and T2 infrahypoid lesions.

Glottis tumor limited to vocal cord(s) (may involve anterior and posterior commissure with normal mobility.

T1a - Tumor limited to one vocal cord

T1b - Tumor involves both vocal cords

T2 - Tumor extends to supraglottis and/or subglottis and/or with impaired vocal cord mobility.

61 patients were enrolled for the study purpose. 1 patient had succumbed to death due to an unrelated cause during the study. The patients were categorized under T1 and T2 suprahypoid, T1 and T2 infrahypoid supraglottic cancers, and T1a T1b and T2 glottic cancers.

Risk factors in the personal history of the patients were recorded, notably alcoholism, smoking and the duration of the abuse. Pretreatment Hb levels were recorded. All the patients were subjected to indirect laryngoscopy and flexible pharyngolaryngoscopy. Computed tomography (CT) neck was taken for all patients. Magnetic resonance imaging (MRI) was done in patients who needed further evaluation on submucosal invasion, cartilage infiltration, involvement of anterior commissure, pre-epiglottic and paraglottic space invasion, which were mandatory for the staging of the tumors. Direct laryngoscopy was done and biopsy specimen was sent to our Pathology Department for histopathological confirmation of SCC.

External beam radiation therapy was administered by standard fractionation modality.⁴ Telecobalt radiation therapy of 66-70 gray in 33-35 fractions for 5 days a week were administered to the patients. The radiation therapy portal extended from the thyroid notch to the inferior border of the cricoid cartilage, the field ranging from 4 cm × 4 cm. The follow-up during the first 6 months was

carried out both at the ENT OP and Radiotherapy OP to assess the post radiation edema and any residual lesion at the primary site. Patients were evaluated at 3 months intervals during the first 1 year and at 6 months intervals during the subsequent period of follow-up or earlier if the patient had any specific complaints after completion of the external beam radiation therapy. Return of hoarseness, pain, increase in edema at the radiation site, fixity of a previously mobile vocal cord, metastatic lymph node were all considered suspicious of recurrence.

Clinically, all patients were assessed by indirect laryngoscopy and flexible pharyngolaryngoscopy. Those who presented with suspicious lesions were sent for radiological studies like CT scan and or MRI to know if there was deep infiltration and also to differentiate between post radiation edema and the mass lesion. As MRI gives a much better soft tissue contrast than with CT and has a higher sensitivity than CT, it is a better choice when it comes to imaging doubtful cases of cartilage and submucosal invasion.³ Though positron emission tomography is most helpful to differentiate between a recurrent tumor and post irradiation sequelae, it was not advocated, being not cost effective⁵ and locally not available.

As the incidence of distant metastasis from laryngeal carcinoma is related to the N stage, screening was not done in these patients for distant metastasis with early laryngeal carcinoma.⁵

Patients with suspected recurrent lesions were subjected to direct laryngoscopy and biopsy for histopathological confirmation. Continuation of the risk factors even after radiotherapy treatment was recorded. A statistical analysis was performed using SPSS software version 16.6.

RESULTS

Among the 60 patients, the maximum number of cases presented between 61 and 70 years of age group, 10 with supraglottic cancer and 16 with glottis cancer, the total number being 26 (Table 1).

28 cases had supraglottic T1 and T2 malignancy, 8 with suprahyoid T1 lesions, 5 with suprahyoid T2, 5 infrahyoid T1 lesions and 10 infrahyoid T2 lesions. 32 patients had T1 and T2 glottic malignancies, 18 T1a, 12 T1b and 2 T2 malignancy (Table 1).

On histopathology, 34 patients presented with well differentiated and 26 with moderately differentiated SCC.

A total of 19 cases had recurrence in the first 3 years giving a local recurrence rate of 31.6%. 78.9% ($n = 15$) cases

were supraglottic and 21% cases ($n = 4$) were glottis cancer recurrence. Out of 13 T1 and T2 suprahyoid supraglottic cancer patients, 2 cases had a recurrence. Whereas, 13 out of 15 T1 and T2 infrahyoid supraglottic cancer patients went on to recurrence, giving an overall recurrence rate of 53.57% for supraglottic cancers. The recurrence rate of T1 and T2 glottic malignancy was only 12.5%.

The first case of recurrence was noted at the 9th month, which was of a T2 infrahyoid supraglottic cancer. A maximum number of recurrence cases ($n=8$) was noted at 18 months among whom, 6 were supraglottic and 2 were glottic laryngeal cancer (Table 2).

The subsite which had maximum recurrence was T2 infrahyoid cancer ($N = 8$) (Table 2). Among the 19 cases of recurrence, 11 were of moderately differentiated and 8 were of well-differentiated SCC.

All the patients were smokers and alcoholics for years with an average of 33.8 years. Among the 19 patients with recurrence, 15 had continued the risk factors of smoking and alcohol throughout the study. Poor Hb levels were found in 15 cases of recurrence.

Association of the recurrence positive and negative cases with the sites of lesions, risk factors, Hb levels, and histopathology were calculated by univariate analysis using Chi-square's test and Fisher's test. Results are given in Tables 3 and 4.

Out of the 13 cases of suprahyoid supraglottic cancer, only 15.4% ($n = 2$) had recurrence, while 86.7% ($n = 13$) of patients out of 15 with infrahyoid supraglottic cancer showed recurrence which was found to be significant. Furthermore, there was a significant increase in the rate of recurrence in supraglottic cancers when compared to glottis cancers (Table 3).

Continuing smoking and alcohol intake significantly increased the rate of recurrence in laryngeal cancer in this study (Table 4). Association between Hb levels with recurrence is given in Table 4. Poor Hb levels at the time of radiotherapy had an increased rate of recurrence. Histopathologically well-differentiated carcinoma had less recurrence than moderately differentiated carcinoma (Table 4) which was not found to be statistically significant.

But when the above factors which were found to be significant from univariate analysis (Chi-square and Fisher's exact test) when put into the logistic regression model, only the fact that recurrence was higher in infrahyoid tumors than suprahyoid tumors of supraglottic carcinoma was significant at a p value of 0.025, odds ratio 0.03 (confidence interval, 0.001-0.65).

Table 1: Age group distribution of carcinoma of the larynx in relation to the different subsites of the supraglottis and glottis

Age group	Number of patients with supra glottic suprahyoid T1	Number of patients with supra glottic supra hyoid T2	Number of patients infra glottic infra hyoid T1	Number of patients with infra glottic infra hyoid T2	Number of patients with s with glottic T1a	Number of patients with glottic T1b	Number of patients with glottic T2	Total number of patients with supraglottic malignancy	Total number of patients with glottic malignancy
31-40	Nil	Nil	Nil	1	Nil	Nil	Nil	1	
41-50	1	Nil	Nil	Nil	3	Nil	Nil	1	3
51-60	2	2	2	3	5	1	Nil	9	6
61-70	4	2	1	3	8	6	2	10	16
71-80	1	1	2	3	2	5	Nil	7	7
Total number	8	5	5	10	18	12	2	28	32

Table 2: Correlation of the associated factors in patients of T1 and T2 carcinoma of the larynx who developed recurrence after radiotherapy

Age in years	Site of lesion	Risk factor Tobacco and Alcohol	Duration in years of exposure to risk factor	Hb level	Whether exposure to risk factor was continued	HPE type Squamous cell carcinoma differentiated	Recurrence period in months
54	1	Present	31	Good	Yes	Well differentiated	18
67	7	Present	26	Poor	Yes	Well differentiated	24
39	6	Present	16	Poor	No	Moderately differentiated	24
74	3	Present	38	Poor	No	Well differentiated	36
64	4	Present	31	Good	Yes	Moderately differentiated	9
60	4	Present	40	Poor	Yes	Moderately differentiated	18
68	7	Present	32	Poor	No	Moderately differentiated	18
71	3	Present	43	Good	Yes	Well differentiated	12
68	6	Present	45	Poor	Yes	Moderately differentiated	18
73	2	Present	46	Poor	Yes	Well differentiated	18
56	4	Present	29	Poor	Yes	Moderately differentiated	36
69	3	Present	39	Poor	Yes	Moderately differentiated	18
69	4	Present	40	Poor	Yes	Moderately differentiated	18
58	3	Present	27	Poor	Yes	Well differentiated	24
69	4	Present	40	Poor	No	Well differentiated	36
59	3	Present	39	Poor	Yes	Moderately differentiated	30
73	4	Present	34	Poor	Yes	Moderately differentiated	18
72	4	Present	39	Good	Yes	Well differentiated	12
71	4	Present	43	Poor	Yes	Moderately differentiated	12

Hb: Hemoglobin, HPE: Histopathological examination

Table 3: Association of the recurrence of T1 and T2 laryngeal cancers with the sites of lesion

Site of lesion	Recurrence positive	Recurrence negative	Marginal row totals
Supraglottic	15 (8.87) [4.24]	13 (19.13) [1.97]	28
Glottic	4 (10.13) [3.71]	28 (21.87) [1.72]	32
Marginal column totals	19	41	60 (grand total)
Chi-square=11.6413	P=0.000645		
Supraglottic suprahyoid	2 (6.96) [3.54]	11 (6.04) [4.08]	13
Supraglottic infrahyoid	13 (8.04) [3.07]	2 (6.96) [3.54]	15
Marginal column totals	15	13	28 (grand total)
Chi-square=14.2272	P=0.000162		

DISCUSSION

Glottic cancers are discovered at a relatively early stage with hoarseness being the initial symptom, while supraglottic

cancers may present late with dysphagia, metastatic lymph node or hoarseness with stridor. Glottis of the larynx is devoid of lymphatic drainage, but the supraglottis is rich in lymphatic drainage.⁴

Suprahyoid lesions of the supraglottis usually produce exophytic masses with little tendency to spread. Infrahyoid lesions of the supraglottis tend to invade the porous epiglottic cartilage and thyroepiglottic ligament onto the pre-epiglottic fat space. They can grow circumferentially to involve the false vocal cords, aryepiglottic fold and medial wall of the pyriform sinus and thyroid cartilage. The frequency of nodal metastasis is at least 20-50%.⁴ Bilateral metastasis is also not uncommon, as supraglottis is a midline structure.⁶

The goals in treating the early stages of cancer of the larynx include cure, voice preservation, and minimal morbidity.

Table 4: Association of the recurrence in T1 and T2 laryngeal cancers with the risk factors, Hb levels and histopathology

Parameters	Recurrence positive	Recurrence negative	Marginal row totals
Risk factor			
Risk factor continued	15 (7.92) [6.34]	10 (17.08) [2.94]	25
Risk factor discontinued	4 (11.08) [4.53]	31 (23.92) [2.1]	35
Marginal column totals	19	41	60 (grand total)
Chi-square=15.8995	P=0.000067		
Hb level			
Good Hb level	4 (11.4) [4.8]	32 (24.6) [2.23]	36
Poor Hb level	15 (7.6) [7.21]	9 (16.4) [3.34]	24
Marginal column totals	19	41	60 (grand total)
Chi-square=17.5738	P=0.000028		
Histopathology			
Well-differentiated	8 (10.77) [0.71]	26 (23.23) [0.33]	34
Moderately well differentiated	11 (8.23) [0.93]	15 (17.77) [0.43]	26
Marginal column totals	19	41	60 (grand total)
Chi-square=2.4009	P=0.121264		

Hb: Hemoglobin

Considering the important role the larynx plays in speech, measures have to be taken to preserve the function of the larynx as well treating cancer. Radiotherapy, chemotherapy, conservative laryngeal surgeries, transoral laser surgeries are nowadays being considered against total laryngectomy.⁴

Both radiotherapy and surgery (transoral laser surgery or conservative laryngeal surgery) are advocated in treating T1 and T2 laryngeal carcinoma with equally good results. The selection of treatment usually depends on the location and site of the tumor, occupation of the patient (professional voice users), facility available at the hospital, general medical fitness of the patient and the choice made by the patient.⁶

The local control rates after treatment for T1-T2 laryngeal cancer vary. The most important parameter that influences the local control after RT is the tumor extent and staging. Other factors that are likely to influence are tobacco and alcohol abuse, histologic differentiation, pretreatment Hb, sex and p53 etc.⁶

Tobacco smoking and alcohol intake are the most important etiological factors. Both can act synergistically and independently. Even after stopping the abuse, the chance of developing laryngeal SCC, still remains high when compared to lifelong nonsmokers with a 3 fold risk.⁷ Alcohol might promote carcinogenesis through acetaldehyde exposure, malnutrition, and desiccation of mucosa. Polycyclic hydrocarbons like benzopyrene are the main culprits in tobacco in promoting carcinogenesis.¹

An association between a low Hb-content and a poor response on radiation therapy has been established in patients with SCCs. Pre-treatment poor Hb levels and poor levels at the end of treatment have been found to reduce the disease-free survival period after radiotherapy.^{8,9}

Histologic differentiation also influences the local control rate, with better prognosis for well differentiated than for poorly differentiated carcinoma.⁶

The increasing T stage and N stage are the most important prognostic factors for laryngeal cancers. Tumor bulk, submucosal invasion, deep tissue and cartilage invasion affect the prognosis adversely.¹⁰

Tumors involving the infrahyoid supraglottis tend to be aggressive, with frequent pre-epiglottic space involvement and deep tissue infiltration. Recurrence occurs in 40-50% of cases.^{11,12}

In our study, local control rate of 68.3% was achieved for both supraglottic and glottic T1 and T2 malignancy at the end of 3 years with a local control rate of 53.57% for supraglottic cancer and 87.5% for glottis cancer. Supraglottic infrahyoid cancers had the maximum number of recurrence ($n = 13$). Recurrence of laryngeal cancer was associated with the tumor extent, poor Hb levels, histological differentiation and continuing smoking and alcohol which was significant at univariate analysis. But on logistic regression, recurrence was significantly higher with infrahyoid than suprahyoid suprahglottic carcinoma.

The reasons for irradiation failure in SCC of the larynx may be due to geographical miss due to undiagnosed extensions, inadequate technique to assure daily coverage of the tumor, inadequate dose for larger tumor volume, poor penetration of hypovascular tissue and in deep infiltration with fixation, the possibility of new cancer instead of recurrence.¹³

Standard fractionation was the radiation schedule used in this study. Hyperfractionation and accelerated fractionation with concomitant boost schedule may yield better control of tumor recurrence.^{4,14}

LIMITATIONS

1. A small group of patients were studied. Statistical significance of the risk factors could not be assessed.
2. Prognostic factors like p53 were not included in the study.
3. A comparative study with surgical treatment of T1 and T2 laryngeal cancers could not be done.
4. Only one modality of radiation schedule was

administered for all cases which may have affected the outcome result.

5. The neck was not irradiated in T2 supraglottic carcinoma, which may have led to the increased recurrence due to occult metastasis.
6. The role of concurrent chemoradiotherapy was not explored.

Those patients who had recurrence were advised conservative laryngeal surgery.

Since larger tumor volume ($>5 \text{ cm}^3$), impaired vocal cord mobility and infrahyoid lesions had a better result with conservative surgery in the literature, these patients may be considered for conservative partial laryngectomy or transoral endoscopic laser surgery as the first line of management. Also as supraglottic lesions present with occult nodes, selective neck dissection may also be advised. Poor Hb levels, long duration of smoking and alcohol adversely affect the prognosis. Improvement of nutritional status and cessation of these risk factors will definitely improve the outcome of treatment by radiotherapy.

CONCLUSION

A multidisciplinary approach is necessary for the management of laryngeal cancer. Both radiotherapy and conservative laryngeal surgery can be advised for T1 and T2 supraglottic and glottis lesions of laryngeal malignancy. The choice of therapy depends on patient factors like occupation (professional voice user), duration of treatment, pulmonary reserve status and the place of treatment. Radiotherapy may be preferred for patients who are professional voice users, those with poor pulmonary reserve and with high anesthesia risk. Large tumor volume, deep tissue invasion, impaired vocal cord mobility, infrahyoid supraglottic lesions which have the potential to involve the adjoining pre and paraglottic spaces may be managed with transoral endoscopic laser surgery or with conservative partial laryngectomy. All the patients in this study had undergone external beam irradiation. Other radiation techniques like hyperfractionation may be tried in early laryngeal cancers to improve the local control rate.

Those who continued the personal habits of smoking and consuming alcohol had a higher recurrence rate than those who discontinued. It was also noted that poor Hb levels were a poor prognostic factor in the treatment of laryngeal cancers. Educating patients over these factors can considerably bring up the local control rate, irrespective of the choice of treatment.

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How to cite this article: Santhi T, Rajan KV. Recurrence Rate in Post Irradiated T1 and T2 Supraglottic and Glottic Carcinoma of the Larynx. *Int J Sci Stud* 2016;3(11):233-238.

Source of Support: Nil, **Conflict of Interest:** None declared.

Maternal and Perinatal Outcomes in Cases of Acute Renal Failure in Pregnancy and Puerperium in Tertiary Care Centre

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Abstract

Introduction: This was a prospective observational study to determine to maternal and perinatal outcome in cases of acute renal failure (ARF) in pregnancy.

Materials and Methods: It was the prospective observational study carried out in Department of Obstetrics and Gynaecology, at Government Medical College, Nagpur, Maharashtra, India during the period of September 2012 to October 2014. Permission from the Ethical Committee was taken. The data were retrieved, tabulated, and analyzed. Patients were followed until they were discharged from the hospital. Data were analyzed using the appropriate software.

Results: Total number of cases were 83 in 2-year study period out of 25,391 deliveries. Thus, the proportion of ARF cases in pregnancy and puerperium was 0.37%. The average age of our patients was 25.60 ± 4.01 . Maximum number of patients were postpartum (68.67%). Cesarean section required in a maximum number of patients, i.e. 55.42%. Most common causes of ARF in our study were sepsis (26.05%) cases and severe pre-eclampsia in 18.07%. Maximum deaths (15) occurred in 0-5 days of admission. Mean duration of hospital stay was 10.71 ± 8.51 days. In dialysis group, 6 (31.57%) patients died and 13 (68.42%) patients survived. The improvement was more in dialysis as compared to a conservative group in reducing blood urea and serum creatinine. Leukocytosis, deranged liver function test, and international normalized ratio were seen in 60.24%, 45.78%, and 31.32% cases, respectively. Anuria found in 27.71% and oliguria in 39.75% while 32.53% had a non-oliguric renal failure. 24 (28.91%) patients expired, and 64 (77.10%) patients survived.

Conclusion: Proportion of ARF in pregnancy and puerperium was 0.37%. The majority of cases belonged to a rural area and that too lower socio-economic class. A significant number (86.74%) were booked cases; still the risk factors were not detected in the early stage may be due to lack of expertise and the patients referred late. Puerperal sepsis, pre-eclampsia, eclampsia, and obstetric hemorrhage were leading causes of ARF in the present study.

Key words: Acute renal failure, Acute tubular necrosis, Maternal and perinatal morbidity

INTRODUCTION

Pregnancy-related acute renal failure (ARF) is one of the most common causes of ARF. The important causes of pregnancy-related ARF are divided into (1) causes during

early pregnancy, which may include septic abortion leading to septic shock and acute tubular necrosis (ATN) and (2) causes in late pregnancy, i.e. after 34 weeks of gestation and immediate puerperium are antepartum hemorrhage (APH), abruptio placentae, postpartum hemorrhage (PPH), hemolytic uremic syndrome (HUS), HELLP syndrome, pre-eclampsia, puerperal sepsis, and hemolysis. Among these causes, ATN is most common pathological lesion, but it has excellent prognosis as compared to other pathological lesions associated with eclampsia, HELLP syndrome, disseminated intravascular coagulation (DIC), and HUS, in which glomerular involvement is predominant^{1,2} However, in rare case of septic abortion leading to acute tubular

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Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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necrosis (ATN), the mortality is high if the causative agent was clostridium.² It is postulated that all these diseases are manifestations of thrombotic microangiopathy caused by endothelial injury, due to deficiency of nitric oxide-dependent endothelial relaxing factors.³ The bad prognostic lesion seen in pregnancy induced ARF is acute bilateral renal cortical necrosis. The incidence of cortical necrosis is still high in developing countries, in Pakistan, it is about 13% as reported by Ramzan,⁴ and about 24% in India as reported by Prakash *et al.*⁵ It is frequently seen after APH and prolonged retention of a dead fetus.^{2,6,7} Mortality in pregnancy-related renal failure depends on the underlying renal lesion and associated complications. It is high when associated with severe pre-eclampsia, HELLP syndrome, and acute fatty liver of pregnancy, sepsis, DIC, HUS, and cortical necrosis. Obstetrical renal failure is a challenging health problem of population, especially of rural areas of developing the country. Ours being tertiary care center situated in central India with referrals not only from districts around but also from adjoining states of Madhya Pradesh and Andhra Pradesh. Hence, the study of pregnancy-related ARF was undertaken. The aim of the study was to know the magnitude of pregnancy-related ARF, factors responsible for it and maternal and neonatal morbidity and mortality associated with it.

Aims and Objectives

1. To study proportion and underlying conditions associated with ARF in pregnancies and puerperium.
2. To study maternal and perinatal outcome in ARF.

MATERIALS AND METHODS

The present study was carried out in the Department of Obstetrics and Gynaecology, at Government Medical College, Nagpur, Maharashtra, India during the period of September 2012 to October 2014. Permission from the ethical committee was taken. It was the prospective observational study.

Inclusion Criteria

All patients having urine output <400 ml/24 h and or serum creatinine >2 mg% during pregnancy and puerperium during the study period.

Exclusion Criteria

Patients with chronic renal disease, chronic hypertension, diabetes mellitus, and renal stones.

Sample Size

Sample size calculated with reference to study by Agrawal *et al.* (2014) assuming expected the incidence of sepsis was 40%, with precision = 10% and confidence interval = 95% and hence sample size = 80.

Methodology

The data retrieved for analysis contained demographic parameters, routine obstetric, menstrual, past, personal, family history and general, systemic and obstetric examination of patients included in the study. Baseline investigations including investigations supporting renal functions such as complete blood count, renal function test, urine analysis, serum electrolytes, renal scan, and abdominal ultrasound were carried out. Patients were followed until they were discharged from the hospital. Partial recovery due to patchy cortical necrosis is suspected when renal function shows improvement but does not return to normal even after 12 weeks. Patients were managed in collaboration with the nephrology department when required dialysis.

Statistical Analysis

A continuous variable was presented as mean \pm standard deviation. A categorical variable was expressed in actual number and percentage. Student's *t*-test was applied to compare pre-dialysis and post-dialysis level of serum creatinine and blood urea among dialysis and conservative group. The difference between two means is calculated by applying Student's *t*-test. $P < 0.05$ was considered as significant.

OBSERVATION AND RESULTS

The present study was carried out in the Government Medical College and Tertiary Care Institute, Nagpur, Maharashtra, India during the period of September 2012 to October 2014. All patients with ARF in pregnancy and puerperium who met the inclusion criteria were studied. A total number of cases in the Department of Obstetrics and Gynaecology, medicine and nephrology fulfilling the inclusion criteria were 83 in 2-year study period out of 25,391 deliveries. Thus, the proportion of ARF cases in pregnancy and puerperium was 0.37%.

Table 1 depicts that average age of our patients was 25.60 ± 4.01 . 37.34% of cases were primiparous, and 61.44% cases were multiparous. 86.74% patients were booked. Maximum patients belonged to a rural area (62.65%). According to Prasad classification, 61.43% patients were from lower class while rest belonged to the middle class. Maximum number of patients included in the study were PP (68.67%) followed by 14.45% cases with gestational age above 36 weeks.

Table 2 shows that cesarean section was required in a maximum number of patients, i.e. 55.42% followed by vaginal delivery (38.55%). 3 patients aborted spontaneously while 2 patients remained undelivered.

Table 3 depicts that most common causes of ARF in our study were sepsis (26.05%) cases, followed by severe pre-eclampsia in 18.07%. APH encountered in 12.04% of cases as eclampsia, and acute febrile illness leads to 8 (9.63%) cases each. HELLP syndrome was associated with 6 (7.22%) of cases.

Table 4 shows that maximum patients, i.e. 36 (43.37%) had duration of 5-10 days in hospital followed by 19 (22.89%) patients had stay of 0-5 days. In a total of 19 patients with duration of hospital stay >20 days, 9 required dialysis. Maximum deaths (15) occurred in 0-5 days of admission as the patients were referred in critical condition and with

Table 1: Demographic parameters

Demographic parameters	Observations (%)
Mean age in years	25.60±4.01
Primipara	37.34
Multipara	61.44
Rural	62.65
Urban	37.34
Booked	86.74
Unbooked	13.25
Lower class	61.43
Middle class	38.55
Duration of pregnancy (%)	
<28 weeks	6 (7.22)
28-36 weeks	8 (9.63)
>36 weeks	12 (14.45)
Postpartum	57 (68.67)

Table 2: Distribution according to mode of delivery

Mode of delivery	Number of cases (%)
Vaginal delivery	32 (38.55)
Cesarean delivery	46 (55.42)
Undelivered	2 (2.40)
Abortions	3 (3.61)
Total	83 (100)

Table 3: Distribution according to underlying conditions in cases of ARF

Underlying condition	Number of cases (%)
Sepsis	22 (26.50)
Severe pre-eclampsia	15 (18.07)
Antepartum hemorrhage	10 (12.04)
Eclampsia	8 (9.63)
Acute febrile illness	8 (9.63)
Postpartum hemorrhage	5 (6.02)
HELLP syndrome	6 (7.22)
DIC	3 (3.61)
ARDS	2 (2.40)
Septic abortion	2 (2.40)
Acute fatty liver	1 (1.20)
Blood transfusion reaction	1 (1.20)

ARF: Acute renal failure, DIC: Disseminated intravascular coagulation, ARDS: Adult respiratory distress syndrome

early onset ARF. The mean duration of hospital stay was 10.71 ± 8.51 days.

Table 5 shows that cases, with output <400 ml/24 h and serum creatinine >2 mg/dl, 21 patients expired of which 6 underwent dialysis, 35 (62.5%) patients survived, out of which 9 required dialysis and rest were managed conservatively. In cases with urine output >400 mg/24 h and serum creatinine >2 mg/dl, 3 (11.11%) patients expired and 24 (88.88%) patients survived of which 4 required dialysis and rest were managed conservatively.

Table 6 depicts the outcome of patients receiving only conservative treatment and dialysis treatment. In dialysis group, 6 (31.57%) patients died and 13 (68.42%) patients survived. Similarly, in conservative group, 18 (28.12%) patients died and 46 (77.87%) patients survived.

Table 7 shows improvement in blood urea and serum creatinine after either conservative and dialysis group. Both groups show significant (*P* < 0.05) improvement in blood urea and serum creatinine level at post-treatment as compared to pre-treatment. The improvement was, however, more in dialysis as compared to the conservative group.

Table 8 depicts that anemia, thrombocytopenia, and leukocytosis seen in 30.12%, 33.73%, and 60.24%,

Table 4: Distribution of cases according to duration of hospital stay

Duration of stay (days)	Number of cases (%)
0-5	19 (22.89)
5-10	36 (43.37)
10-20	16 (19.27)
>20	12 (14.45)
Total	83 (100)

Table 5: Distribution of cases according to outcome of two groups

Groups	Groups	Number of cases (%)
U/O<400 ml/24 h	Deaths	21 (37.5)
Serum creatinine>2 mg/dl	Survival	35 (62.5)
U/O>400 ml/24 h	Deaths	3 (11.11)
Serum creatinine>2 mg/dl	Survival	24 (88.88)
	Total	83 (100)

Table 6: Distribution of cases according to treatment and outcome

Treatment	Deaths (%)	Survived (%)	Number of cases (%)
Conservative	18 (28.12)	46 (71.87)	64 (77.10)
Dialysis	6 (31.57)	13 (68.42)	19 (22.89)
Total	24 (28.91)	59 (71.08)	83 (100)

Table 7: Comparison of biochemical parameters between conservative group and dialysis group after treatment

Variable	Groups	Pre-T/T	Post-T/T	P value
Blood urea	Dialysis	177.42±39.30	106.05±41.33	0.0001
	Conservative	131.17±74.76	96.29±85.50	0.015
P value		0.001	0.63	
Serum creatinine	Dialysis	8.73±2.52	4.65±1.47	0.0001
	Conservative	5.33±3.22	3.91±3.65	0.021
P value		0.001	0.40	

Table 8: According to laboratory finding in cases of pregnancy-related acute renal failure

Laboratory finding	Number of cases (%)
Anemia (Hb<8 g)	25 (30.12)
Thrombocytopenia (platelet<1,00,000)	28 (33.73)
Leukocytosis (TLC>11,000)	50 (60.24)
Deranged liver function test	38 (45.78)
SGOT>80 U	
SGPT>80 U	
ALP>300 U	
D-dimer (>200 ng/dl)	1 (1.20)
INR>1.4	26 (31.32)
Hyponatremia (Na<135 meq/l)	26 (31.32)
Hypernatremia (Na>145 meq/l)	7 (8.43)
Hypokalemia (K<3.5 meq/l)	18 (21.68)
Hyperkalemia (K>4.5 meq/l)	26 (31.32)
Anuria (U/O<100 ml/24 h)	23 (27.71)
Oliguria (U/O<400 ml/24 h)	33 (39.75)
Non-oliguria (U/O>400 ml/24 h)	27 (32.53)

Hb: Hemoglobin, TLC: Total leukocytic count, SGOT: Serum glutamic oxaloacetic transaminase, SGPT: Serum glutamate pyruvate transaminase, ALP: Alkaline phosphatase, INR: International normalized ratio

respectively. Liver function test and international normalized ratio were deranged in 45.78% and 31.32% cases, respectively. Hyponatremia was seen in 26 cases and hypernatremia was seen in 7 cases. Hypokalemia and hyperkalemia were seen in 18 and 26 cases, respectively. Anuria found in 27.71% and oliguria in 39.75% while 32.53% had the non-oliguric renal failure.

Table 9 shows that 24 (28.91%) patients expired and 64 (77.10%) patients survived. Out of those who survived, 50 (84.74%) cases showed complete recovery while 8 (13.55%) cases had a partial recovery. Puerperal sepsis accounts for maximum number of mortality, i.e. 8 (33.33%), followed by APH (3 = 12.5%), and HELLP syndrome (3 = 12.5%). DIC, PPH, and adult respiratory distress syndrome (ARDS) accounted for 2 (8.33%) deaths each. Acute fatty liver of pregnancy, acute febrile illness (Dengue fever), septic abortion, and acute gastroenteritis accounted for 1 (4.66%) deaths each.

Table 10 shows a total number of live birth were 49 (62.82%) and 29 (37.17%) were stillbirth. Out of 20

Table 9: Distribution of cases according to maternal outcome

Maternal outcome	Number of cases (%)
Death	24 (28.91)
Survival	59 (71.08)
Complete recovery	50 (84.74)
Partial recovery	8 (13.55)
Left against medical advice	1 (1.69)

Table 10: Distribution of cases according to perinatal outcome

Outcome	Number of cases (%)
Live birth	49 (62.82)
Stillbirth	29 (37.17)
Perinatal deaths	06 out of 20 NICU admission (30)

NICU: Neonatal intensive care unit

neonatal intensive care unit (NICU) admissions, 6 perinatal deaths occurred. Most neonates died due to prematurity, i.e. 3 (50%), followed by sepsis, hyperbilirubinemia, and birth asphyxia with one case each.

DISCUSSION

A total number of cases in the Department of Obstetrics and Gynaecology, Medicine and Nephrology fulfilling the inclusion criteria were 83 in 2-year study period out of 25,391 deliveries. Thus, the proportion of ARF cases in pregnancy and puerperium was 0.37%. Mean age in the present study was 25.6 ± 4.01 which is comparable to study by Goplani *et al.*,⁸ which was 25.6. In the present study, 37.34% of cases were primiparous, and 61.44% cases were multiparous which is comparable to study by Goplani *et al.*⁸ (primipara = 31.4% and multipara = 68.57%). In present study, 68.67%, 7.22%, and 24.08% cases were from PP cases, 1st and 2nd trimester combined cases, and 3rd trimester cases, respectively, which is comparable to study carried out by Kumar *et al.*⁹ (PP = 75.61%, 1st two trimester = 7.32% and third trimester = 17.07%). We have 37.37% cases from urban and 62.65% cases from a rural area similar to results found in a study carried out by Rashid *et al.*,¹⁰ who observed 30% cases from rural and 70% cases from the urban population. We had more booked cases (86.74%) than unbooked cases (13.25%) which show disparity with a study by Rashid *et al.*¹⁰. However, most of the patients were booked at referring health care centers. In present study, we had maximum number of cases with cesarean delivery (55.42%) followed by vaginal delivery (38.55%) and abortions (3.61%) similar to study conducted by Arrayhani *et al.*¹¹ (cesarean = 40.5%, vaginal = 40.5%, and abortion = 18.9%). Most common causes of ARF in our study were sepsis (26.05%) cases, followed by severe pre-eclampsia in 18.07%. Patel *et al.*¹² found that 38.33%

cases required dialysis, 75% had a complete recovery, 17% had a partial recovery while 8.4% cases had no recovery and deaths occurred in 15% cases. In the present study, 22.89% cases required dialysis, 84.74% cases recovered completely, 13.55% recovered partially, and 28.91% cases died. In a study by Aggarwal *et al.*, (2014)¹³ 78% cases had anemia, 12% cases had thrombocytopenia, and 64% cases had leukocytosis. In our study, anemia was in 30.12%, thrombocytopenia in 33.73%, and leukocytosis was in 60.24% cases. The incidence of oliguria and anuria was comparable to study carried out by Patel *et al.*¹² (oliguria = 37% and anuria = 23%). In a study by Goplani *et al.*⁸ reported total mortality of 18.57%, most common cause was sepsis (39.02%) followed by HELLP syndrome (15.38%), pulmonary edema (15.38%), and hepatic encephalopathy (7.69%). In present study, puerperal sepsis accounts for maximum number of mortality, i.e. 8 (33.33%), followed by APH (3 = 12.5%) and HELLP syndrome (3 = 12.5%). DIC, PPH, and ARDS accounted for 2 (8.33%) deaths each. Patel *et al.*¹² in their study reported perinatal mortality of 41.3%, whereas in the present study, the total number of live births were 62.82%, 37.17% were stillbirths, and 18.60% were NICU admissions.

RECOMMENDATIONS

Rural women have poor access to MCH services. There is a need to provide better and expert antenatal care up to the grass root level. Development of standard protocols for detection of pre-eclampsia and timely referral to higher centers will definitely prevent eclampsia and associated life-threatening complications such as ARF.

Conducting mock drill for prompt management of hemorrhagic shock in obstetrics will definitely help in the training of both medical and paramedical staff and will contribute to reducing the mortality and morbidity associated with it, which is still higher.

CONCLUSION

During recent years, ARF in obstetrics has decreased significantly. The probable factors:

1. Diminished number of criminal abortion with liberalization of abortion law
2. Early detection of pre-eclampsia and judicious and early termination of pregnancy
3. Availability of blood transfusion and prompt treatment of hemorrhage and shock.

In the present study, the proportion of ARF in pregnancy and puerperium was 0.37%. The majority of cases belonged to a rural area and that too lower socioeconomic class. A significant number (86.74%) were booked cases; still the risk factors were not detected in the early stage may be due to lack of expertise and the patients referred late. Puerperal sepsis, pre-eclampsia, eclampsia and obstetric hemorrhage were leading causes of ARF in the present study.

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How to cite this article: Patankar A, Wakankar R, Raut S. Maternal and Perinatal Outcomes in Cases of Acute Renal Failure in Pregnancy and Puerperium in Tertiary Care Centre. *Int J Sci Stud* 2016;. *Int J Sci Stud* 2016;3(11):239-243.

Source of Support: Nil, **Conflict of Interest:** None declared.

Effect of 0.5% Bupivacaine Versus 0.75% Ropivacaine - Onset, Duration and Quality of Brachial Plexus Block through Supraclavicular Approach

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Abstract

Introduction: The brachial block can be employed in upper limb surgery such as soft tissue surgery, bone surgery, and in plastic surgery. Local anesthetics are drugs that block reversibly the conduction of impulses in the peripheral nervous system. The aim of the present study is to compare the efficacy of 0.5% bupivacaine and 0.75% ropivacaine - the onset, duration and quality of the brachial plexus block through supraclavicular approach.

Materials and Methods: A total of 60 patients belonging to ASA Grades 1 and 2 between 20 and 60 years age of either sex were included in this study. The onset of sensory and motor block were tested every 1 min interval for a maximum of 35 min after injection of local anesthetics through supraclavicular plexus block. All patients were kept under observation for 24 h. All the observed characteristics were analyzed.

Results: The actual difference between mean duration of the onset of sensory and motor blockade in Group A and in Group B was 1.6 and 2.7 min, respectively. Duration of analgesia of Groups A and B were 678.75 ± 187 and 648.17 ± 180.91 , respectively. The most number of cases attained Grade IV that means complete block of sensory and motor functions among both Groups A and B. Complete blockade was more in Group B when compared to Group A about 66.67% and 58.62%, respectively.

Conclusion: There were no much clinical differences in onset, duration and analgesia among 0.5% bupivacaine and 0.75% ropivacaine when injected in equal volumes for brachial plexus block by the supraclavicular approach. Ropivacaine has potentially improved safety profile compared with bupivacaine.

Key words: Bupivacaine, Ropivacaine, Supraclavicular plexus

INTRODUCTION

The brachial block can be employed in upper limb surgery such as soft tissue surgery, bone surgery, and in plastic surgery.

The advantages of regional anesthesia are that it is simple, easy to learn and practice and no untoward effects of

general anesthesia agents. It can be employed in patients with a systemic disease where general anesthesia is hazardous. It is used in prolonged duration of surgery by a continuous infusion technique. It gives prolonged duration of post-operative analgesia.

Local anesthetics are drugs that block reversibly the conduction of impulses in the peripheral nervous system. Local anesthetics may be combined for rapid onset of action (chloroprocaine) and prolonged duration of action (bupivacaine). Local anesthetics toxicity of combination of drugs is additive rather than synergistic.¹

Bupivacaine has been used for all the types of nerve blocks, lumbar and caudal epidurals, paracervical blocks and intravenous regional analgesia. Bupivacaine is available

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Month of Submission : 12-2015
 Month of Peer Review : 01-2016
 Month of Acceptance : 01-2016
 Month of Publishing : 02-2016

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for clinical use as racemic mixtures (50:50 mixtures) of enantiomers. Local anesthetics prevent transmission of nerve impulses (conduction blockade) by inhibiting passage of sodium ions through ion-selective sodium channels in nerve membranes² so that action potential is not propagated. Bupivacaine rarely causes allergic reactions about <1%.³

Ropivacaine is new, long-acting local anesthetics, pure (S-isomer) enantiomer. Ropivacaine is chemically similar to bupivacaine, the butyl group being replaced by a propyl group. Though it has similar structure, pharmacology and pharmacokinetics to that of bupivacaine, ropivacaine has lower potential for the toxic effect. One mg basis ropivacaine shows greater selectivity for the sensory blockade and a lower systemic toxicity as compared to bupivacaine.

When clinically effective doses and concentrations are used, there are no clinically relevant differences in the comparative efficacy of ropivacaine and bupivacaine.^{4,5} With a mean dose of ropivacaine shows maximum tolerable central nervous system (CNS) effect,^{6,7} maximum tolerated total venous plasma concentration⁶ and higher arterial unbound plasma concentration⁷ of ropivacaine when compared to bupivacaine.

Both bupivacaine and ropivacaine can be used for all types of nerve blocks, epidural, Spinal anesthesia, infiltration of field block, acute pain management. They can cause minimal side effects which are depending on plasma concentration of drug,⁸ such as numbness of tongue and circumoral tissues, restlessness, tinnitus, vertigo, slurred speech, seizures, hypotension, cardiac arrhythmias,⁹ cardiac arrest,¹⁰ hepatotoxicity.¹¹

The aim of the present study is to compare the efficacy of 0.5% bupivacaine and 0.75% ropivacaine - the onset, duration and quality of the brachial plexus block through supraclavicular approach.

MATERIALS AND METHODS

After institutional approval, a prospective comparative study was conducted in the Department of Anesthesiology, Government General Hospital, Siddhartha Medical College, Vijayawada for 2 years - 2010 and 2011.

Inclusion Criteria

A total of 60 patients belonging to ASA Grades 1 and 2 between 20 and 60 years age of either sex were included in the study, scheduled for various surgical procedures on below elbow, forearm and hand.

Exclusion Criteria

Include patients with local infection, pneumothorax, peripheral neuropathy, severe liver or kidney disease, history of previous adverse reactions to local anesthetic drugs and coagulopathy.

After explaining the details of the procedure, written consent was taken from each patient. Pre-operative assessment was carried out in every patient 1 day before surgery. All the patients were premedicated in the night before doing surgery with tablet diazepam 10 mg and tablet ranitidine 150 mg.

The patients were randomly allocated into two groups according to the drug received.

Group A: Patients were given 30 ml of 0.5% bupivacaine

Group B: Patients were given 30 ml of 0.75% ropivacaine

Maximum care was taken in proper positioning of the patient. Before injecting the local anesthetics, the patient was explained about the accidental paraesthesias that may occur during the introduction of needle. By following aseptic precautions either bupivacaine or ropivacaine was injected into supraclavicular brachial plexus.

As soon as the block was given, the patient was kept comfortably with arm by the side. Electrocardiogram, blood pressure, pulse rate, respiratory rate, and arterial saturation were noted every 5 min. Signs for drug toxicity were observed.

The onset of sensory and motor block were tested every 1 min interval for a maximum of 35 min. All patients were kept under observation for 24 h. All the observed characteristics were analyzed.

Statistical Analysis

The patient data were analyzed using the unpaired *t*-test, $P < 0.05$ is considered as statistically significant.

RESULTS

A total of 60 patients were studied in the age group of 20-60 years of either sex. A most number of surgeries were performed in the age group of 20-30 years about 53.3%. A more number of males were underwent surgeries when compared to females about 80% and 20%, respectively.

The onset of sensory blockade was measured from the commencement of injection of anesthetic solution until the loss of pinprick sensation. The onset of motor blockade was measured from commencement of injection

of anesthetic solution until the loss of finger movements. The actual difference between mean duration of onset of sensory blockade and motor blockade in Group A and in Group B was 1.6 min and 2.7 min, respectively (Table 1).

Duration of sensory blockade was measured from the time of sensory loss of pinprick sensation to the time of return of pinprick sensation. Duration of motor blockade was measured from the time of loss of finger movements to time of return of finger movements. The actual difference between mean duration of sensory and motor blockade in Groups A and B was 36.36 and 14.51 min, respectively (Table 2).

The duration of analgesia of Groups A and B were 678.75 ± 187 and 648.17 ± 180.91 , respectively. The difference in duration between two groups is 30.58 min.

Grading of sensory and motor blockade was assessed in both groups and results were tabulated in Table 3. Most number of cases attained Grade IV which means complete block of sensory and motor functions among both Groups A and B. Sensory blockade in Grade IV was observed in more number of patients about 72.8% when compared to Motor blockade about 62.7%.

Quality of blockade was assessed which is expressed in terms of complete blockade, incomplete blockade and

failure (Figure 1). Complete blockade was more in Group B when compared to Group A about 66.67% and 58.62%, respectively. Incomplete block observed in 41.37% of Group A and 26.67% of Group B patients. Failures were not observed in Group A, but in Group B failures were 2 patients (6.66%).

Drug supplementation is needed in few patients and the requirement of supplementation with drugs like ketamine or pentazocine or midazolam among Groups A and B (Table 4). The Chi-square test shown not significant.

Complications were noted during and after surgery in both groups. Various complications occurred were depicted

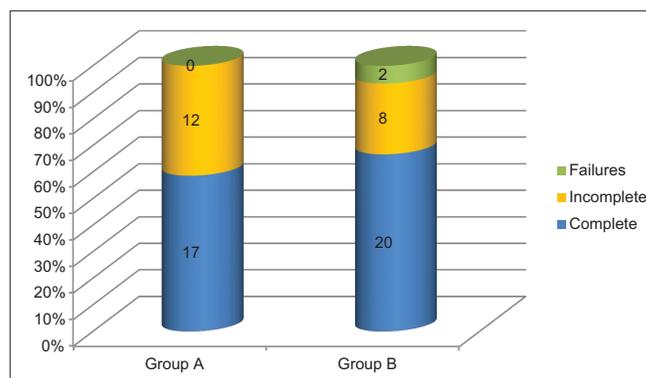


Figure 1: Representing quality of blockade of bupivacaine and ropivacaine

Table 1: Onset of sensory and motor blockade in minutes

Parameter	Time in minutes		t value	P value	Significance
	Group A	Group B			
Loss of pinprick sensation (mean±SD)	14.06±4.13	12.46±2.28	1.7998	>0.05	NS
Loss of finger movements (mean±SD)	19.48±6.0	16.78±4.63	1.8921	>0.05	NS

SD: Standard deviation, NS: Not significance

Table 2: Duration of sensory and motor blockade in minutes

Parameter	Time in minutes		t value	P value	Significance
	Group A	Group B			
Recovery of pinprick sensation (mean±SD)	612.82±150.3	576.46±179.3	0.899	>0.05	NS
Recovery of motor paralysis (mean±SD)	478.79±143.4	464.28±187.6	0.328	>0.05	NS

SD: Standard deviation, NS: Not significance

Table 3: Grade of sensory and motor blockade in both groups

Grade of blockade	Group A				Group B				Total number of cases	
	Number of cases		% of cases		Number of cases		% of cases		Sensory	Motor
	Sensory	Motor	Sensory	Motor	Sensory	Motor	Sensory	Motor		
Grade I	0	0	0	0	2	2	6.67	6.67	2	2
Grade II	8	1	27.59	3.44	6	0	20	0	14	1
Grade III	0	11	0	37.93	0	8	0	26.66	0	19
Grade IV	21	17	72.41	58.63	22	20	73.33	66.67	43	37
Total	29	29	100	100	30	30	100	100	59	59

in Table 5. Hematoma, horners syndrome, bradycardia, hypertension, brachial neuritis, pneumothorax, hemothorax not occurred in the present study.

DISCUSSION

The selection of optimal long-acting local anesthetic and concentration for brachial plexus block must take into consideration the available anesthetics, the time to onset, duration of blockade and side effects of each drug and dose.

A most number of surgeries were performed in the age group of 20-30 years about 53.3%. Many studies^{12,13} observed that most number of surgeries was performed in the age group of 21-30 years. Male predominance was seen in this study. This may be due to males in younger age group go for outside works, they are more prone for trauma.

In the present study, the onset of sensory and motor blockade was faster with 0.75% of ropivacaine when compared to 0.5% of bupivacaine. Duration of sensory and motor blockade is lesser with 0.75% ropivacaine when compared with 0.5% of bupivacaine. However, there is no much clinical difference in onset, duration of sensory and motor blockade and duration of analgesia.

In line with this study Misolek *et al.*,¹⁴ Vainionpää *et al.*,¹⁵ Hickey *et al.*,¹⁶ Katz *et al.*¹⁷ also concluded that there was no important clinical difference between 0.75% ropivacaine and 0.5% bupivacaine in terms of onset, duration and quality of analgesia.

Few studies such as Raeder *et al.*,¹⁸ McCrae *et al.*,¹² documented that the onset time of both sensory and motor blockade between 11 and 20 min. Other studies like Bertini *et al.*¹⁹ were observed prolonged time about 23-48 min and

Klein *et al.*²⁰ observed less time about <6 min than our study. These differences may be attribute to the anatomic location of the different nerve blocks (supraclavicular, interscalene, and subclavicular) and the technical procedure used. Akerman *et al.*,²¹ ropivacaine is longer acting than bupivacaine upon infiltration, equally effective in peripheral nerve block and slightly shorter acting in subarachnoid and epidural anesthesia.

As per this study, 58.62% of patients in Group A and 66.67% of cases in Group B had complete block. 41.37% in Group A and 26.67% cases in Group B had incomplete block. There are no failures in Group A, but Group B has 66.6% of failure cases (2 patients) in the present study. In the study by Raeder *et al.*,¹⁸ axillary brachial plexus block with 40 ml of 0.75% ropivacaine versus 0.5% bupivacaine found that, there was significantly higher quality scores for anesthesia, partial and complete motor block in ropivacaine patients, whereas analgesia scores were similar.

In the present study, 41% of patients in Group A needed further supplementation whereas 26.67% of cases in Group B needed further supplementation of drugs. Hematoma, Horners syndrome, bradycardia, hypertension, brachial neuritis, pneumothorax, hemothorax not occurred in the present study. One case of convulsions noted with bupivacaine. Arterial puncture and tachycardia was observed with bupivacaine and also ropivacaine.

Scott⁶ documented that ropivacaine caused less CNS symptoms and was at least 25% less toxic than bupivacaine. The majority of symptoms occurred early and as a maximum effect with bupivacaine ($P < 0.05$). Chazalon *et al.*,¹⁰ Huet *et al.*²² reported that cardiopulmonary resuscitation following ropivacaine injection was successful. In contrast, this Long *et al.*,²³ Tsai *et al.*,²⁴ documented that cardiac arrest is difficult to treat and may require cardiopulmonary bypass. In this study, there was no incidence of ropivacaine toxicity.

Although appears to be a considerable difference, when these results are subjected to statistical analysis by using Chi-square test, they are statistically insignificant.

CONCLUSION

About 30 ml of 0.5% bupivacaine or 30 ml of 0.75% ropivacaine for supraclavicular brachial plexus block produced satisfactory and comparable sensory, motor block related to onset, duration, quality and duration of analgesia. The lower CNS and cardiotoxicity of ropivacaine may help in reducing risk to the patient. There were no much clinical differences in onset, duration and analgesia among

Table 4: Need of further drug supplementation

Group	Supplementation of drug		Total
	Required	Not required	
A	12	17	29
B	8	22	30
Total	20	39	59

Table 5: Complications due to bupivacaine and ropivacaine injections

Complications	Group A (n=30)	Group B (n=30)	Total
Arterial puncture	2	1	3
Tachycardia	6	4	10
Seizures	1	0	1

0.5% bupivacaine and 0.75% ropivacaine when injected in equal volumes for brachial plexus block by supraclavicular approach. Hence, the choice of local anesthetic should not be based on onset and duration time alone. Ropivacaine has potentially improved safety profile compared with bupivacaine, it may offer an advantage.

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How to cite this article: Gonuguntla SB. Effect of 0.5% Bupivacaine Versus 0.75% Ropivacaine - Onset, Duration and Quality of Brachial Plexus Block through Supraclavicular Approach. *Int J Sci Stud* 2016;3(11):244-248.

Source of Support: Nil, **Conflict of Interest:** None declared.

Ultrasound Guided Fine-Needle Aspiration Cytology of Liver Lesions: A Prospective Study

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Abstract

Background: The liver is a common site for metastatic tumor deposits most often from carcinomas originating in the abdominal cavity, but also for sarcomas and lymphomas. The main indication of fine-needle aspiration cytology (FNAC) of the liver single or multiple nodular lesions, demonstrated by palpation, nuclear scan, computed tomography, or ultrasonography.

Purpose: Purpose of the study is to evaluate various neoplastic lesions, whether primary or metastatic and non-neoplastic conditions of the liver.

Materials and Methods: This study was hospital-based prospective study including all the patients with space occupying lesion of the liver mass. Mass lesions on US examination of liver were subjected for FNAC under ultrasound (US) guidance.

Results: A total number of cases registered were 78. A maximum number of cases were in 7th decade (32, 41.02%). The average age of sample population was 59.37 years (standard deviation \pm 10.66) with a range of 30-80 years. Male to female ratio was 1.69:1. Out of 78 cases, 11 (14.10%) were benign and 67 (85.90%) were malignant. Among benign, reactive changes (5, 6.41%) and in malignant lesions, metastatic adenocarcinoma (37, 47.44%) were most common. The most common neoplastic liver lesion was metastatic adenocarcinoma (37, 55.22%) and least common were metastatic sarcoma and metastatic anaplastic carcinoma (1, 1.49%) each. Metastatic tumor was the most common malignancy detected, noted in 57 cases (85.07%). In the present study, hepatocellular carcinoma (HCC) was the most common primary malignant tumor of the liver.

Conclusion: We found that incidence of malignant hepatic lesions was more than benign. In benign lesions, the most common lesion was reactive changes and cirrhosis. Adenocarcinoma was most common metastatic tumor. While in the primary tumor, HCC was most common. US guided FNAC was less time consuming, safe, useful, and highly accurate technique for making diagnoses of hepatic lesions.

Key words: Carcinoma, Fine-needle aspiration cytology, Liver, Ultrasound

INTRODUCTION

Fine-needle aspiration (FNA) has proven to be a very effective means of obtaining tissue from many different body sites for diagnosis.

Most of the mass lesions of the liver and gallbladder discovered clinically or by imaging techniques are easily

assessable to FNA cytology (FNAC). It is important to establish primary or metastatic nature of the lesion and in case of the latter to comment upon the probable site of the primary tumor.¹

FNAC is a major indicative procedure in the diagnosis of hepatic lesions. Ultrasound guided FNAC (US-FNAC) in the diagnosis of hepatic lesions including focal liver lesions showed high sensitivity in identifying liver lesions. The diagnostic technique yields adequate pathological materials in the majority of cases. The advantages of US guided FNAC in the diagnosis of liver diseases cannot be overemphasized. The advantages of this technique are its high diagnostic accuracy and low cost, thereby rendering the older technique of blind percutaneous biopsy using a coarse needle obsolete.²

Access this article online



www.ijss-sn.com

Month of Submission : 12-2015

Month of Peer Review : 01-2016

Month of Acceptance : 01-2016

Month of Publishing : 02-2016

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The main indication of FNAC of the liver is single or multiple nodular lesions, demonstrated by palpation, nuclear scan, computed tomography (CT), and ultrasonography (USG). The purpose of the study is to evaluate various neoplastic lesions whether primary, metastatic or non-neoplastic conditions of the liver and to correlate with histopathology wherever possible.³

Also to compare and standardized the cytomorphological features of various types of hepatic lesions *viz.* cirrhosis, neoplastic and metastatic lesions.

The development of cytology has been based on cytomorphologic and cytochemical studies of tumor cells. Cytology is a diagnostic procedure which can precisely allow a decision as to whether the cells are malignant, precancerous or benign cytology at present.

The sensitivity of FNAC for malignancy was 91%, the specificity was 100%, predictive value of the positive result was 100%, and the predictive value of the negative result was 73%.

FNA of the liver was considered a very safe procedure. Anecdotal cases of fatality secondary to hemorrhage have been reported (Riska *et al.*, 1975), and bleeding disorders were considered a contraindication. The other reported complication was bile peritonitis (Schultz, 1976).⁴

One of the major advantages of radiologically guided percutaneous FNA biopsy is that it can sample malignancy anywhere in the liver, such as in the left lobe or in the area of the porta hepatis, where the use of a large-bore needle may be too risky. Therefore for any mass or masses in the liver suspected to be malignant, radiologically guided FNA biopsy is the method of choice.

US guided FNAC is a safe, quick and precise diagnostic procedure for early diagnosis and management of gallbladder cancer in developing countries.⁵ Only a few large studies on US/CT guided percutaneous FNA of gallbladder are available in the literature until date. Moreover, the cytologic findings have not been illustrated in detail.

MATERIALS AND METHODS

The study was carried out in the Department of Pathology, Sardar Patel Medical College and associated group of hospitals, Bikaner. This study was hospital based prospective study including all the patients with space occupying lesion of the liver and gall bladder mass who attended hospital.

After obtaining the detailed clinical and radiological data, the patients were subjected for FNAC under US guidance. The consent of the patient was taken before undertaking the procedure.

Inclusion Criteria

1. All patients with hepatobiliary mass confirmed by radiological examination.

Exclusion Criteria

1. Patients with marked hemorrhagic diathesis
2. Patients with skin infection at the site of aspiration
3. Critically ill patients
4. Non cooperative patients.

Procedure

The area (based on clinical examination and radiological finding) is sterilized with spirit and infiltrated with 2% xylocaine. The needle of length 15-20 cm, 22-23 G disposable needle is fixed on the 10 ml dispovan syringe that is prefixed to FNAC gun. The cellular material will be aspirated into a syringe under US guidance and expelled onto slides. Four to five slides will be prepared for each patient. The wet-fixed smears will be stained with hematoxylin and eosin (H and E). While air dried smears will be stained with May-Grünwald–Giemsa (MGG) stain, and other two smears will be kept for special stains as per requirement.

RESULTS

In the present study entitled “A Prospective Study On US guided FNAC of liver lesions” was carried out in the Department of Pathology Sardar Patel Medical College, Bikaner on 78 cases with the clinical or radiological suggestion of hepatic lesions.

In the present study, indications of FNAC were hepatomegaly, abnormal USG finding of benign and malignant hepatic lesions.

A detailed clinical information and laboratory investigation were obtained. FNA was performed, and the smears stained by H and E and MGG stains and special stain are used whenever needed. The role of FNAC was evaluated for diagnosing different type of hepatic lesions.

A total number of cases registered were 78. A maximum number of cases were in the 7th decade 41.02% followed by 24.35% in 6th decade, 20.51% in 5th decade, 8.97% in 8th decade, 3.84% in 4th decade and 1.28% in 3rd decade.

The average age of sample population was 59.37 years (standard deviation [SD] ± 10.66) with a range of 30-80 years.

The outcome of FNAC diagnosis among liver aspirate in 78 patients studied. Among this benign aspirates were 11 (14.10%), malignant aspirate were 67 (85.90%).

Table 1 reveals age wise distribution of benign and malignant liver lesions. A maximum number of malignant cases were found in 61-70 years of age groups with 27 cases (40.29%) next in order of frequency were in 51-60 years with 16 cases (23.52%), maximum number of benign case were found in 61-70 years of age groups with 5 cases (45.45%).

Gender wise distribution of benign and malignant lesions with male to female ratio 1.69:1. Out of 49 male cases, 6 were suffering from benign and 43 were suffering from malignant. Out of 29 female cases, 5 were suffering from benign and 24 were suffering from malignant lesions.

Table 2 reveals incidence of various type of benign and malignant lesions. Out of 78 cases, 11 were benign and 67 were malignant. Among benign, normal liver cytology (6.41%) and in malignant lesions metastatic adenocarcinoma (47.44%) were more common.

Most common neoplastic liver lesion is metastatic adenocarcinoma 55.22% and least common are metastatic sarcoma and metastatic anaplastic carcinoma 1.49% each (Table 3).

Table 1: Age wise distribution of benign and malignant liver lesions

Age (years)	Benign (%)	Malignant (%)
21-30	0 (0)	1 (1.49)
31-40	0 (0)	3 (4.47)
41-50	1 (9.09)	15 (22.38)
51-60	4 (36.36)	16 (23.88)
61-70	5 (45.45)	27 (40.29)
71-80	1 (9.09)	6 (8.95)
Total	11 (100)	67 (100)

Table 2: Incidence of various type of benign and malignant liver lesions

Cytological diagnosis	Frequency (%)
Benign	11 (14.10)
Cirrhosis	3 (3.85)
Fatty liver	1 (1.28)
Normal liver	2 (2.56)
Reactive changes	5 (6.41)
Malignant	67 (85.90)
HCC	10 (12.82)
Metastatic adenocarcinoma	37 (47.44)
Metastatic sarcoma	1 (1.28)
Metastatic SCC	4 (5.13)
Metastatic anaplastic	1 (1.28)
Metastatic unclassified	14 (17.95)
Total	78 (100.0)

SCC: Squamous cell carcinoma, HCC: Hepatocellular carcinoma

Out of 67 malignant lesions, cases of metastatic adenocarcinoma were most common. Males were more commonly affected (Table 4).

Out of 67 malignant cases, there were 43 male and 24 female with maximum number of cases found in 7th decade. Male to female ratio were found 1.79:1 (Table 5).

Table 6 reveals the distribution of different type of metastatic tumors. Out of total 78 cases, 57 cases were

Table 3: Cytological diagnosis of neoplastic liver lesions

Diagnosis	Number of cases (%)
HCC	10 (14.93)
Metastatic adenocarcinoma	37 (55.22)
Metastatic sarcoma	1 (1.49)
Metastatic SCC	4 (5.97)
Metastatic anaplastic	1 (1.49)
Metastatic unclassified	14 (20.89)
Total	67 (100.0)

SCC: Squamous cell carcinoma, HCC: Hepatocellular carcinoma

Table 4: Gender wise distribution of liver lesion

Diagnosis	Female (%)	Male (%)	Total
Cirrhosis	2 (6.9)	1 (2.04)	3
Fatty liver	1 (3.45)	0 (0)	1
Normal liver	1 (3.45)	1 (2.04)	2
Reactive change	1 (3.45)	4 (8.16)	5
HCC	3 (10.34)	7 (14.29)	10
Metastatic adenocarcinoma	14 (48.28)	23 (46.94)	37
Metastatic sarcoma	0 (0)	1 (2.04)	1
Metastatic SCC	3 (10.34)	1 (2.04)	4
Metastatic anaplastic	0 (0)	1 (2.04)	1
Metastatic unclassified	4 (13.79)	10 (20.41)	14
Total	29 (100)	49 (100)	78

SCC: Squamous cell carcinoma, HCC: Hepatocellular carcinoma

Table 5: Gender wise distribution of various types of malignant liver lesion

Diagnosis	Female (%)	Male (%)	Total
HCC	3 (12.5)	7 (16.28)	6
Metastatic adenocarcinoma	14 (58.33)	23 (53.48)	39
Metastatic sarcoma	0 (0)	1 (2.33)	1
Metastatic SCC	3 (12.5)	1 (2.33)	4
Metastatic anaplastic	0 (0)	1 (2.33)	2
Metastatic unclassified	4 (16.67)	10 (23.25)	15
Total	24 (100)	43 (100)	67

SCC: Squamous cell carcinoma, HCC: Hepatocellular carcinoma

Table 6: Distribution of metastatic liver lesion

Type of metastatic tumor	Number of cases (%)
Metastatic adenocarcinoma	37 (64.91)
Metastatic sarcoma	1 (1.75)
Metastatic squamous cell carcinoma	4 (7.02)
Metastatic anaplastic tumor	1 (1.75)
Metastatic unclassified tumor	14 (24.56)
Total	57 (100)

metastatic malignant tumors. Adenocarcinoma was the most common metastatic tumor detected, noted in 37 cases (64.91%).

The study reveals HCC was more common in male. Male to female ratio were 2.33:1.

DISCUSSION

Diseases of the liver include space-occupying lesions, such as cysts, abscesses, and benign or malignant tumors. This group is the target of FNAC, and can also be performed under imaging guidance (USG).⁶

A total number of 80 cases of liver aspiration cytology were studied during this period. It was positive in 78 cases out of 80 cases, and the diagnostic yield of the present study was 97.5%.

Similar results were seen in the earlier studies in which diagnostic yield of FNAC were 96% (Tsui *et al.*⁷ in 1980), 93.5% (Talukder *et al.*⁸ In 2004).

In the present study, out of 78 cases, 29 (37.18%) were female and 49 (62.82%) were male. Male to female ratio was 1.69:1. Maximum number of case was in 7th decade.

Similar results were seen in the earlier study conducted by Talukder *et al.*⁸ In 2004, on 108 cases result were 67 (62.0%) males and 41 (37.96%) females with a mean age 53 years (SD \pm 14) ranging from 2 to 83 years.

Similar result was seen in the earlier study conducted by Nazir *et al.*⁹ in 2010 on 100 cases find out the mean age at presentation was 55(SD \pm 12) years with male to female ratio of 1.7:1.

Out of 49 male cases, 6 were suffering from benign and 43 were suffering from malignant. Out of 29 female cases, 5 were suffering from benign and 24 were suffering from malignant lesions.

Malignant and benign lesions both were more common in male.

Maximum number of malignant cases were found in 61-70 years of age groups with 27 cases (40.29%) next in order of frequency were in 51-60 years with 16 cases (23.88%), Maximum number of benign case were found in 61-70 years of age groups with 5 cases (45.45%).

Similar results were seen in the earlier study conducted by Gatphoh *et al.*,¹⁰ Gaytri in 2003 find out the most common age group of the malignant liver disease was 51-60 years.

Metastatic tumor was the most common malignancy detected, noted in 57 cases (85.07%). Next most frequent malignancy was HCC noted in 10 cases (14.93%).

Similar results were seen in the earlier study conducted by Rasania *et al.*³ in 2007 who found that metastatic tumors were the most common and constituted 70.4% while the hepatocellular carcinoma (HCC) accounted for 26.2% of the malignant liver lesion.

In present study, HCC was the most common primary malignant tumor of the liver. HCC was diagnosed in 14.93% of all malignant lesions.

The results were higher the earlier study conducted by Bottles *et al.*¹¹ in 1988, Gatphoh *et al.*¹⁰ in 2003 (31%).

In the present study, out of 78 cases, 57 cases were metastatic malignant tumor. Adenocarcinoma was the most common metastatic tumor detected, noted in 37 cases (64.91%). Next common was unclassified carcinoma, noted in 14 (17.95%), metastatic squamous cell carcinoma was noted in 4 (5.13%), single case of metastatic sarcoma and metastatic anaplastic was noted. (1.28% each).

Similar result was seen in the earlier study conducted by Das *et al.*¹² studied on 61 metastatic lesions which were included 43 (70.49%) adenocarcinomas, 6 (9.8%) small cell anaplastic carcinomas, undifferentiated carcinoma and soft tissue sarcoma each (1.63%).

The outcome of FNAC diagnosis among liver aspirate in 78 patients studied. Among this benign aspirates were 11 (14.10%), malignant aspirate were 67 (85.90%).

Maximum number of malignant cases were found in 61-70 years of age groups with 27cases (40.29%) next in order of frequency were in 51-60 years with 16 cases (23.52%), maximum number of benign case were found in 61-70 years of age groups with 5 cases (45.45%).

A maximum number of cases were in 7th decade 41.02 % followed by 24.35% in 6th decade, 20.51% in 5th decade, 8.97% in 8th decade, 3.84% cases in 4th decade and 1.28% cases in 3rd decade. Average age was 59.37 years with a range of 30-80 years of age.

Similar results were seen in the earlier study conducted by Nggada *et al.*² A total of 47 patients were studied with a mean age of 47.04 (SD \pm 14.24) years and range between 14 and 75 years. The peak age incidence is between 40 and 59 years age groups.

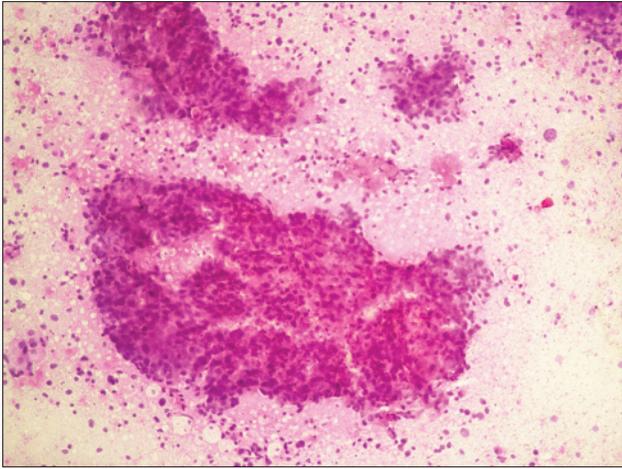


Figure 1: Hepatocellular carcinoma - showing sinusoidal pattern, clusters of cells are surrounded by endothelial wrapping (H and E, x10)

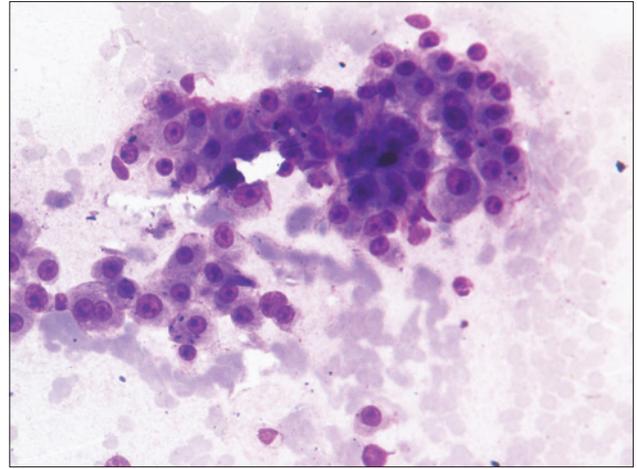


Figure 4: Hepatocellular carcinoma - showing cluster of cells, having moderate amount of cytoplasm, round nuclei and prominent nucleoli (May-Grünwald-Giemsa, x40)

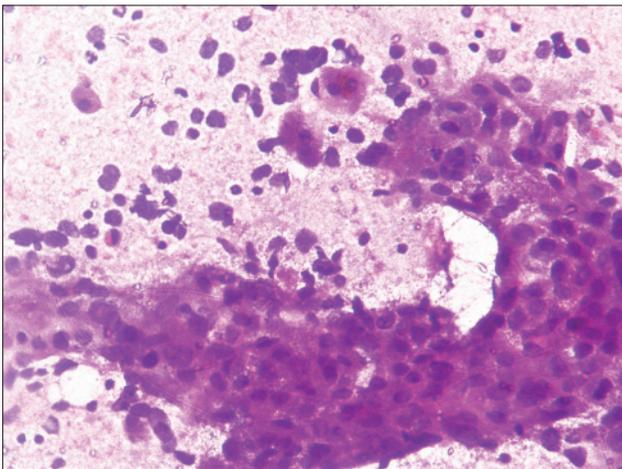


Figure 2: Hepatocellular carcinoma - showing trabecular pattern of cells, one cell shows bile accumulation in the cytoplasm (H and E, x40)

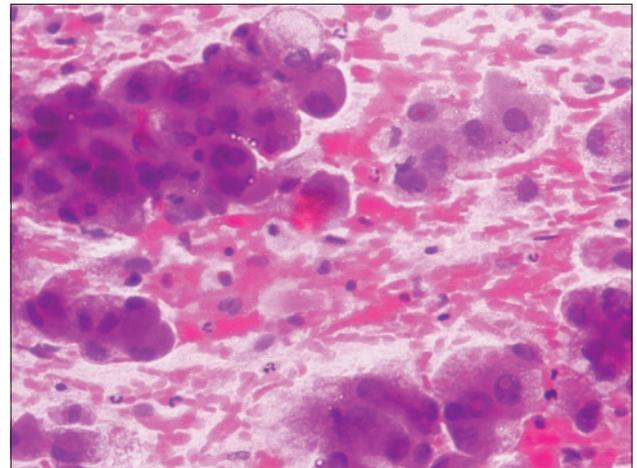


Figure 5: Metastatic adenocarcinoma - showing clusters of pleomorphic cells having abundant cytoplasm and pleomorphic nuclei, normal hepatocytes are also present (H and E, x40)

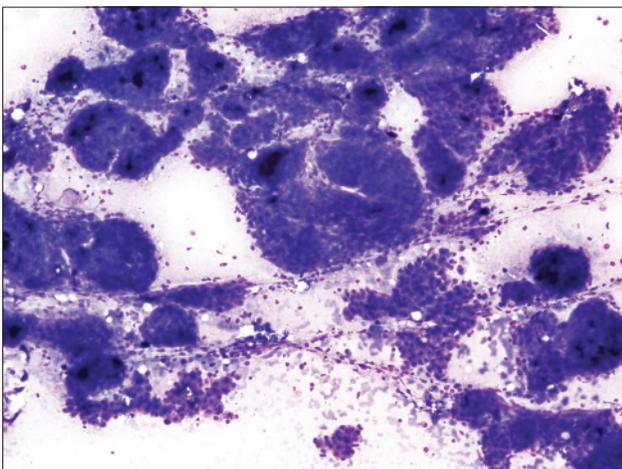


Figure 3: Hepatocellular carcinoma - smear shows sinusoidal pattern, clusters are traversed by endothelium of capillaries (May-Grünwald-Giemsa, x10)

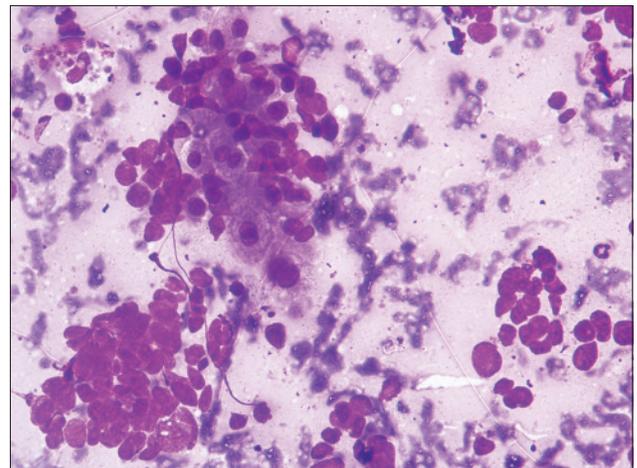


Figure 6: Metastatic anaplastic carcinoma - smear showing cells arranged in clusters and dispersed pattern having scanty cytoplasm, pleomorphic nuclei, nuclei show nuclear molding, along with normal hepatocytes (May-Grünwald-Giemsa, x40)

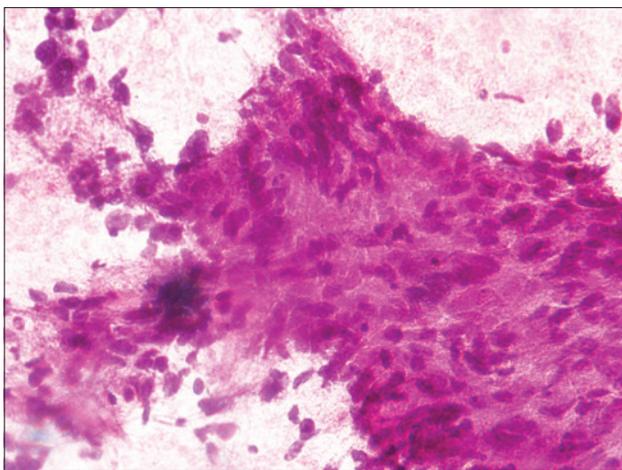


Figure 7: Metastatic sarcoma - showing cluster of spindle-shaped cells (H and E, x40)

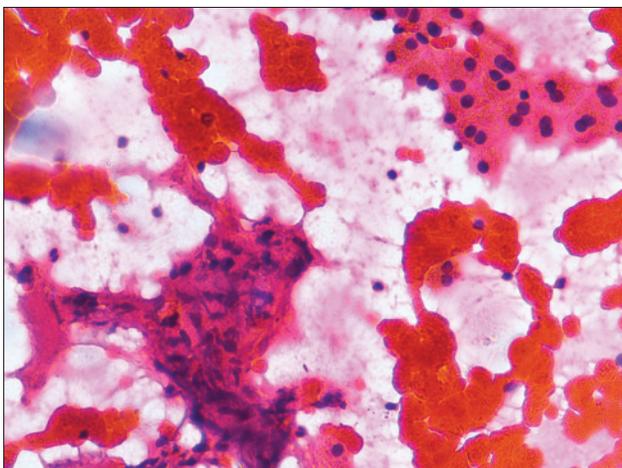


Figure 8: Smear showing clumps of reactive hepatocytes and fragment of fibrocollagenous tissue and hemorrhage in the backgrounds (H and E, x40)

Out of 78 cases 11 (14.10%) were benign and 67 (85.90%) were malignant. Among benign, reactive changes (5, 6.41%) and in malignant lesions, metastatic adenocarcinoma (37, 47.44%) were most common.

Most common neoplastic liver lesion is metastatic adenocarcinoma (37, 55.22%) and least common are metastatic sarcoma and metastatic anaplastic carcinoma (1, 1.49%) each.

Figures 1-8 depict morphological features of different hepatic lesions seen on cytology.

CONCLUSION

We found that incidence of malignant hepatic lesions was more than benign. In benign lesions common were reactive changes and cirrhosis. While in malignant liver lesions, metastatic were more common than primary. Adenocarcinoma was most common metastatic tumor. While in the primary tumor, HCC were most common.

From this study, in present set up it is felt that with the help of US guided FNAC is less time consuming, safe, useful, and highly accurate technique for making diagnoses of hepatic lesions.

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How to cite this article: Tailor SB, Kothari DC. Ultrasound Guided Fine-Needle Aspiration Cytology of Liver Lesions: A Prospective Study. *Int J Sci Stud* 2016;3(11):249-254.

Source of Support: Nil, **Conflict of Interest:** None declared.

Comparative Study of Titrated Oral Misoprostol Solution and Oxytocin to Induce Labor Conducted at Kannur Medical College

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Abstract

Introduction: Various methods are used for inducing labor. Out of these, two common methods are oral misoprostol and oxytocin intravenous drip. A comparative study of titrated oral misoprostol solution and intravenous oxytocin in the effectiveness of induction of labor was conducted at Kannur Medical College during a period of 3-year from 2010 to 2013.

Objectives: (1) To compare the efficacy of misoprostol and oxytocin in inducing labor. (2) To compare the complications of misoprostol and oxytocin. (3) To compare the induction-to-active labor time. (4) To compare the induction-to-delivery time of misoprostol and oxytocin.

Methods: A total number of cases selected for study purpose were 280 for a period from March 2010 to February 2013; all were term pregnancies. Misoprostol group received 25 µg oral solution every 3 h, and oxytocin group received a titrated dose starting from 4 mIU with an increment of 4 mIU every half an hour. The time between onset of induction and delivery has been recorded; so does the time between induction and active labor. Maternal and fetal complications also were noted. Vaginal delivery, not effected and ended with cesarean was considered failure.

Result: Failure of induction by misoprostol was less with misoprostol (19.8%) comparing to oxytocin which was 39.2% with statistical significance ($P < 0.001$). Induction-to-delivery time was shorter for misoprostol group ($P < 0.04$). Induction-to-active labor was also shorter for misoprostol group ($P < 0.05$). Complications, maternal, and fetal were similar in both groups.

Conclusion: Misoprostol is a safe and effective method of induction of labor superior to intravenous oxytocin drip.

Key words: Arrest of descent, Arrest of dilatation, Cesarean, Dysfunctional labor, Labor induction, Misoprostol, Oxytocin, Protracted descent, Protracted dilatation, Vaginal delivery

INTRODUCTION

Induction implies stimulation of contractions before the spontaneous onset of labor, with or without ruptured membranes.¹

Induction is indicated when the benefits of delivery outweigh the risk of continuation of pregnancy in utero.

The more common indications include pre-labor rupture of membranes, gestational hypertension, oligohydramnios, non-reassuring fetal status, post-term pregnancy, and various maternal medical conditions such as chronic hypertension and diabetes.²

Oxytocin has been used for decades to induce or augment labor. Other effective methods include prostaglandins, such as misoprostol and dinoprostone, and mechanical methods those encompass stripping of membranes, artificial rupture of membranes, extra-amnionic saline infusion, transcervical balloons, and hygroscopic cervical dilators. Misoprostol is widely practiced for induction of labor. The American College of Obstetricians and Gynecologists (2013b) reaffirmed its recommendation for use of the drug because of proven safety and efficacy.²

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www.ijss-sn.com

Month of Submission : 12-2015

Month of Peer Review : 01-2016

Month of Acceptance : 01-2016

Month of Publishing : 02-2016

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Importantly, as recommended in Guidelines for Perinatal Care, each obstetrical department should have its own written protocols that describe administration of these methods for labor induction and augmentation.³

Objectives of Study

1. To compare the efficacy of misoprostol and oxytocin in inducing labor
2. To compare the complications of misoprostol and oxytocin
3. To compare the induction-to-active labor time
4. To compare the induction-to-delivery time of misoprostol and oxytocin.

MATERIALS AND METHODS

The study period was 3 years from March 2010 to February 2013. The study was approved by the ethical committee of Kannur Medical College. The total number of cases taken for study purpose were 280.

Inclusion Criteria

1. Term pregnancy
2. Fetus with average weight assessed clinically and ultrasound.

Exclusion Criteria

1. Short women, height <147 cm
2. Cephalopelvic disproportion
3. Antepartum hemorrhage
4. Previous cesarean deliveries.

Informed consent was obtained from each lady. As soon as the pregnant lady entered into the labor room clinical evaluation was done and documented.

Drugs Used

Misoprostol used was Misoprost-200 manufactured by Cipla India Ltd. The strength was 200 µg oxytocin used was Pitocin, manufactured by Pfizer India Ltd, 1 ampoule contains 5 units oxytocin.

Methods

2 groups were created; the first one was induced by misoprostol and the second one induced by oxytocin. Bishop score was calculated for all cases. Scores 3 and 4 were chosen for study purpose. Three indications were considered for induction; postdated pregnancy, pre-eclampsia, and gestational diabetes. Misoprostol was used as solution by dissolving into 40 mL sterile water. Every lady of the first group was fed 5 mL solution (1 teaspoon) every 3 h, maximum 6 doses, 5 mL containing 25 µg. An increment of half teaspoon solution (12.5 µg) was added every 3 h. Oxytocin was administered as drip

infusion. This was prepared by adding 5 units of Pitocin into 500 mL normal saline started with 2 mIU/min (4 drops per minute) and an increment of 2 mIU per minute is added every 30 minutes. Maximum dose was 36 m IU/min. Cervical dilatation was assessed every 4 hours by examination per vaginam. All the pregnant ladies were monitored by partogram and fetuses monitored by continuous electronic monitoring. Induction was stopped on the appearance of the following; presence of tachysystole and non-reassuring FH pattern. Tachysystole is defined as more than 5 contractions in 10 minutes. Tachysystole was controlled by terbutaline injection in one case of misoprostol administration. The active phase of labor is defined by cervical dilatation 4 cm or more. 3 contractions in 10 min are considered adequate. Regular rhythmic uterine contractions resulting into effacement and cervical dilatation was considered effective in labor induction. Failure to progress was assessed by no cervical dilatation in 4 h (arrest of dilatation) or no descent in 4 h (arrest of descent). Failure to achieve dilatation 1 cm/hour (protracted dilatation) or descent 1 cm/hour was also considered failure of progress or dysfunctional labor. The cesarean was done for the following situations; hyperstimulation syndrome, thick meconium stained liquor and failure to progress. Hyperstimulation syndrome is defined as tachysystole plus non-reassuring fetal heart rate (FHR) pattern. The non-reassuring pattern is a sign of fetal hypoxemia. It is diagnosed by the following abnormal features; tachycardia (FHR more than 180 a minute), reduced variability, late deceleration, and variable deceleration. All ladies were given adequate postpartum care and discharged on the 3rd day.

Statistical Analysis

Results were given as mean plus or minus SD. Statistical analysis was performed using the SPSS 16.0 statistical software package (SPSS Inc, Chicago, IL, USA). Time intervals were analyzed with Mann-Whitney U test, and other data were analyzed with the χ^2 for qualitative and Student's *t*-test for quantitative variables. A *P* = 0.05 was considered significant.

RESULT

Pregnant ladies from each group were studied for the demographic variables. No statistically significant difference was found (Table 1).

3 main indications of labor are taken into account (Table 2).

There was statistically significant difference in route of delivery, duration from induction-to-active phase and total duration of labor (Table 3).

Table 1: Demographic variables

Demographic variables	n (%) (n=140)		P value
	Misoprostol	Oxytocin	
Age	25±3 (53)	25±4 (53)	0.80
Gestational age	40±1.2	40±1.3	0.30
Parity nulli	56.0 (40.0)	62.0 (44.3)	0.40
Parity multi	84.0 (60.0)	78.0 (55.7)	0.40
Bishop score	3.2±1.4	3.1±1.4	0.10

Table 2: Indications of induction of labor

Indications	n (%) (n=140)	
	Misoprostol	Oxytocin
Post dated	120.0 (85.7)	118.0 (84.3)
Pre-eclampsia	16.0 (11.4)	17.0 (12.1)
GDM	4.0 (3.0)	5.0 (4.0)

Table 3: Labor details

Variables	n (%) (n=140)		P value
	Misoprostol	Oxytocin	
Vaginal delivery	113 (80.7)	82.0 (58.6)	<0.001
Delivery time [hours]	15.6±5.1	13.2±7.7	<0.05
Interval from induction-to-active labor (hours)	12.9±5.4	10.1±6.1	<0.04
Cesarean	27 (19.2)	58 (41.4)	<0.001

There was a significant increase in the rate of cesarean in oxytocin group ($P < 0.001$). The interval from induction-to-active phase (cervical dilatation ≥ 4 cm) was shorter in misoprostol group ($P < 0.04$) which is significant. The total duration of delivery also decreased in misoprostol group ($P < 0.05$) which also is significant.

There was no statistically significant difference in maternal complications in misoprostol group and oxytocin group. Important maternal morbidities were tachysystole, postpartum hemorrhage, blood transfusion, abruptio placentae, and vomiting (Table 4).

There was no statistically significant difference in the fetal complications also. Important fetal morbidities were aspiration of meconium and abnormal APGAR (Table 5). There was no maternal or fetal death in both groups.

DISCUSSION

Two common drugs used for labor induction are misoprostol and oxytocin.⁴ There are so many studies on the advantages and disadvantages of oxytocin and misoprostol.^{5,6} For example, Hofmeyr *et al.* suggest an effective dose of 25 µg of misoprostol every 4-6 h for reduction of complication rate.⁷ In our study, a dose of 25 µg which was repeated every 3 h in a titrated dose

Table 4: Maternal complications

Variables	n (%) (n=140)		P value
	Misoprostol	Oxytocin	
Tachysystole	18.0 (12.9)	12.0 (8.5)	0.40
Postpartum hemorrhage	10.0 (7.1)	17.0 (12.1)	0.40
Blood transfusion	1.0 (0.7)	3.0 (2.3)	0.60
Placental abruption	2.0 (1.4)	2.0 (1.4)	1.00
Gastrointestinal symptoms	13.0 (9.3)	5.0 (3.6)	0.03

Table 5: Neonatal outcome

Variables	n (%) (n=140)		P value
	Misoprostol	Oxytocin	
Birth weight	3100±250	3150±250	0.50
1 m APGAR<4	3.0 (2.3)	4.0 (3.1)	1.0
5 m APGAR≤7	1.0 (0.7)	1.0 (0.7)	1.0
Meconium staining	0.0 (0.0)	1.0 (0.7)	1.0
NICU admission	1.0 (0.7)	5.0 (3.9)	0.2

for 6 doses was administered. Studies of Fonseca *et al.*⁸ and de Aquino and Cecatti,⁹ showed significant maternal and fetal complications in misoprostol-induced cases; tachysystole, meconium stained liquor and reduced APGAR. However, our study does not show such increased complications in misoprostol group. Maternal and fetal complications are more or less equal in both groups. A study by Fonseca *et al.*⁸ and Kramer¹⁰ show no statistical significance in the rate of cesarean and vaginal deliveries. Our study clearly reveals an increase of vaginal deliveries in the misoprostol group ($P < 0.001$). Two important separate studies by Oliveira *et al.*¹¹ and Sanchez-Ramos *et al.*¹² show significant reduction of induction-to-vaginal delivery time. Our study supports this ($P < 0.001$)

CONCLUSION

The following conclusions have been arrived at by our study. Titrated orally administered misoprostol is as safe as titrated oxytocin. Misoprostol is superior to oxytocin in the following aspects. Reduction in cesarean rate. Induction-to-delivery time is shorter. Induction-to-active phase duration is also shorter in misoprostol-induced labor.

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Asokan and Santhosh: Comparative study of titrated oral misoprostol solution and oxytocin to induce labor

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How to cite this article: Asokan KM, Santhosh S. Comparative Study of Titrated Oral Misoprostol Solution and Oxytocin to Induce Labor Conducted at Kannur Medical College. *Int J Sci Stud* 2016;3(11):255-258.

Source of Support: Nil, **Conflict of Interest:** None declared.

Routine Elective Induction of Labor by 38-39 Weeks Advantages and Safety Concerns

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Abstract

Introduction: Since the idea of active management of labor by Kieran O'Driscoll came into practice, there is a lot of debate as to whether routine elective induction of labor has any advantage in relation to the outcome for mother and fetus without compromising safety to mother and fetus. We have taken an endeavor to study the above aspect.

Objectives: The objectives of this study were as the following section. (1) To evaluate the efficacy of elective induction between 38 and 39 weeks. (2) To assess the maternal and fetal complications of elective induction.

Materials and Methods: This prospective study consisted of a sample size of 420 subjects. Induction done by misoprostol and stripping and augmentation by oxytocin. SPSS 16.0, Mann-Whitney U test, the χ^2 for qualitative, and Student's *t*-test for quantitative variables. A *P* = 0.05 was considered significant.

Result: Vaginal delivery was 90.7% and cesarean 9.3% induction delivery time 12 h and 20 min for primigravidae and 7 h and 40 min for multigravidae.

Conclusion: Routine elective induction of labor between 38 and 39 weeks can be resorted safely by misoprostol and oxytocin. Normal vaginal delivery and cesarean are comparable to spontaneous onset of labor at 40 weeks. Fetal complications are comparable to spontaneous labor at 40 weeks. Elective induction is a more convenient to obstetrician and mother.

Key words: Artificial rupture of membranes, Elective induction of labor, Maternal and fetal outcome misoprostol induction, Oxytocin augmentation

INTRODUCTION

Pregnancy can be terminated once the fetus has attained lung maturity at 37 completed weeks. There are institutional variations in the management of term pregnancies. Elective induction is an accepted procedure among the public since most of them are concerned with horoscopic propriety. Elective induction is also convenient for obstetrician because of the efficient management of complications in a planned atmosphere. Here, we have planned routine elective induction of labor by 38-39 weeks and explored its advantages and safety.^{1,2}

MATERIALS AND METHODS

The study was conducted in Kannur Medical College Obstetrics and Gynecology department for a period of 14-month from 1st July, 2013, to 30 September, 2014. A total of 420 cases of term pregnancies were selected for study purpose. All pregnancies were terminated by elective induction of labor at 38-39 weeks. Out of 420, 284 ladies (67%) were primigravidae and the rest multipara (33%) (Table 1).

Inclusion Criteria

- Gestational age between 38 and 39 weeks
- Vertex presentation
- No obstetrical complications
- No medical complications.

Exclusion Criteria

- Previous cesarean
- Macrosomia

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Month of Submission : 12-2015

Month of Peer Review : 01-2016

Month of Acceptance : 01-2016

Month of Publishing : 02-2016

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- Contracted pelvis
- Malpresentations.

Study Design

This is a prospective study. The patients were admitted on the previous day of induction. All cases had undergone a biophysical profile scanning by the first author. This helped to assess the gestational age and estimated fetal weight. All cases had a non-stress test done on the date of admission. Routine blood investigations were performed. Cross matched blood and operation theater availability for emergency caesarean section were assured. A Bishop score³ was calculated at the time of admission by a vaginal examination. Our practice was to introduce 25 µg of misoprostol into the posterior fornix by 5 AM on the next day of admission.⁴ A repeat dose was given after 4 h in 92 cases, and 18 cases required a third dose, 4 h later. 8 cases had to be postponed 1 or 2 days due to lack of response. A Foley's catheter was inserted transcervically in nonresponders. Sweeping were performed to cases while assessing Bishop score whenever feasible.³

Sweeping alone initiated labor pain in 63 cases. True labor pain started within 2-4 h of the first dose of misoprostol in 294 cases. Enema (proctoclysis) was given once pain started. Intrapartum fetal and maternal monitoring were done by partograph.

Once the lady is in active labor (cervix dilatation of more than ≥ 4 cm), we performed artificial rupture of membrane (ARM). Oxytocin drip was started in titrating dose of 2 mIU/min and an increment of 2 mIU/min, in those cases with inadequate uterine contractions. Ampicillin 2 g IV was given to mother after ARM. Sedation with injection pentazocin 30 mg + promethazine 25 mg was the usual practice, especially in primigravidae. Intravenous (IV) hydration was ensured. The patient was kept on empty stomach in cases of delayed progress. Intrapartum monitoring of mother and fetus was done observing the NICE clinical guidelines (Table 2).⁵

RESULTS

Successful vaginal delivery was accomplished in 381 (90.7%) cases. Caesarean section was done in 39 cases (9.3%) which are statistically significant ($P < 0.001$). Indications were fetal heart variations, meconium stained amniotic fluid and inadequate progress with poor cervical dilatation and descent of head.

The mean induction delivery time was 12 h 20 min for primigravidae and 7 h 40 min for multigravidae which are also statistically significant ($P < 0.001$). 29 cases were vacuum-assisted vaginal deliveries (Table 3).

Table 1: Split up of case by Gravida

No. of Primi Gravida	284
Para I Gravida II	88
Para II Gravida III	32
Para III Gravida IV and above	16
Total cases	420

Table 2: Method of induction

Single dose misoprostol	310 cases
Second dose	92 cases
Third dose	18 cases
Postponed (failed third dose)	8 cases
ARM	368 cases
ARM pitocin	342 cases

ARM: Artificial rupture of membranes

Table 3: Mode of delivery

Vaginal delivery	381	90.71%
Caesarean Primi	33	7.86%
Caesarean multi	6	1.43%
Total	420	

About 10 units oxytocin infusion and per rectal application of 600 µg misoprostol were done to prevent postpartum hemorrhage (PPH) in all cases. Only 3 patients had mild to moderate atonic PPH which was controlled with injection prostodin 250 µg. One of them was transfused with one unit of blood. Cervical tear resulting in traumatic PPH was not seen in any case. No maternal complications such as tachysystole cases or hypertonic uterine action leading to fetal distress were present.

All babies had a good APGAR SCORE. 6 babies had poor 1 min APGAR SCORE (<5) which improved with simple resuscitation measures by a pediatrician. We ensured pediatric care in all deliveries.

DISCUSSION

The American College of Obstetrics and Gynecology do not recommend elective induction of labor before 39 completed weeks of gestation for non-medical indications,⁶ the main reasons are compromised fetal lung maturity and increased cesarean rate, i.e. 23.8% in induction and 13% in spontaneous labor.⁷

American College of Obstetrics and Gynecology further revised the name "Term" pregnancies in 2013⁸ as follows:

38 ⁰ to 38 ⁺⁶ days	Early term
39 ⁰ to 40 ⁺⁶ days	Term
41 ⁰ to 41 ⁺⁶ days	Late term
$\geq 42^0$ weeks	Post term

We have followed the WHO guidelines for induction of labor wherever possible.⁹ Clinical guidelines for induction of labor by National Institute of Clinical Excellence also were followed.¹⁰ However in our study with a proper selection of cases and confirmed of dates, neonatal respiratory distress was not observed in any of the cases. In the present study, the cesarean rate was only less than only 9.3%, which is statistically significant, $P < 0.001$ Early Ultrasonography for fetal gestational age and late ultrasonography for the biophysical profile (Doppler study in selected cases) are essential for a successful induction. Continuous fetal monitoring, ideally with partogram and supervision by a senior obstetrician are essential. Service of the blood bank, operation theater, anesthesiologist, pediatrician and supporting staff should be ensured.

CONCLUSION

Routine elective induction of labor between 38 and 39 weeks can be achieved safely by misoprostol and oxytocin. There is a definite benefit to mother and fetus with almost no complications. The induction can be scheduled for convenience which eliminated messy middle of night deliveries and late pregnancy discomforts. A single obstetrician in a busy unit has definite advantage with planned induction, not compromising safe motherhood. However, all precautions mentioned earlier should be adhered to. Hospital staff and resources should be adequate and vigilant for a successful outcome.

ACKNOWLEDGMENTS

We express our sincere gratitude to the Ethical Committee, Kannur Medical College for granting permission to conduct the study.

We also express our gratitude to the management Kannur Medical College for funding the project and giving permission to publish the article.

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How to cite this article: Warrier HG, Asokan KM. Routine Elective Induction of Labor by 38-39 Weeks Advantages and Safety Concerns. *Int J Sci Stud* 2016;3(11):259-261.

Source of Support: Nil, **Conflict of Interest:** None declared.

A Step toward Precision: A Review on Surgical Guide Templates for Dental Implants

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Abstract

Dental implants are becoming a more common treatment option nowadays with a large number of patients opting for this treatment option. For a good prognosis of implant treatment, proper implant placement is the major criteria. To establish a logical continuity between diagnosis, prosthetic planning and surgical phases, use of transfer device is essential. To increase the precision of implant placement, use of surgical guides had been suggested by various authors. Accurate pre-surgical planning taking into account anatomical limitations and prosthetic demands is mandatory to ensure a predictable treatment, without incurring possible intra- and post-operative complications. This article reviews the ideal requisites of a surgical guide along with basic methods of surgical guide fabrication and certain common recent advances in this field.

Key words: Cone beam computed tomography, Implants, NobelGuide, Stereolithography, Surgical template

INTRODUCTION

The protocol for a successful implant is one that demonstrates osseointegration, as well as optimal position of the implant for the fabrication of an esthetic and functional restoration. Ideal placement facilitates the establishment of favorable forces on the implants and prosthetic components while ensuring an esthetic outcome. To increase the predictability of success, it is essential that the implants are placed properly.¹

To establish a logical continuity between diagnosis, prosthetic planning and surgical phases, use of transfer device is essential. The surgical guide template is fabricated by the restoring dentist after the pre-surgical restorative appointments, the final prosthesis design, optional abutment number and location, occlusal scheme, and implant angulation have been determined.

A surgical guide is “A guide, derived from the diagnostic wax-up, used to assist in the preparation for, and placement of, dental implants. It dictates drilling position and angulation.” A number of types of guides and templates have been described in the literature.²

IDEAL REQUISITES

The surgical guide should accurately translate diagnostic information from pre-surgical diagnostic work-up to direct implant placement in three dimensions (Figure 1):

- Bucco-lingually
- Mesio-distally, and
- Apico-coronally.²

The guide should, if possible, be able to carry radiographic markers to provide contrast between the guide and sites selected for implant trajectory to be used in diagnostic imaging. The American Academy of Oral and Maxillofacial Radiology has recommended the use of surgical templates with radiographic markers in conjunction with imaging.

Ideally, the surgical guide should possess the following characteristics:³

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Month of Submission : 12-2015

Month of Peer Review : 01-2016

Month of Acceptance : 01-2016

Month of Publishing : 02-2016

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- Simple and cost-effective to fabricate
- Stable retention in surgical field (adjacent teeth or landmark)
- Easy access of drills/guide pins/osteotomes intraoperatively (Figure 2)
- Ability to translate pre-surgical work-up information accurately to operating field.

Extensions

If the arch treated has remaining teeth, the template should fit over and/or around enough teeth to stabilize and position the guide stent.

When no remaining teeth are present, the template should extend onto unreflected soft tissue regions, that is, the palate and tuberosities in the maxilla, or the retromolar pads in the mandible. In this way, the guide template may be used after the soft tissue has been reflected from the implant site, and during preparation for the implant osteotomy.

Implant Angulation

The ideal angulation for implant insertion should be visualized during surgery and requires, at least, two reference points for each implant. For that purpose, the surgical guide must be elevated above the edentulous site. The distance between the occlusal surface of the abutment crown and the crest of the ridge represents 8 mm or more. As a result, these two points of reference correspond to the path of ideal implant insertion. The ideal angulation is perpendicular to the occlusal plane and parallel to the most anterior abutment joined to the implant.

Gingival Contouring

The surgical template should relate the ideal gingival contour position. Lost bone and gingival width may be replaced during implant insertion by an onlay graft of dense hydroxyapatite and demineralized freeze-dried bone. The amount of augmentation required to support the tissue can be determined by the surgical template.

Construction of Surgical Templates

The easiest method to construct the implant surgical template is to use a modification of Preston's clear splint for the diagnosis of tooth contours, tooth position, and occlusal form (Figure 3). The diagnostic wax-cast is completed to determine tooth size, position, contour, and occlusion in the edentulous regions where implants will be inserted. A full arch irreversible hydrocolloid impression is made and poured in dental stone. On the duplicate cast of the wax-up teeth, a vacuum acrylic shell is pressed and trimmed to fit over the teeth and gingiva contours of the buccal aspect of the ridge. If no natural teeth remain, the posterior portion of the template should be maintained and cover the retromolar pads or tuberosities to aid in positioning.

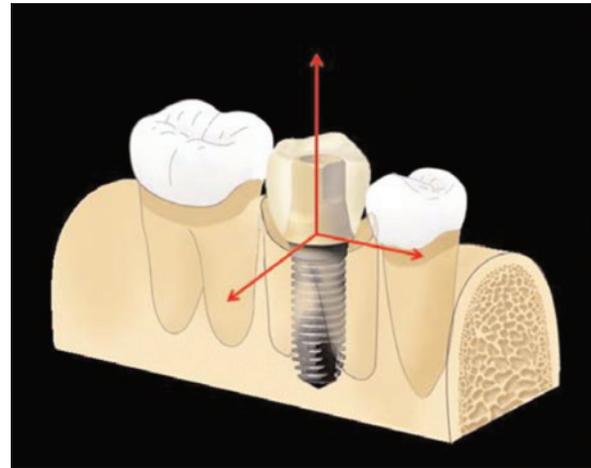


Figure 1: An ideal surgical guide should facilitate placement of a dental implant in the optimal bucco-lingual, mesio-distal, and apico-coronal dimension



Figure 2: A surgical guide should have easy access to drills, osteotomes, and other devices commonly used during implant surgery



Figure 3: Clear vacuum shell adapted over diagnostic wax up duplicate cast

The occlusal acrylic is removed over the ideal and optional implant sites, maintaining the facial and facio-occlusal line angle of the surgical template. This provides maximum

freedom for implant placement, yet communicates the ideal tooth position and angulation during surgery. In the edentulous arch, the vacuum form may be of the existing removable prosthesis, if within accepted guidelines.⁴

The surgical template for complete denture engaging occlusal aspect of opposing arch (Laney Poitras Template) contains an acrylic stent on the opposing arch with projecting orthodontic wires at the desired implant sites.

This allows each pin of the template to contact bone, once the tissue is reflected during surgery, without modifying the occlusal vertical dimension and consequently the emergence position of the implant. The wire should approach within 1-3 mm of opposing arch.

Once the soft tissue is reflected the template is positioned over teeth of the opposing arch. The patient may occlude on pins and each one determines the ideal center position of teeth. A pilot drill can be used to mark each implant body positions (Figure 4).⁴

Proper preparation of the dental office is essential for the prompt recognition, and successful management, of medical emergencies that do arise in dental offices. Following are some suggestions for the basic emergency drugs and items of equipment needed in the well-equipped dental office (Figures 2a and b).

Advantages

- Angulation of the osteotomy can also be determined
- Easily determines the implant position yet surgeon can have complete access and vision
- Template may also be used with osteoprotegrin before surgery
- Can also be used for second stage surgery to determine

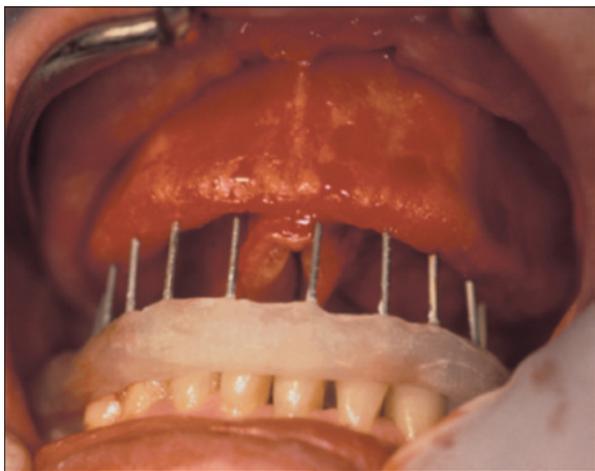


Figure 4: Once the tissues are reflected, the template is seated on the opposing arch and indicates the position and angulation of each implant

the exact position of implants for conservative soft tissue reflection.

RECENT ADVANCES

Computer-Aided Design (CAD)/Computer-Aided Manufacturing (CAM) Surgical Guides

Treatment planning decisions made with CAD can be easily transferred to the surgical treatment phase, be performed, in turn, with CAM. CAD can be conducted through reading and interpreting multiplanar computerized tomography (CT) scans or cone beam CT (CBCCT), performing measurements, and evaluating anatomic relationship by placing virtual images on the screen. In the CAM process, stereolithography method can be used for the fabrication of three-dimensional (3D) surgical templates. The method includes a laser beam traveling above the photosensitive liquid acrylic, allowing the surgical template to be polymerized in the layers according to the design. Then, stainless steel tubes are inserted in the spaces that represent implant location. After insertion the tubes, the surgical template is ready for use. Thus, CAD/CAM surgical templates allow the software-based planning to transfer to the surgical field.⁵

Nokar *et al.* investigated the accuracy of implant placement using a CAD/CAM surgical guide by means of an *in vitro* study. The results showed that the average differences between the planned and actual entry points in the mesiodistal and buccolingual directions, lengths, and angles of the implants and the osteotomy showed a considerable reduction in the CAD/CAM group versus the conventional group and it was concluded that accuracy of implant placement was improved using an innovative CAD/CAM surgical template.⁶

Stereolithography

Once CT scan data are segmented, the software interpolates the data on all three planes to form a smooth 3D model. A computer file of this model can be alternatively transferred to stereolithography equipment where a physical model of the patient's bone structure is created. The finalized treatment plan is thus used for fabrication of a surgical template using this technique.

In oral implantology, this technology develops a precise evaluation of anatomic points such as the size of the maxillary sinus in the upper jaw and the location of the alveolar nerve in the lower jaw. It also provides information about size, direction, and bone location for accurate positioning of implants.⁵

Using this technique, surgical procedure would be simplified, reliable, and easily reproducible. Wound size

and bone surface exposure would be minimal and no soft tissue trauma would be derived by use of burs during bone drilling. Furthermore, during the operative procedure, there will be no major problems of bleeding or nerve lesion. The post-operative time would be without complications.

This technique offers many advantages which include:

- Correct management of the tissues with minimal trauma and a superior planned treatment
- In cases of severe atrophy, this methodology allows fixture measurements by the indication of exact surgical limitations and prevents complications related to poor stability of a denture.

DRAWBACKS

The main drawback of the surgical template can be seen in the possible movement of the template during surgery and reproducibility of the splint position between the CT exam and surgical procedure.

The degree of the difference between the proposed and actual implant direction may be influenced by various factors, such as the construction accuracy of the template, the surgical accuracy using these templates, the accuracy of the study model, the accuracy of the stereolithographic machines and the measurement accuracy.

The CT scan involves a higher dose/higher cost method. However, the CT scan is less time consuming when multiple implants are required, and it allows imaging of the entire jaw, making it possible to use software for virtual implant placement. As long as radiographic imaging has been enhanced by the development of various techniques, multi-slice, and spiral CT are being replaced by CBCT systems for oral and maxillofacial imaging, enabling a significant reduction dose (Loubele *et al.*, 2008).

NOBELGUIDE COMPUTERIZED SURGICAL TEMPLATE SYSTEM

Nobel Biocare's NobelGuide is a planning and surgical concept that allows dentists to place implants in a single visit so that the patient leaves the office with a fully functioning tooth or teeth. NobelGuide uses Nobel Biocare's Procera® surgical planning software and flapless surgery, alternatively described as "keyhole surgery." Using Procera software, dentists can plan complete implant treatment, including number, length, and angulation. CT or a plaster model taken of the patient's teeth and mouth provide the basis for determining the bone's shape and location. Planning data allow Nobel Biocare or a dental laboratory to create a surgical template permitting less invasive, flapless surgery.

The surgical template, secured over the patient's soft tissue, allows the dentist to drill directly into the bone through the soft tissue through guide holes.

NobelGuide allows the simultaneous placement of implant, abutment, and restorative crown or bridge; furthermore, conventional or computer aided-3D design can be used to construct the surgical template for placing implants in the exact position and depth needed for completion of the restorative plan.⁷

CONCLUSION

In a research to determine the "Effect of Surgical Guide Design and Surgeon's Experience on the Accuracy of Implant Placement," it was found that surgical guide design, surgeon's experience, and size of the edentulous site all statistically significantly affect the accuracy of implant placement. An angulation error in the buccal-lingual direction was shown to be less likely to occur in the experienced group.⁸ An electronic and hand search of the literature revealed three categories, namely, non-limiting, partially limiting, and completely limiting design. Most clinicians still adopt the partially limiting design due to its cost-effectiveness and credibility. Moreover, clinicians use cross-sectional imaging during the pre-implant assessment of surgical sites.⁹ Precision has been improved and uncertainty, and surgical time have been reduced with the use surgical templates, thus addressing complex rehabilitation with greater confidence. A study was done to determine the accuracy of computer-aided template-guided oral implant placement and it was concluded that computer-aided flapless implant surgery seemed to provide several advantages to the clinicians as compared to the standard procedure; however, linear and angular deviations are to be expected. Therefore, accurate pre-surgical planning taking into account anatomical limitations and prosthetic demands is mandatory to ensure a predictable treatment, without incurring possible intra- and post-operative complications.¹⁰ In addition, predictable positioning allows for the better prosthetic outcome by simplifying abutment selection and avoiding complex laboratory fabrication when misalignment must be corrected.

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How to cite this article: Pawar A, Mittal S, Singh RP, Bakshi R, Sehgal V. A Step towards Precision: A Review on Surgical Guide Templates for Dental Implants. *Int J Sci Stud* 2016;3(11):262-266.

Source of Support: Nil, **Conflict of Interest:** None declared.

Applications of 3-D Printing in Orthodontics: A Review

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Abstract

The art and science of dentistry have evolved over the past few years more importantly in clinical and laboratory workflows with a progression from an analogous, manipulation of materials manually to a systematic, digitally verifiable process. The field of orthodontics in its new era is stepping ahead to newer technologic perspective. Three-dimensional (3-D) printing application in orthodontics has made the treatment procedures easy, time saving, cost-effective apart from the initial investments. This article is to provide recent trends and updates of application of 3-D printing in orthodontics.

Key words: 3-D printing, Appliances, Digitization

INTRODUCTION

A three-dimensional (3-D) printing is also known as additive manufacturing or desktop fabrication. It is a process of making 3-D solid objects from a digital file. The digital 3-D model is saved in STL format and then sent to the 3-D printer where the layer by layer design of an entire 3-D object is formed.^{1,2} This creation of the 3-D printed object is achieved using additive processes. Each of these layers can be observed as a thin sliced horizontal cross-section of the eventual object.²

HISTORY

1984 seems to be the beginning when Charles (Chuck) Hull of 3-D Systems developed the first working 3-D printer.⁶ Later, in 1986, Charles Hull founded 3-D Systems and developed the first commercial 3-D Printing machine and it was called as Stereo

lithography Apparatus.³ He obtained patency for this Stereo lithographic technique. In 1993, Massachusetts Institute of Technology (MIT) patented “3-D Printing techniques.” It is similar to the inkjet technology used in 2D Printers.

In 2010 - Organovo, Inc., a regenerative medicine company prioritized on bio printing technology, announced the release of data on the first fully bio printed blood vessels.³

WHAT IS A 3-D PRINTER

The 3-D printer is unlike of the common printers in which the object is printed by 3-D (Figure 1). A 3-D model is built up layer by layer. Therefore, the whole process termed as rapid prototyping or 3-D printing.³

The biggest drawback for the individual home user is still the high cost of 3-D printer, and also it takes hours or even days to print a 3-D model (depending on the complexity and resolution of the model). Besides above, the professional 3-D software and 3-D model design are also in a high-cost range.³

Alternatively, there are already simplified 3-D printers for hobbyist which are much cheaper and the material it uses is also economical. Such 3-D printers for home use are not

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www.ijss-sn.com

Month of Submission : 01-2015
Month of Peer Review : 01-2016
Month of Acceptance : 02-2016
Month of Publishing : 02-2016

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as accurate as commercial 3-D printer.³

ADVANTAGES OF 3-D PRINTING

1. Enhanced treatment procedures;
2. Patient treatment becomes fast, smooth and with greater precision;
3. Dependably superior appliances.

MATERIALS USED TO PRINT 3-D OBJECTS

Various materials that can be used for 3-D printing are ABS plastic, PLA, polyamide (nylon), glass filled polyamide, stereo lithography materials (epoxy resins), silver, steel, titanium, photopolymers, wax, polycarbonate.³ The Objet 500 and 260 Dental Selection 3-D Printers work with the full range of PolyJet dental materials.⁴ Materials for dental application is available in convenient sealed cartridges.

The known three PolyJet dental materials, specially engineered for dentistry are:-

1. Clear Bio-compatible (MED610),
 - Can produce orthodontic appliances
 - Delivery and positioning trays and
 - Surgical guides for temporary in
 - Mouth placement.
2. Vero Dent Plus (MED690),
A dark beige material that creates amazingly fine features and finish, and offers excellent strength, accuracy and durability placement.
3. Vero Glaze (MED620),
An opaque material with A2 shading designed to provide the suitable color match for veneer try-ins and diagnostic wax-ups. Vero Glaze is medically approved for temporary in-mouth placement, up to 24 h.

Website with 3-D models database:

- 3-D Marvels
- 3-D Via
- GrabCAD
- Google 3-D Warehouse
- Ponoko Product Plans
- Shapeways 3-D Parts Database
- Thingiverse
- Turbosquid: Free objects.

3-D modeling software which can be downloaded for free:

1. Google SketchUp
2. 3-Dtin - The simplest 3-D software
3. Blender

4. Open SCAD: Focus on CAD aspect
5. Tinkercad.

REVOLUTION

As 3-D printing can replicate the human form more accurately than traditional manufacturing techniques. Orthopedics and dental implants are the most common medical uses of the technology.⁵ Estimates of IBIS World (2013) are that there are already more than half million 3-D printed dental implants in patients worldwide. The University of Toronto's Bio Printer project is exploring the use of 3-D printed tissue for the treatment of burned patients. 3-D printing also allows the production of complex shapes (such as hollow figures) and lightweight parts that can be used to create implants a growing demand in countries with aging populations. Bone replacements and support structures for growing body parts made by 3-D printers are at different stages of research.

Another possible application in the medical industry is to use 3-D printers to create models of human parts from computed tomography scans or magnetic resonance imaging images to assist surgeons during complex surgeries (Figures 2 and 3). Designers and engineers are also exploring the development of new and specialized surgical tools made by 3-D printers.

APPLICATIONS OF 3-D PRINTING IN DENTISTRY

1. Dental restorations, especially dental prostheses, including crowns, veneers, inlays and on lays, fixed bridges,
2. Dental implant restorations,
3. Dentures (removable or fixed),
4. Orthodontic appliances.
5. Print craniofacial structures for reference before complex surgeries.⁵

ORTHODONTIC PERSPECTIVE

Orthodontist creates beautiful smile and crafting smile is a time-consuming process. But with digitization, it has become easy. 3-D printing is revolutionizing the orthodontic process, providing digital advantages over the traditional workflow process.⁶ After the 3-D scan is done, it is transferred to the computer to get 3-D images of patient's teeth. Either these files can be sent out to labs for fabrication or in office set up where the 3-D CAD file is dragged into the 3-D printer. Compact 3-D Printers

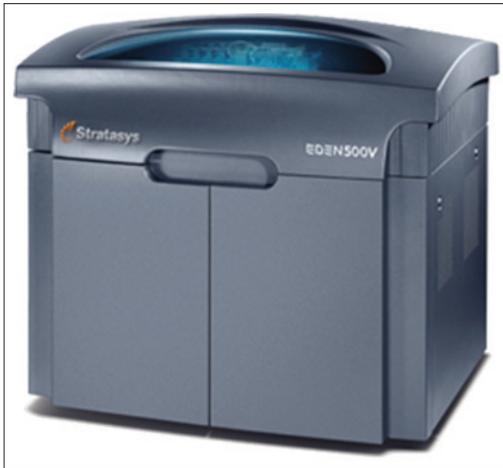


Figure 1: 3-D Printer. Source: <http://ObjetEden500V3-DPrinter>



Figure 3: Colored 3D print of craniofacial structure

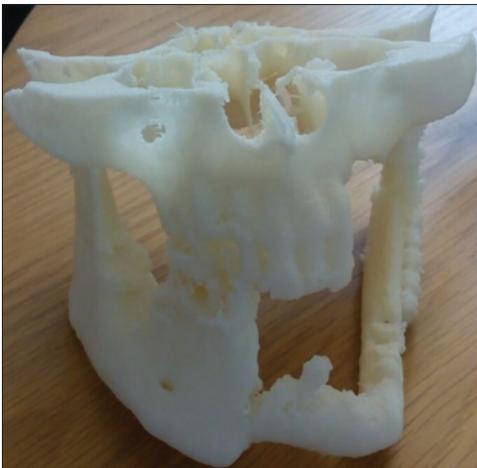


Figure 2: 3-D print of craniofacial structure in cancer patient after computed tomography scan



Figure 4: Orthodontic study models. Source: <http://3dprint.com/29835/e-appliance-envisiontec/>

for clinical setup and small labs are introduced by various companies (e.g.: Objet30 Orthodesk from Stratasys). Here, 20 models per printer can be created.⁶ Various removable appliances (like Hawleys retainer, splints), functional appliances, arch expansion appliances, clear aligners, retainers, arch wires, brackets, auxiliaries, trays for indirect bonding, set up models which will make lingual orthodontics and mock surgeries fast and easy, also study models (Figure 4). The process is quick, clean and accurate. These factors can dramatically accelerate professional time of an orthodontist, eliminate physical impression, and put an end to bulky physical model storage.

Many years back digital orthodontics was only a dream. For those eager for the day when everything from scheduling to final appliances can be achieved digitally and automatically, the future is here. With a 3-D printer doing the hard work, dental labs eliminate the manual modeling and let the business grow.⁷⁻¹⁰

CONCLUSION

Automated model-making with the 3-D printer dramatically reduces fabrication times and exponentially increases output per technician. Thus by transitioning to a fully digital process, there is no need to store bulky physical models and keep all your cases digitally, for as long as you need.

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How to cite this article: Mahamood S, Khader MA, Ali H. Applications of 3-D Printing in Orthodontics: A Review. *Int J Sci Stud* 2016;3(11):267-270.

Source of Support: Nil, **Conflict of Interest:** None declared.

Linear Syringocystadenoma Papilliferum with Unusual Presentation: A Rare Case Report

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Abstract

Syringocystadenoma papilliferum (SP) is a skin hamartoma also known as nevus syringocystadenomatous papilliferus. The histogenesis of this tumor is unclear. It is believed to derive from undifferentiated pleuripotential cells with either apocrine or eccrine differentiation and still classified under tumors with apocrine differentiation because of evidence of decapitation secretions pointing toward an apocrine origin. It is relatively a rare neoplasm, and most of the patients presented with solitary lesions in the head and neck region at birth or early childhood. Multiple erythematous papules like lesions are rarely a presentation and often misdiagnosed clinically. We report a case of SP in a 10-year-old female, which was located in axilla and was clinically misdiagnosed as molluscum contagiosum.

Key words: Molluscum contagiosum, Skin hamartoma, Syringocystadenoma papilliferum

INTRODUCTION

Syringocystadenoma papilliferum (SP) is a rare hamartomatous skin adnexal tumor which is believed to originate from undifferentiated pleuripotential cells which may show apocrine or eccrine differentiation but still considered under the category of tumors with apocrine differentiation.¹ It is predominantly a childhood tumor and is present since birth in almost 50% of cases another 15-30% of them developing before puberty with equal frequency in both sexes. Mostly, it is seen on the head and neck region with face and scalp being the most common locations, however, these tumors may be seen in other locations like vulva, external ear, lower leg, scrotum eyelids and breast.^{1,2}

A present case report is of linear SP in 10-year-old female, which was located in axilla. Though clinically it was very much similar to that of molluscum contagiosum but could

not be considered as a differential diagnosis because of the history of long duration.

CASE REPORT

A 10-year-old female child was brought with a complaint of multiple asymptomatic papules over the right axillary region since birth which gradually increased in size. The lesion developed a change in texture and grew rapidly over the last 1 year. There were no associated systemic symptoms.

On examination, there were multiple erythematous papules of size 1-10 mm in linear pattern of arrangement. Most of the papules were discrete, pink, and dome shaped few of the papules were eroded with yellowish creamy slough on it. Central umbilication and crusting were also noted on some of the papules. There was no regional lymphadenopathy. Hematological, biochemical and radiological investigations were normal. Lesions were similar to that of molluscum contagiosum but because of long duration history no particular presumptive diagnosis was made, and skin biopsy was performed for the final diagnosis (Figure 1 and Table 1).

Pathological Findings

We received two punch biopsies of skin each measuring 5 mm.

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Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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Microscopic Findings

Section showed epidermis and dermis. Epidermis revealed hyperkeratosis, parakeratosis acanthosis, and papillomatosis mimicking like a verrucous lesion (Figure 2). Adjacent to it was a focus of cystic, papillary and ductal invagination extending into deep dermis. These invaginations were lined by double layers of cells made of outer layer of cuboidal cells with round nuclei and scanty cytoplasm and a luminal layer of tall columnar cells with oval nuclei and eosinophilic cytoplasm (Figure 3). The core of the papillae was filled with dense plasma cell infiltrate, few lymphocytes and dilated capillaries (Figure 4).

Deep in dermis groups of tubular glands with large lumina were seen. The cells lining the lumina were flattened and showed evidence of active decapitation secretion.

On the basis of clinical features and histopathological finding diagnosis of linear SP was made.

DISCUSSION

In the present case report, the lesions were located in axilla in a linear pattern of arrangement, this particular location and the pattern of arrangement is highly uncommon and has not been described in available literature.

Three clinical subtypes of SP have been described:^{1,2,4}

- a. Plaque type: They present mostly as a hairless area in the scalp and enlarge during puberty to become nodular, verrucous or crusted. It is often seen in

Table 1: Distribution of sites and sub types of SP

Case report	Type	Site	Age group
Vyas <i>et al.</i> ²	Plaque	Scalp	12 year female
Chauhan <i>et al.</i> ¹	Linear	Right lower abdomen	10 year female
Park <i>et al.</i> ³	Nodular	Right supra pubic	65 year male
Present case report	Linear	Axilla	10 year female

SP: Syringocystadenoma papilliferum



Figure 1: Linear, multiple erythematous papules with crusting and umbilication on axilla

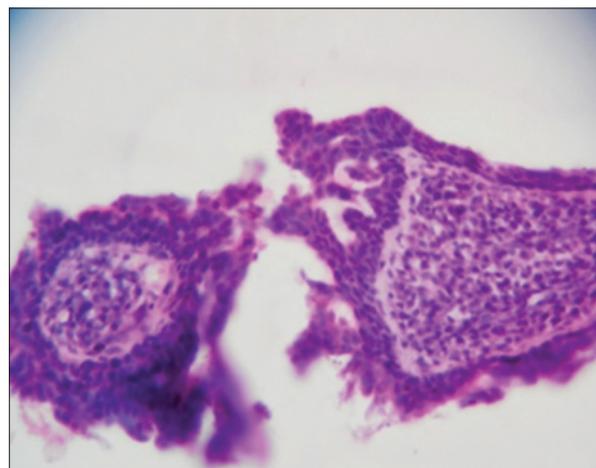


Figure 3: Papillary projections lined by two rows of epithelial cells. Luminal row is high columnar outer row consist of small cuboidal cells

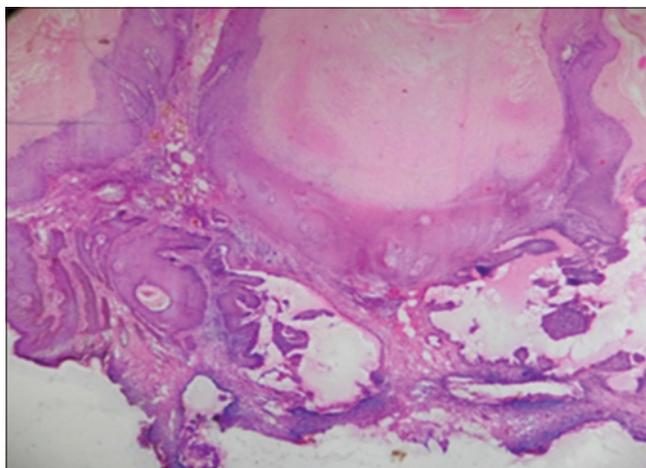


Figure 2: Epidermis with hyperkeratosis, parakeratosis and cystic invaginations with papillary projection into the lumen of cyst

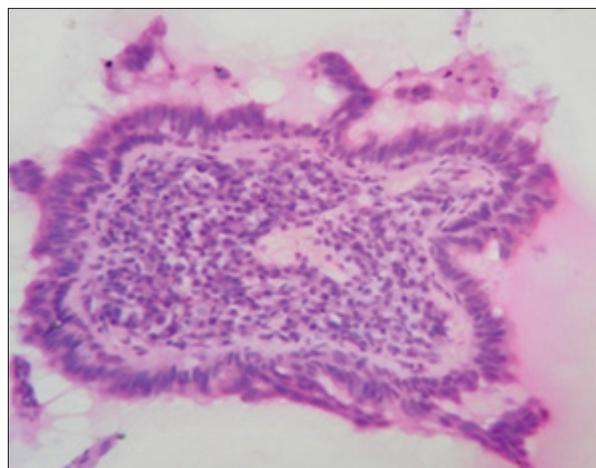


Figure 4: Plasma cells infiltrate in the core of papilla, decapitation secretion at the luminal surface

association with sebaceous nevus of Jadassohn or may appear *de novo* without preexisting lesions.

- b. Linear type: Nearly, all cases involve neck and rarely chest arm abdomen and thigh. The lesions are present since birth and consist of multiple linear reddish pink firm papulovesicles with dome-shaped surface of size 1-5 mm, as age progresses it may increase in size and number sometimes show central umbilication, ulceration, crusting, and yellowish foul smelling creamy discharge. At puberty, it may become verrucous and papillomatous.
- c. Solitary nodular type: This type show predilection for the trunk, shoulders, axillae, and the genital area and occasionally extensive verrucous or papillary plaques can be seen. It consists of solitary pedunculated nodules up to 5-10 mm.

A long list of lesions which are reported to be associated with SP includes viral warts, nevus sebaceous, linear nevus verrucous, nevus comedonicus, apocrine poroma, apocrine hidradenoma, tubulopapillary hidradenoma, hidradenoma papilliferum, papillary eccrine adenoma, verrucous carcinoma, apocrine acrosyringial keratosis, poroma folliculare, linear nevus verrucosa, atypical fibro xanthoma, clear cell syringoma, basal cell epithelioma, sebaceous epithelioma, trichoepithelioma and verruca vulgaris.⁵⁻⁹ It can be seen in association with malignant tumors such as verrucous carcinoma, basal cell carcinoma, sebaceous carcinoma and ductal carcinoma. The most common association is with a nevus sebaceous.^{10,11}

Differential diagnosis is syringoma for solitary lesions,⁴ other adnexal tumors which show linear arrangements include nevus comedonicus, trichodiscoma, trichoepithelioma, basaloid follicular hamartoma, cylindroma, eccrine nevus, syringoma, eccrine poroma, eccrine spiradenoma, and basal cell carcinoma.¹ Umblicated nodules may mimic molluscum contagiosum, warty lesions often confused with verruca vulgaris. Clinical features of SP vary widely

but histopathology is invariably uniform and confirmatory in all clinical subtypes.^{1,4}

Results of enzyme histochemistry immunohistochemistry and electron microscopy obtained have been conflicting.¹¹ A complete surgical excision is a treatment of choice.⁴

CONCLUSION

The presented case illustrates a yet un-described location and pattern of the rare skin tumor linear SP, leading to a clinical misdiagnosis. Correct diagnosis rest on histopathology since clinical information does not narrow down among many differential diagnoses.

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How to cite this article: Shubhada B, Umesh K, Suresh C, Renuka G. Linear Syringocystadenoma Papilliferum with Unusual Presentation: A Rare Case Report. *Int J Sci Stud* 2016;3(11):271-273.

Source of Support: Nil, **Conflict of Interest:** None declared.

Retroperitoneal Ancient Schwannoma: A Benign Tumor

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Abstract

Schwannomas are uncommon benign neoplasms arising from the Schwann cells lining the nerve sheath. Retroperitoneal schwannomas are extremely rare constituting about 0.3-3.2% of all retroperitoneal masses. Pancreatic schwannomas are obsolete and less than 50 cases reported until date in the literature. Ancient schwannomas is a histological variety in which there would be degenerative changes occurring with increasing duration of these tumors. We report 4 cases of retroperitoneal ancient schwannomas with one of pancreatic origin. Patients underwent pre-operative imaging studies (computed tomography/magnetic resonance imaging). All cases underwent exploration and *en bloc* excision of the tumors. The diagnosis was confirmed on both histopathological and immunohistochemical analysis. Pre-operative diagnostic dilemma in retroperitoneal schwannomas arises as they are either asymptomatic or have vague symptoms and signs. The radiological findings are not characteristic in the majority of the time. Fine-needle aspiration cytology is inconclusive and accessibility is always challenging due to its location. Pancreatic ancient schwannoma described here is unique due to the extreme rarity of location and was diagnosed intraoperatively on frozen section. As most of these tumors are in the paravertebral position in close proximity to important neurovascular structures it causes a technical challenge for a surgeon to operate. Resection of the tumor in toto is the treatment of choice for all tumors.

Key words: Benign, Excision, Schwannoma, Tumor

INTRODUCTION

Schwannoma is an uncommon benign neoplasm arising from the Schwann cells lining the nerve sheath. They are usually found in extremities, head, and neck region. Retroperitoneal schwannomas are quite rare accounting to 0.3-3.2% of all schwannomas. Pancreatic schwannomas are very rare and only 50 cases being reported in the literature. Some Schwannomas are termed “ancient” because of the degenerative changes which occur with increasing duration of these tumors. We present 4 cases of retroperitoneal ancient schwannomas with one of pancreatic origin.

CASE REPORTS

Case 1

A 48-year-old female presented with a mass in the right lower abdomen of 6 years duration which was painless, slowly progressive in size with no co-morbidities. On abdominal examination, fullness was noted in the right iliac fossa with no other findings on inspection of the abdomen. On palpation, a 10 cm × 6 cm vertically oval shaped non-tender mass was felt in the right iliac fossa which had a smooth surface and hard consistency. The mass was immobile, the plane being retroperitoneum.

Her routine blood investigations were within normal limits. Contrast enhanced abdominal computed tomography (CT) showed a smooth well-defined mass measuring 10 cm × 8 cm in the right retroperitoneum, displacing the right ureter and the iliac vessels with no local infiltration.

The mass was approached through a midline abdominal incision. The ileocecal junction was mobilized to expose

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Month of Submission : 12-2015

Month of Peer Review : 01-2016

Month of Acceptance : 01-2016

Month of Publishing : 02-2016

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the peritoneum overlying the tumor in the retroperitoneum. The peritoneum was incised, and the tumor capsule was exposed. A 12 cm × 8 cm tumor was noted extending from the level of the right renal artery to the bifurcation of common iliac artery and the tumor was found to be pushing the common iliac vein anteroinferiorly. The right ureter was coursing inferiorly over the tumor. On further dissection, the tumor was noted to be arising from the right lumbar sympathetic trunk (Figure 1a). The tumor was excised into sparing the nerves.

Gross examination showed the tumor to be well encapsulated and on cut section; there was heterogeneous yellow cheesy xanthomatous degeneration (Figure 1b).

Post-operative period was uneventful (Figure 1c) and at 1 year follow-up; there were no clinical or radiological evidence of recurrence.

Case 2

A 35-year-old female presented with a history of mass and vague pain in the lower abdomen since 1 year. She was asymptomatic otherwise. On abdominal examination, lower abdominal distension was noted with no visible peristalsis or prominent veins. A 20 cm × 15 cm mass was palpable in the lower abdomen, the lower border of which was extending into the pelvis. Per vaginally, no mass was palpable in the fornices.

She underwent contrast enhanced CT of abdomen and pelvis which revealed a heterogeneous mass in the left retroperitoneum measuring 20 cm × 10 cm. A midline laparotomy incision was performed, and a huge mass was found to be occupying the lower abdomen from umbilicus to the pelvis (Figure 2a). The left ureter was coursing over the mass. The mass was expected to be originating from the organ of Zuckerkandl. The tumor was excised with meticulous dissection and thorough hemostasis.

On gross examination, the tumor was nodular with a breach in the capsule (Figure 2b). On cut section, the tumor showed white cheesy areas with cystic degeneration. The histopathological examination showed malignant schwannoma. Her post-operative period was uneventful. During her follow-up, she was clinically and radiologically disease free until 1 year.

Case 3

A 27-year-old female presented with 1 month history of pain abdomen in the right hypochondrium and epigastrium. The pain was insidious in onset, dull aching in nature and associated with nausea, decreased appetite and early satiety. There was no significant past history. Abdominal examination revealed tenderness in the epigastrium

and right hypochondrium with no palpable mass or organomegaly.

All laboratory investigations including complete blood count, liver function and renal function profiles, coagulation profile, serum amylase, serum lipase, carcinoembryonic antigen and cancer antigen 19-9 were within normal limits.

Contrast-enhanced CT abdomen and pelvis (plain and contrast) showed a well-defined round to oval heterogeneously enhancing lesion with areas of central calcification in the region of the head and uncinate process of pancreas measuring 38 mm × 43 mm × 49 mm. The pancreatic duct appeared normal measuring 2 mm. Anteromedially, the lesion was abutting the gastric antrum, gall bladder, portal vein. Posteriorly the lesion was abutting the right kidney and inferior vena cava. Cranially the lesion was abutting the caudate lobe of the liver (Figure 3a).

At laparotomy, a globular firm to hard mass measuring 4.5 cm × 3.5 cm × 3.2 cm was noted in the region of head and uncinate process of pancreas which was abutting the second part of duodenum (Figure 3b). The lesion appeared

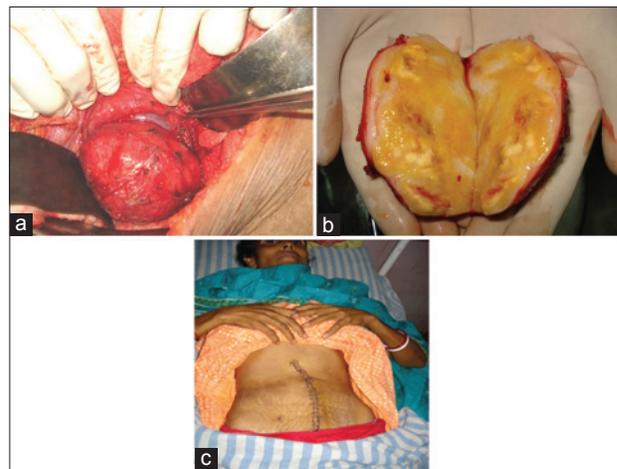


Figure 1: (a) Tumor arising from right lumbar sympathetic trunk. (b) Cut section of the tumor showing yellow cheesy xanthomatous degeneration (c) Patient in postoperative period with midline sutured wound

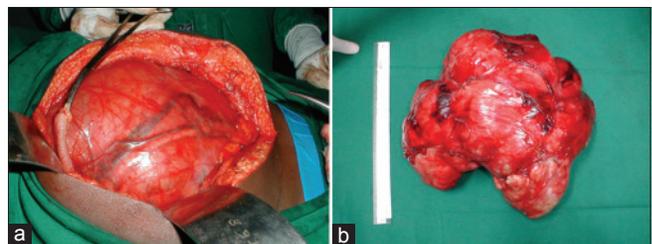


Figure 2: (a) A huge mass occupying the lower abdomen from umbilicus to the pelvis with left ureter and vessels coursing over it. (b) Nodular tumor with breach in the capsule

encapsulated and well circumscribed. A single 1×1 cm lymph node was noted along the right gastroepiploic vessels. Rest of the viscera was normal. The patient underwent wide local excision of the mass (Figure 3c) and excision of the lymph node with frozen section analysis.

Frozen section of pancreatic mass was suggestive of benign spindle cell lesion, and the lymph node showed reactive changes. Hence, in view of the benign nature of the pancreatic lesion, Whipple's procedure was deferred. Complete hemostasis confirmed and abdomen closed with 28 Fr abdominal drain in the lesser sac.

Until the 3rd post-operative day, her drain output was 50 ml/day. Next day onward, the drain output increased to 300-500 ml/day and remained persistently elevated until the day of discharge. Pancreatic fistula was expected in this case because during the surgery it was hardly possible to identify and avoid injury to the undilated main pancreatic duct. Abdominopelvic sonography revealed no obvious collection. Enteral feeding was initiated on 7th post-operative period and she was discharged with drain *in situ*. On the 15th post-operative period, she got admitted in view of accidental removal of the abdominal drain. Since abdominopelvic sonography revealed no significant collection in the abdominal cavity, she was managed with stoma bag around the drain site (Figure 3d), prophylactic intravenous antibiotics, appropriate nutritional support, and regular dressings. The patient got discharged after 2 weeks. She is on regular follow-up monthly and on the 10th month of follow-up, she is asymptomatic and has gained weight.

Case 4

A 72-year-old female presented with pain in the lower abdomen of 3 months duration. She did not have any other gastrointestinal symptoms. She was a known diabetic and hypertensive on regular medications. Per abdominal examination revealed a vague mass in the left lumbar region, with the plane being retroperitoneum. CT abdomen and pelvis showed a central hypodense lesion with partial enhancement and calcification displacing the kidney laterally (Figure 4).

Abdomen was explored with a left paramedical incision. By a retroperitoneal approach, descending colon was mobilized. Left ureter was identified and mobilized laterally. Tumor was found to be arising from the left sympathetic trunk displacing the aorta medially. Tumor was excised sparing the nerve trunks. Postoperatively, the patient developed abdominal distension. A diagnosis of paralytic colon was made, and colonoscopic decompression was done. The patient is asymptomatic and free of disease both clinically and radiologically after 1 year of follow-up.

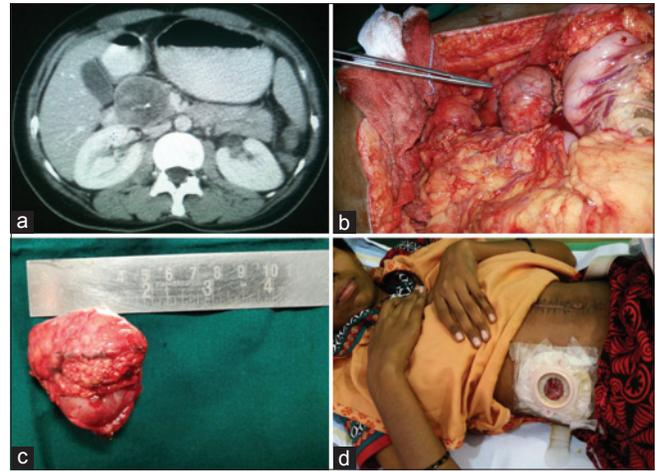


Figure 3: (a) A well-defined round heterogeneously enhancing lesion with areas of central calcification in the region of the head and uncinate process of pancreas. (b) A globular firm to hard mass measuring 4.5 cm x 3.5 cm x 3.2 cm in the region of head and uncinate process of pancreas abutting the second part of duodenum. (c) Excised tumor with a margin of pancreatic tissue. (d) Pancreatic fistula through the drain site managed with stoma bag

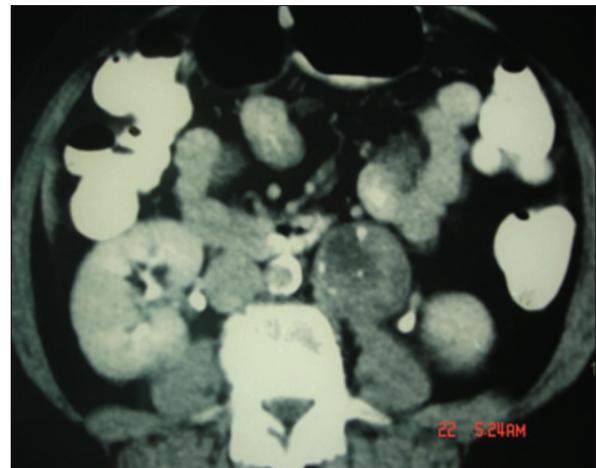


Figure 4: A central hypodense lesion with partial enhancement and calcification displacing the left kidney laterally

DISCUSSION

Schwannoma belongs to the benign peripheral nerve sheath tumors which also includes neurofibroma.¹ The neoplastic cells of both neurofibroma and schwannoma are closely related to the normal Schwann cells which are derived from the neural crest.² Schwannoma is less common compared to neurofibroma accounting for approximately 5% of all benign soft tissue tumors.³ Schwannomas are usually located in the head, neck, and flexor aspect of the extremities. They are rarely situated in mediastinum, pelvis and rectum. Up to 20% of these cases are associated with Neurofibromatosis Type 1.⁴

Retroperitoneal schwannomas are rare, and they account for 0.3-3.2% of all schwannomas.⁵ Most of the retroperitoneal tumors are considered malignant and retroperitoneal schwannomas mimic retroperitoneal sarcomas. Even though pancreas is richly supplied by both sympathetic and parasympathetic nerves, schwannomas arising from the nerves supplying the pancreas are extremely rare.⁶

Retroperitoneal tumors constitute a difficult management problem due to their anatomic location, late presentation and proximity to adjacent vital structures thus making resection difficult or even impossible. Retroperitoneal schwannoma often attains a large dimension due to the presence of loose areolar tissue in the retroperitoneum, with non-specific vague clinical symptoms leading to a delay in diagnosis. They usually arise in women between the ages of 20 and 50 years.⁷ Patients present with poorly localized pain and discomfort, accompanied by non-specific digestive disturbances.⁸ Atypical presentations include flank pain and hematuria, headache, varicose veins of lower extremities, secondary hypertension, and recurrent renal colic pain.⁹

Pancreatic schwannomas are usually diagnosed at the age ranging from 20 to 87 years (mean of 56 years) with equal sex distribution. In 40% of the cases, the tumor is located in the head of the pancreas followed by its body (20%). The size of the tumor ranges from 1 to 20 cm.¹⁰⁻¹² Schwannoma usually occurs as a solitary lesion in the majority of cases, but can occasionally be multiple when associated with von Recklinghausen's disease. Patients present with nonspecific symptoms, usually with upper abdominal pain and discomfort (60%). Recent reports have shown that in 70% of cases, it can be symptomatic.¹⁰ Other symptoms include nausea, vomiting, melena, abdominal mass, jaundice, and gastrointestinal bleeding.

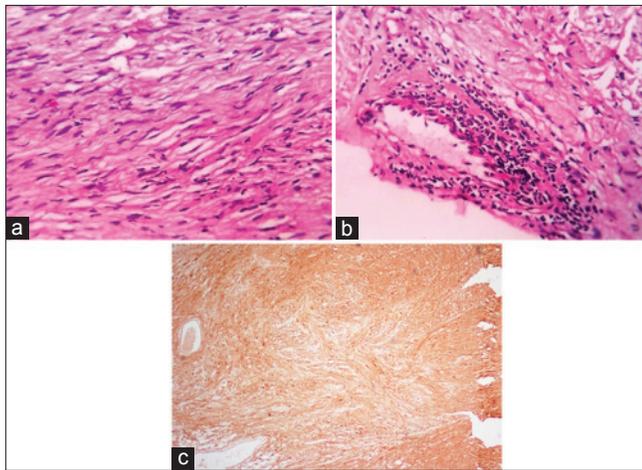


Figure 5: (a) Hypercellular (Antoni A) and hypocellular (Antoni B) areas. (b) Tumor cells strongly immunoreactive to S-100

Laboratory investigations will not provide any assistance for the diagnosis of pancreatic schwannomas.¹⁰⁻¹² Macroscopically, schwannomas are characteristically cystic, thin-walled, and hemorrhagic masses. However, solid and mixed tumors have also been reported. Cut section will show well-demarcated, encapsulated mass with or without myxomatous and hemorrhagic areas.^{10,11,13} Microscopically, there will be two characteristic components, a highly ordered cellular component (Antoni A areas) consisting of closely packed spindle cells arranged in palisading and interlacing fashions (Figure 5a), and a loose myxoid/hypocellular component with degenerative changes (Antoni B areas) (Figure 5b). Verocay bodies without mitotic figures can also be noted.²

Ancient schwannoma is a rare variant of benign peripheral nerve sheath tumor. Ackermann and Taylor coined the term "ancient schwannoma" in 1951. It morphologically resembles malignancy but is, in fact, a benign tumor. They are deep-seated and can attain large size. There will be less Antoni A areas and more hypocellular areas with areas of secondary degenerations such as hyalinization, calcification, necrosis, hemorrhage, cystic, and fatty degenerations. All these changes are believed to be due to the aging of the tumor, hence the term "ancient."¹⁴ Sometimes because of the presence of nuclear atypia and pleomorphism, such tumors are mistakenly diagnosed as malignant. In such cases, mitotic count will provide the benign nature of these tumors.¹⁵ Ogren *et al.* described the use of flow cytometry to assess DNA ploidy and thus, helps in distinguishing benign schwannomas from malignant schwannomas.¹⁶ Immunohistochemically, the tumors are strongly immunoreactive for S-100 protein (Figure 5c), vimentin and CD56, and negative for cytokeratin AE1/3, CD34, CD117 (c-kit), desmin, and smooth muscle myosin.¹⁷⁻¹⁹

CT of abdomen and pelvis usually show well-defined, round masses with multiple, low-attenuation, cystic necrotic areas. Antoni A areas (cellular component) in CT show inhomogeneous, hypodense, solid masses with contrast enhancement. Antoni B areas (loose myxoid) will be homogeneously cystic without significant contrast enhancement.¹³ Cystic changes occur more commonly in retroperitoneal schwannomas (66%) compared to other retroperitoneal tumors.²⁰

On magnetic resonance imaging (MRI), they appear as masses of low signal intensity on T1-weighted images and of high signal intensity on T2-weighted images.¹⁷ The signal intensity on T2-weighted images may differ depending on cell density. These findings are characteristic but not specific for schwannomas and have been reported to be present in only 57% of the cases.²¹ Hence, pre-operative diagnosis of retroperitoneal schwannomas is unusual.

Pre-operative radiological diagnoses as pancreatic cystic neoplasms,²² hepatic tumors,²³ ovarian tumors,²⁴ and psoas abscess²⁵ have been reported. Gadolinium enhanced MRI may provide enhancement of tissue inhomogeneities within the tumor. MRI is generally accepted as the imaging modality of choice for most soft tissue lesions but is incapable of distinguishing between benign and malignant tumors reliably.

Question will arise whether to perform pre-operative biopsy when the radiological investigations provide a suspicion of neoplasm. Making pre-operative histological diagnosis by fine-needle aspiration biopsy or core needle biopsy has been shown to be unnecessary. Fine-needle aspiration cytology (FNAC) from degenerated areas will provide cells with pleomorphism giving a false interpretation of malignancy. Such large tumors will have large engorged veins coursing over the surface or within the tumor substance and these tumors are very close to aorta and inferior vena cava. Hence performing FNAC can cause torrential hemorrhage, tumor seeding and can introduce infection.

It is advised to perform FNAC and core needle biopsy under CT guidance. Proponents argue that pre-operative histological diagnosis enables to plan the proper intervention. If the radiologically diagnosed asymptomatic lesion is benign, one may consider regular timely radiological follow-up, especially in elderly individuals and the exemption from surgery, which is associated with high risk of complications.

Wide surgical resection has been advocated as the treatment of choice in retroperitoneal schwannomas based on the belief that malignant transformation occurs very rarely (0.7-2.6%)²⁶ and that pre-operative histological confirmation of malignancy is not possible most of the times.²⁷ Because of the benign nature of most of the retroperitoneal schwannomas, some authors have recommended simple intralesional enucleation of the tumor²⁸ and laparoscopic piecemeal excision.²⁹ The proponents argue that because of the indolent nature of the tumor, local recurrence will take considerable time and the resection of involved viscera and neurovascular bundles to attain clear margin can be avoided, thus reducing the morbidity and mortality associated with the radical surgery. Opponents argue that the rate of local recurrence after enucleation ranges from 16% to 54%, whereas recurrence after resection with a wide surgical margin has been reported in only 11.7%.³⁰ Concern regarding the margin status arises when the histology reveals malignant transformation if the tumor had been excised in piecemeal fashion.

Management of pancreatic schwannomas remains to be controversial. Most of the pancreatic schwannomas are

benign and hence if the histopathological diagnosis is obtained during the surgery, local excision of these tumors is sufficient and safe. If the definitive histopathological diagnosis cannot be confirmed, or if the tumor is of malignant potential during surgery, radical resection of the pancreas is contemplated based on the region involved.¹⁰ Hence, intra-operative histopathological confirmation of the pancreatic schwannoma will become important to avoid morbidity and mortality associated with radical resection. In our case, based on the frozen section report, we deferred a radical surgery on the patient with pancreatic ancient schwannoma, avoiding major post-operative complications and hospital stay.

CONCLUSION

We have described 4 cases of retroperitoneal ancient schwannomas with varied ages and symptoms of presentations and the methodical approach to the diagnosis and expert management. The majority of the retroperitoneal schwannomas presented with vague symptoms and were diagnosed when they attained a large size. The pancreatic ancient schwannomas described here is unique because the ancient variety developing in such young age and in such a small tumor is very rare.

There will be a pre-operative diagnostic dilemma because there are no specific findings in the imaging studies and FNA may not be conclusive because sampling from the representative area is a mere chance. Resection of the tumor in toto is the treatment of choice for benign schwannomas and wide local excision in the case of malignant ones. Most of the retroperitoneal ancient schwannomas are paravertebral in a location with close proximity to iliac vessels, aorta, ureter and other vital structures. Hence, it is a challenge for the surgeons to have adequate margin during dissection.

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How to cite this article: Chetty YV, Sreevathsa MR, Koruth S, Krishnan S. Retroperitoneal Ancient Schwannoma: A Benign Tumor. *Int J Sci Stud* 2016;3(11):274-279.

Source of Support: Nil, **Conflict of Interest:** None declared.

Neurenteric Cyst of Posterior Mediastinum in an Infant: A Case Report

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Abstract

Neurenteric cysts are one of the rare congenital disorders that present within first 5 years. Neurenteric cysts are the enterogenous type of duplication cyst when associated with vertebral anomalies. These can be located anywhere in the body from intracranial to abdomen, but the posterior mediastinal neurenteric cysts are very rare, which presumably arise from misplaced epithelium of nasopharynx and intestinal tract. It is rare in incidence, with male predominance. Neurenteric cyst represents a failure of complete separation of the notochord from the foregut during embryogenesis. There are many types of the bronchopulmonary foregut malformations among which neurenteric cysts are the least common. The most common form consists of a simple epithelium resting on a delicate fibrovascular capsule. It is septate and has different varieties of epithelium (ciliated or non-ciliated, columnar, intestinal glands, pancreatic and salivary gland tissue) and a muscular wall with smooth mucosal lining. The treatment is complete resection of the cyst.

Key words: Infant, Neurenteric cyst, Posterior mediastinum

INTRODUCTION

Neurenteric cysts are rare congenital anomalies, with only about 35 cases reported in the literature.¹ Neurenteric cysts develop during the 3rd week of development due to the abnormal connection between the primitive ectoderm and endoderm. These cysts are the result of the failure of complete separation of the notochord from the foregut. It is assumed that a cyst lined with enteric and neural tissue is formed when the foregut becomes incorporated into the notochord tissue.^{2,3} Foregut duplication cysts are presently classified into three subtypes: (1) Enterogenous cysts (lined by intestinal epithelium), (2) Bronchogenic cysts (lined by respiratory epithelium), and (3) Neurenteric cysts (associated with apparent vertebral anomalies).

Neurenteric cyst can manifest in any age group (usually discovered during first 5 years of life) and can be found anywhere from intra-cranium to the abdomen, but many of the times they are located in the posterior mediastinum.^{2,3} Neurenteric cysts are usually associated with vertebral anomalies and hemivertebrae may also be included.⁴ Cervical and upper thoracic vertebrae are usually affected.

Neurenteric cyst can be diagnosed antenatally using ultrasound as early as 18 weeks gestation.^{2,3}

CASE REPORT

A 7-month-old female child with the history of a cough, fever, and left upper lobe pneumonic patch was referred to Krishna hospital for further management. The history revealed that a cough and fever were since last 2 months, for which she took treatment, symptoms subsided for few days and then recurred again. She also had dull pain in the front and back of the left chest. A clinical examination showed normal respiratory findings. Abdominal examination and spine were normal.

Access this article online



www.ijss-sn.com

Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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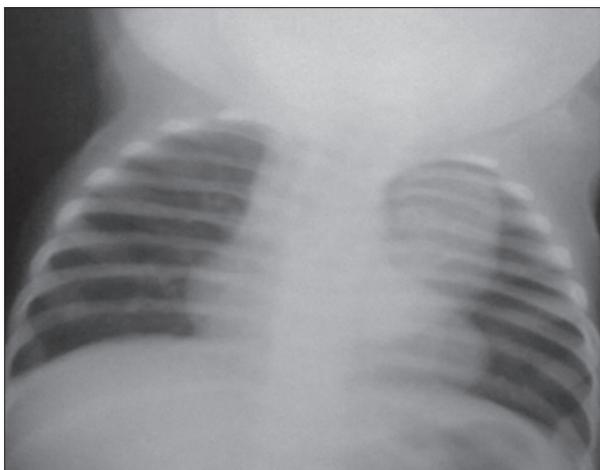


Figure 1: Posteroanterior roentgenogram of chest reveals a well-defined radio-opaque density with smooth sharp margins in the left hemithorax, paraspinal region with density less than that of heart as well as vertebral anomalies (hemivertebrae) with the adjacent vertebrae



Figure 3: Axial 5mm CT scan showing well defined cystic lesion with smooth sharp margins in the retroperitoneum on the left side anterior to left kidney and getting connected to L1 vertebral body

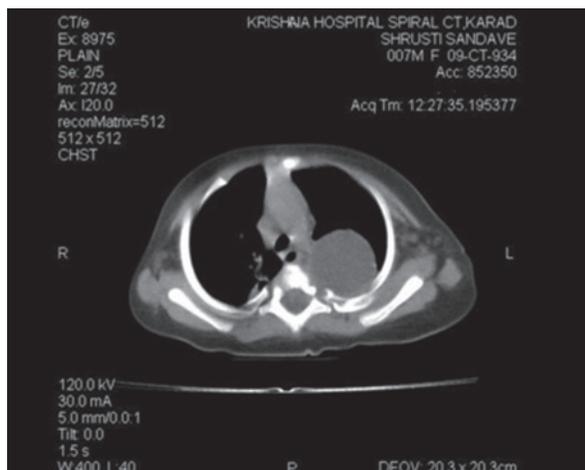


Figure 2: Axial 5 mm computed tomography scan showing well defined well-circumscribed hypodense (6-12 HU) cystic lesion in left hemithorax in posterior aspect in close proximity to vertebral body and posterior margin of rib, causing erosion of the rib



Figure 4: T2 weighted MRI showing well defined rounded hyperintense lesion with smooth, sharp and regular margins in the left paraspinal region extending from D2 – D7 vertebral bodies and getting attach to D3 – D5 vertebral bodies (which are hemivertebrae). Single septa present in the inferior aspect of the lesion

Chest radiograph showed a left posterior mediastinal mass, which was extrapulmonary (Figure 1). Contrast-enhanced computed tomography (CECT) (Figures 2 and 3) and magnetic resonance imaging (MRI) (Figures 4 and 5) confirmed the presence of a cystic mass (5 cm × 3 cm × 3 cm in diameter) extending from D2-D7 vertebral bodies and getting attached to D3-D5 vertebral bodies that are hemivertebrae.

The CT and MRI also revealed another cystic mass (4 cm × 2 cm × 2 cm in diameter) in front and above the left kidney, showing a connection to L1 vertebrae. Other investigations were within normal limits. Pre-operative diagnosis of the neurenteric cyst was being made and by left posterolateral thoracotomy, the cyst was excised. Histopathology confirmed the diagnosis of the neurenteric cyst.

DISCUSSION

Split notochord theory is the explanation for the neurenteric cysts.⁵ Neurenteric cysts can appear in any age group, but it is the first 5 years of life in which they are mostly seen. The failure of separation of the notochord from the foregut during the 3rd week of development gives rise to these posterior enteric remnants. 1842 was the year in which Roth first reported vertebral column attachment to an enteric cyst, but Mc Ritchie, Purves, and Saunders coined the term “neurenteric.”²⁶ The first case reported in 1934 by Pusser.

Neurenteric cysts can be either multiloculated or septate and may look similar to gastric, duodenal or intestinal mucosa. These cells are mostly Periodic acid–Schiff positive and can contain mucus and globules, with occasional squamous cell

metaplasia. Neurenteric cyst lined with gastric columnar epithelium can develop hemorrhage, ulceration or erosion. Neurenteric cyst is also susceptible to infection, perforation or rupture.

In the pediatric population, one-third of the patient with mediastinal cysts remains asymptomatic while two-third present with complains of the respiratory system. These cysts are usually benign, but due to their size they can cause compression of the structures within its vicinity.

Neurenteric cysts are associated with cervical and upper thoracic vertebral abnormalities, such as hemivertebrae, as noted in our case, anterior and posterior spina bifida, the absence of vertebrae, scoliosis, and diastematomyelia. The most common symptoms were difficulty in breathing, stridor or a persistent cough.^{4,7} Ganglion cells, lymphatic tissue, pancreatic tissue, salivary glands, or muscular tissue may be present in the cyst wall without serosa. The cartilaginous tissue is never present.⁸

A clinical trial of respiratory symptoms or distress, a chest radiograph demonstrating cervical or thoracic vertebral anomalies, and a posterior mediastinal cyst suggest neurenteric cyst. Neurenteric cyst can present with a vast spectrum of symptoms and can be life-threatening. When the gastric epithelium lines the cyst, hemorrhage, anemia, and pain can be the chief complaints. The majority of the children with these cyst presents with central nervous system symptoms such as back pain, sensory, or motor deficit or gait disturbances. A persistent cough and fever were the chief complaints of our case.

The radiological evaluation of the neurenteric cyst has evolved with advances in technology. Before MRI, CT metrizamide myelography has been the single best

diagnostic study in the diagnosis of the neurenteric cyst. CT and MRI both are very good in diagnosing the condition.

The surgery of these lesions is actually straight forward. If an asymptomatic or less symptomatic lesion is found out, elective excision is recommended unless operative risks are too high. The symptomatic lesion must undergo excision first as seen in our case. The treatment of choice remains complete excision of the cyst (Figures 6 and 7).^{8,9} Neurenteric cyst is a type of foregut duplication cyst.¹⁰

CONCLUSION

The aim of presenting this case is because of its rarity. Neurenteric cysts are one of the rare congenital disorders that present within first 5 years.¹¹ These are the enterogenous type of duplication cyst associated with vertebral anomalies. The intrathoracic cyst is within the

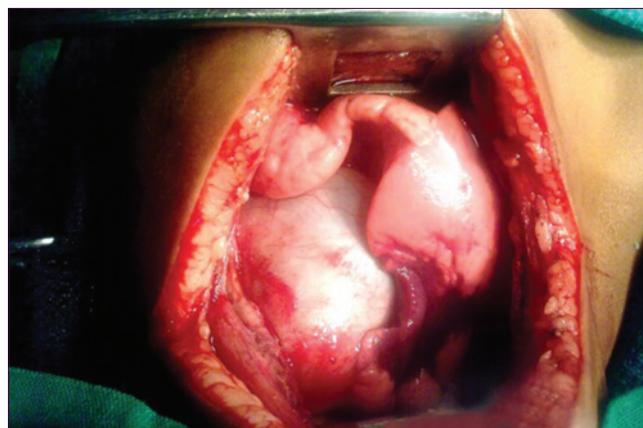


Figure 6: Gross photograph showing posterior mediastinal cystic mass displacing left lung anteriorly.



Figure 5: Flair MRI showing the lesion is getting suppressed indicating cystic nature of the lesion.

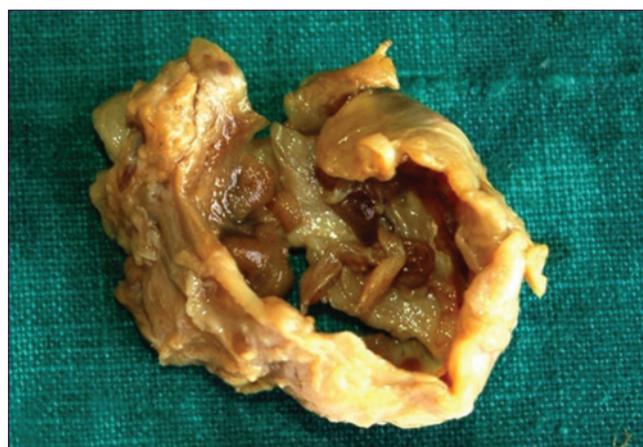


Figure 7: Gross specimen of cut opened cyst showing smooth internal surface

mediastinum, 90% posteriorly, as seen in our case and 60% of the cysts are seen superior to the carina. 66% of the cysts are seen on the right side.¹² Early and complete excision of the lesion is the treatment of choice.

ACKNOWLEDGMENT

We would like to thank Dr. A.Y, Kshirsagar, Professor of the Dept. of Surgery and Medical Director, for allowing us to publish this data. We are also thankful to Mrs. M.C. Deshingkar for her secretarial help.

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How to cite this article: Bagwan MR, Reddy SM, Pardeshi CZ, Panicker S, Kumar K. Neurenteric Cyst of Posterior Mediastinum in an Infant: A Case Report. *Int J Sci Stud* 2016;3(11):280-283.

Source of Support: Nil, **Conflict of Interest:** None declared.

Guillain-Barre Syndrome after General Anesthesia for Endoscopic Retrograde Cholangiopancreatography: A Case Report

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Abstract

Guillain-Barre syndrome (GBS) is a rare acute immune-mediated neuropathy. Predisposing factors being respiratory or gastrointestinal infection occurring 1-4 weeks before the symptoms. The knowledge about GBS occurring after surgery or anesthesia is limited by the number of cases reported. Anesthesia, especially the general anesthesia is known to cause delayed recovery, muscular weakness in susceptible individuals. Regional anesthesia leads to sensory and motor block to the area given. The symptoms of GBS, which is muscular weakness including respiratory muscles, tend to confuse the diagnosis after anesthesia. The etiology is not known. Here, we report a case of GBS occurring few hours after the general anesthesia given for the procedure of endoscopic retrograde cholangiopancreatography in the patient with 1 week history of gastrointestinal infection.

Key words: Demyelinating, Endoscopic, General anesthesia, Guillain-Barre syndrome, Respiratory insufficiency

INTRODUCTION

Guillain-Barre syndrome (GBS) is an acute immune-mediated demyelinating polyradiculoneuropathy disorder. If respiratory muscles are affected or the autonomic nervous system is involved, then life-threatening complications can occur. About 5% of the patients die, and more than 5% live with a disabling motor deficit.¹ Epidemiology suggests an annual incidence of 1.55/100,000 with incidence rate being more in patients older than 75 years than in patients lesser than 35 years. Male:female ratio being 1.5:1.² There are no incidence studies of GBS in the Indian population, but some case based studies are reported.^{3,4} It is associated mostly following respiratory tract infection (40%), gastrointestinal infection (20%).⁵ Death is documented in 4-15% of GBS patients⁶ and 12-20% of patients with GBS may require ventilator support.⁷

Surgery, though is a rare cause of GBS, certain mechanical factors such as compression, stretch, or contusion are attributable. There are case reports of GBS occurring on days 4, 7, 9, 11 after surgery.⁸⁻¹⁰ Furthermore, there are some case reports of GBS following epidural anesthesia.¹¹⁻¹³ GBS occurring after general anesthesia for hepatobiliary surgery is also reported.¹⁴

At this moment, reporting a case of GBS occurring in a patient who suffered from acute gastroenteritis (GE) for about a week and manifesting 5 h after the general anesthesia given for endoscopic retrograde cholangiopancreatography (ERCP) procedure.

CASE REPORT

A diabetic, hypertensive female patient aged 50 years came to our hospital referred from some other hospital for the procedure of ERCP. She was in the previous hospital for the complaints of diarrhea and abdominal pain for evaluation for the past 5 days. She was diagnosed to be having acute GE and common bile duct stone. Due to lack of ERCP facility in that hospital, she was referred here. She was on antibiotics and other supportive treatment for acute GE.

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Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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Pre-anesthetic evaluation of the patient was done. She was conscious, oriented, moving all four limbs and comfortable weighing 82 kg. Her blood pressure was 150/80 mm of Hg on tablet telmisartan 40 mg, pulse rate 84/ min, respiratory rate 14/min and oxygen saturation 98% on room air. She was on tablet metformin 500 mg BD. Auscultation of chest revealed no abnormality. Investigations hemoglobin (Hb) 10 g/ dl, total white blood cell count 12,000 cells/cu mm (N84 L12 E03 M01 B00), random blood sugar 136 mg/dl, HbA1C 7, urea 35 mg/dl, creatinine 1.1, electrocardiography, thyroid function tests, and chest X-ray were normal. Liver function test slightly deranged due the pathology. Nil by mouth and medication protocols followed.

18G cannula was in place in the upper limb and fluid on flow. The patient was made to lie in a prone position, head turned toward the gastroenterologist. Head and eyes well protected from pressure points. Mouth gag inserted, oxygen given through nasal cannula. Injection glycopyrrolate 0.2 mg, midazolam 1 mg, fentanyl 50 µg given. Injection propofol was given in titrated doses to induce sleep. The procedure started which lasted for 30 min. Anesthesia maintained with boluses of 10 mg of propofol and one more dose of 25 µg of fentanyl. Total propofol dose given was 90 mg and fentanyl 75 µg. 750 ml of crystalloids given intravenous (IV) during the procedure. The patient turned supine. Blood pressure was 130/80 mm of Hg, pulse rate 80/min, respiratory rate 12/min and oxygen saturation 100% on room air.

The patient shifted to the recovery room where her vitals remained stable. After 3 h of observation in recovery and being stable, she was shifted to the ward. There, after 2 h, she became tachypneic and then had difficulty in breathing. Oxygen saturation went down to 85% and was not responding to oral commands. She was immediately intubated with 7.5 internal diameters endotracheal tube, bilateral air entry confirmed and shifted to ICU with Ambu ventilation with 4 L of oxygen. In the ICU, she was connected to mechanical ventilator (synchronized intermittent mandatory ventilation mode - tidal volume 450 ml, rate 12/min, positive end-expiratory pressure 5, FiO₂ 40%). She tolerated the ventilator mode well with minimal sedation responding to oral commands. Blood pressure was 120/80 mm of Hg and pulse rate 76/min. Arterial blood gas sample taken on the ventilator with FiO₂ 40% was normal except for slight high PCO₂ of 50 which normalized after 2 h of ventilation. She also complained of inability to move her lower limbs and weakness in both upper limbs.

Neurological examination revealed her to be conscious, responding to oral commands and bilateral symmetrical ascending flaccid quadriparesis. Tone and power of the

both lower and upper limbs were diminished. Power in both upper and lower limbs was 2/5. All deep tendon reflexes were absent. Bilateral plantar responses nonreactive. Cranial nerve examination was normal. Pupils were bilaterally symmetrical and reacted to light. Sensory functions were normal. There was no abnormality in spine and cranium.

Routine blood investigations showed mild infection. Hb – 10 g%, total leukocyte count - 12000/cu mm (N84 L12 E03 M01 B00) platelet - 1, 65,000/cu mm. However, Blood, stool and urine culture showed no growth of the organism on day 5 of admission into ICU probably due to the use of antibiotics for acute GE. Serum electrolytes were within normal limits.

Cerebral spinal fluid (CSF) study revealed – protein – 150 mg/dl, mononuclear cells - 5/cu mm, glucose - 75 mg/dl with plasma glucose - 95 mg/dl. CSF study showed increased number of proteins with few mononuclear cells (albuminocytological disassociation). Hence, a diagnosis of GBS was done. Nerve conduction studies not done due to non-availability.

Immediately, treatment with IV immunoglobulin was initiated and given as a total dose of 400 mg/kg body weight/day for 5 days. Simultaneously respiratory therapy, physiotherapy, nutritional care, postural support, deep vein thrombosis prophylaxis were given. Measures to prevent bed sores undertaken.

Gradually with treatment, power and tone of both upper limb and lower limb improved. Weaning trials from the ventilator carried out, and she was out of it after 2 weeks of support. The patient shifted to the ward from ICU and then discharged.

After 30 days, she came for follow-up while her recovery was satisfactory and was advised to escalate her exercising capabilities.

DISCUSSION

GBS is the one of the common causes of acute polyradiculoneuropathy in adults. It has slight predominance in males and in older individuals. The weakness starts in the lower extremities, and over the course of hours or days, it ascends to the arm, the respiratory and the facial muscles. Most of the patients have a history of upper respiratory tract or gastrointestinal system infections in the 1-4 weeks before the symptoms.¹⁵ GBS patients have preceding bacterial enteritis caused by *Campylobacter jejuni*.¹⁶ Our patient was suffering from acute GE for 1 week being treated with antibiotics. Stool cultures done in the 2nd week were, however, negative for any organisms.

The occurrence of GBS after surgical operations and anesthesia are increasingly debated in recent times.⁸⁻¹⁴ Our patient who was otherwise normal except for the history of gastrointestinal infection manifested symptoms of GBS 5 h after the general anesthesia given to her for the procedure of ERCP.

Anesthetic agents are often known to cause prolonged muscle weakness, but here general anesthesia was given in the forms of propofol, fentanyl, and midazolam and none of these are reported for such weakness. Muscle relaxants were not at all used.

Electrolyte imbalance to cause muscle weakness cannot be considered as the patient's higher functions and serum electrolytes level were normal. History of prolonged use of steroid was negative, which may cause the same clinical picture.¹⁷

One of the variants of GBS is AIDP (acute inflammatory demyelinating Polyradiculopathy) involving the cranial nerves especially 3rd and 7th leading to ptosis, facial nerve palsy and pupillary dysfunction. The patient did not have any cranial nerve involvement as per the examination.

The pathophysiology of post-operative GBS is not clear yet. The stress associated with the surgery or anesthesia triggers the immune response leading to inflammatory macrophage infiltration into the nerve.¹⁸ Without clear evidence yet, it is hypothesized that inflammation is induced by ischemia, general trauma after surgery which causes humoral and cytokines response by the immune system.¹⁹ The calculated Relative risk of GBS within 6 weeks of surgery is 13.1 times greater than the incidence in study population.²⁰

In our patient, gastrointestinal infection receiving treatment added with surgery and anesthesia had aggravated and hastened the onset of GBS symptoms. Fortunately, our patient was saved with timely diagnosis and treatment.

CONCLUSION

The symptom of GBS, which is muscular weakness starting from lower limbs, ascending to upper limbs and respiratory

muscles leading to respiratory insufficiency, confuse the scenario, especially after anesthesia. Timely diagnosis and intervention is important in improving the patient's condition. Although the incidence of GBS is rare, it has to be kept in mind in the presence of relevant predisposing factors and symptoms.

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How to cite this article: Smitha KS, Patil M, Babu AS. Guillain-Barre Syndrome after General Anesthesia for Endoscopic Retrograde Cholangiopancreatography: A Case Report. *Int J Sci Stud* 2016;3(11):284-286.

Source of Support: Nil, **Conflict of Interest:** None declared.

Fallopian Tube Prolapse: An Unusual Complication of Surgical Drainage Site

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Abstract

The fallopian tube prolapse after hysterectomy is a rare occurrence. Cases of prolapse of the fallopian tube into the vaginal vault after vaginal hysterectomy have been reported. The prolapse of the fallopian tube via the surgical drainage site is a very rare occurrence. Surgical drains have been used in clinical practice for a long time, but their use is not without complication. A 40-year-old multigravida was admitted with grade 3 abruptio placenta. Lower segment caesarean section was done and subsequently proceeded with subtotal hysterectomy in view of the atonic uterus not responding to conservative medical and surgical measures. The drainage tube was removed on the 3rd post-operative day and prolapsed reddish fallopian tube was noticed at the drain site. By presenting this case report, we aim to reduce such complications in future. Drains are used to drain body fluids in certain circumstances but do not prevent infection or promote wound healing. Drainage tubes are not a substitute to a good surgical technique.

Key words: Fallopian tube prolapse, herniation, drainage site

INTRODUCTION

Drains inserted after surgery to drain accumulated fluid content sometimes become the focus of infection, such as blood and pus. They do not promote wound healing or prevent infection. In current clinical practice, their use is restricted by good surgical techniques and confidence of surgeons, but their use is unavoidable in certain clinical situations. The surgical drain use is associated with complications such as hemorrhage, infection, tissue damage, pain, blockage and herniation of viscera.¹

CASE REPORT

A 40-year-old G₆P₅L₅ referred from a Taluk headquarter hospital to government medical college hospital as a

case of 8 months amenorrhea with abruptio placenta and intrauterine fetal death. Under general anesthesia, emergency Lower segment Caesarean section was proceeded and a fresh, dead female baby was delivered. Active management of the third stage of labor followed, uterus was found to be atonic. All uterotonics were given. Conservative surgical measures were also followed. In spite of these measures uterus was flabby and hence subtotal hysterectomy was done. Both fallopian tubes were unduly long - 15 cm. In view of prolonged surgery (2 h and 30 min), a drain was inserted through a separate incision in right iliac fossa and placed intraperitoneally in the pouch of Douglas. Abdomen was closed after securing perfect hemostasis. 6 units of fresh frozen plasma and 4 units of whole blood were transfused intraoperatively. On the 3rd post-operative day, drainage tube removed. At the drain tube site, there was a prolapse of a reddish tissue, which was suspected to be omental prolapse (Figure 1). Surgeon's opinion was suspected small bowel prolapse and laparotomy was advised. Laparotomy proceeded via the previous suprapubic transverse incision. The prolapsed tissue via the drainage tube site was reduced and traced and was found to be the fimbrial portion of the oedematous right fallopian tube (Figure 2). Since the tube was congested and oedematous,

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Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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right salpingectomy was done. Left tube was found to be normal and healthy. Omentum, small bowel, and large bowel were inspected and found to be intact and normal. Post-operative period was uneventful. The patient was discharged in good condition. The excised right fallopian tube was sent for histopathological examination and was reported as the fallopian tube with submucosal edema, congestion, and features of acute inflammation (Figure 3).



Figure 1: Right fallopian tube prolapsed, congested and oedematous like a small bowel



Figure 2: Fimbrial portion of congested and inflamed right fallopian tube (intra-operative)

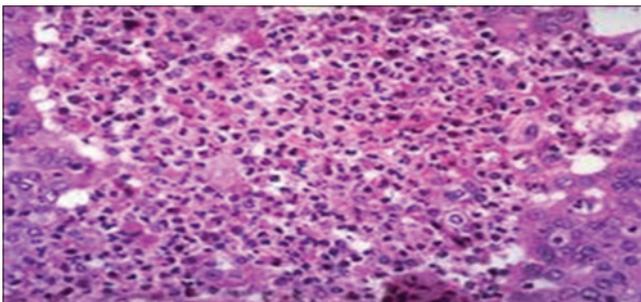


Figure 3: Histopathological examination with inflammatory changes

DISCUSSION

Drains are not used routinely, and their use is restricted in unavoidable circumstances only. Depending on the amount of collection patient may have the drain in place for 1 day to weeks. Patency of tube must be assessed and maintained frequently. Cavities and sacs in the body are potential fluid collection areas. Drains used following abdominal surgeries are closed one, consists of tube draining into a bottle or a bag. Complications due to drains in the post-operative period are mainly due to poor drain selection, poor drain placement, and inadequate post-operative management. Indications for surgical drains may be therapeutic (to evacuate existing collection of fluid) or prophylactic (to prevent the collection of fluid). In literature, there are reports of herniation of intestine,² appendix³ and omentum⁴ through the surgical drainage site but fewer cases of the fallopian tube prolapse have been reported. The incidence of prolapsed tube via port following laparoscopic surgeries is 65-2.5%.⁵ We have used prophylactic drain in our patient, a no. 32 closed penrose drain with openings, kept in pouch of Douglas. Large studies revealed that prophylactic drains should be minimized in uncomplicated surgeries.⁶ It has been reported that herniation of viscera increases with increase in port size more than 10 mm. Factors which increase intra-abdominal pressure such as coughing, straining, prolonged surgery poor nutrition, infection, obesity, and steroid use may cause poor wound healing and herniation.⁷ In our patient, prolonged surgery may be the cause for the prolapse of the fallopian tube. In our case, the length of the fallopian tube was long - 15 cm as against the usual 10 cm. The wrong technique of insertion and removal is another causative factor.

CONCLUSION

Drains are not a substitute for good surgical techniques. Although a large number of cases of herniation of omentum and intestine have been reported, herniation of fallopian tube is uncommon. Prevention of tubal prolapse can be achieved by suturing the adnexae high in the pelvis at abdominal hysterectomy and by the proper closure of the pelvic peritoneum. In this particular case, the unduly long fallopian tube and prolonged surgery could have been the causes for herniation.

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Poovathi and Kalarani: Fallopian Tube Prolapse

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How to cite this article: Poovathi M, Kalarani E. Fallopian Tube Prolapse: An Unusual Complication of Surgical Drainage Site. *Int J Sci Stud* 2016;3(11):287-289.

Source of Support: Nil, **Conflict of Interest:** None declared.

Angioleiomyoma of Broad Ligament: A Rare Variant of Leiomyoma

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Abstract

Angioleiomyoma, which is synonymous with vascular leiomyoma, is an extremely rare and uncommon variant of leiomyoma which is a benign mesenchymal tumor. It originates from the smooth muscle cells and contains numerous thick-walled blood vessels. Although the common location is in the skin of the lower extremities, a few cases of uterine leiomyoma have also been reported in middle-aged women.¹ Patients with uterine leiomyomas usually present with abdominal pain, menorrhagia, and abdominal mass. Angioleiomyoma in the broad ligament is extremely rare. We present one such rare case of broad ligament angioleiomyoma occurring in a 40-year-old female patient.

Key words: Angioleiomyoma, Benign, Broad ligament mesenchymal tumor

INTRODUCTION

Angioleiomyoma or vascular leiomyoma is a benign mesenchymal tumor of smooth muscle cell origin. It is most often seen in the subcutis of the lower extremities. Although a few cases of uterine angioleiomyoma have been reported in literature, broad ligament angioleiomyomas are extremely rare.¹ Keeping this in view, a rare case of broad ligament angioleiomyoma is reported here. Angioleiomyomas are commonly seen in the 4th and 5th decade of life. Uterine angioleiomyomas usually present with menorrhagia due to local dysregulation of uterine vascular structures, the presence of venous plexuses and elaboration of certain growth factors by tumor cells.² They are benign mesenchymal tumors composed of interlacing bundles of smooth muscle cells with interspersed thick blood vessels. They have to be differentiated from other closely related mesenchymal tumors with proliferated vascular channels.

CASE REPORT

A 40-year-old female patient presented with a mass per abdomen of 6 months' duration. A vaginal examination revealed a firm mass measuring 6/5 cm in the left fornix. A speculum examination revealed no abnormalities.

Ultrasonography revealed a homogenous solid mass in the left lower abdominal region. The mass was hypodense in attenuation and showed mottled heterogenous enhancement.

A provisional clinic-radiological diagnosis of broad ligament fibroid was offered.

The patient underwent total hysterectomy with bilateral salpingo-oophorectomy, and the specimen was submitted for histopathological examination.

Gross Examination Findings

Uterocervix with bilateral adnexae and a mass in the left sided broad ligament was received (Figure 1). Cut section of uterocervix showed an endometrial thickness of 0.2 cm. The broad ligament mass was measured 10 cm × 6 cm × 5 cm. A external surface was smooth with congested and dilated blood vessels. Cut surface was gray-white, firm with whorling patterns. Areas of hemorrhage and multiple

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www.ijss-sn.com

Month of Submission : 12-2015
 Month of Peer Review : 01-2016
 Month of Acceptance : 01-2016
 Month of Publishing : 02-2016

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tiny cysts were shown in Figure 2. Bilateral adnexae were normal in appearance.

Microscopy

Uterocervix and bilateral adnexae showed no significant abnormalities. The broad ligament mass showed a benign mesenchymal tumor with prominent vascular channels lined by flattened endothelium and surrounded by loosely arranged interlacing fascicles and bundles of spindle cells with oval and bland nuclei (Figure 3).

Final Diagnosis

Angioleiomyoma

DISCUSSION

Angioleiomyoma a benign mesenchymal neoplasm composed of smooth muscle cells and thick-walled blood vessels. Although commonly seen in the skin of extremities, it is uncommon in the uterus.¹ Broad ligament angioleiomyoma is a more uncommon than the uterine counterpart.³ The patients with uterine angioleiomyomas usually present with abdominal pain which is believed to be related to ischemia due to vascular contraction.⁴ However, our patient presented with a mass per abdomen. On gross examination, the tumor exhibits a whorling pattern and a multi cystic appearance due to the dilated vascular channels as in our case. Histologically, angioleiomyomas are divided into three subtypes namely, capillary, cavernous and mixed. Our case belonged to the capillary subtype.⁵ Unlike uterine leiomyomas which are presumed to arise from parenchymal myometrial cells, angioleiomyomas arise from the smooth muscle cells of the vessel walls.⁶ Differential diagnosis includes angiofibroma, angiomyolipoma, angiomyofibrosarcoma and perivascular epithelioid tumors. Duhig and Ayer in their study observed that there was no recurrence following excision in any of their cases.⁷ Other complications like spontaneous rupture of the tumor, consump coagulopathy, and pseudo-Meigs syndrome have been reported.⁸⁻¹⁰ Our patient had an uneventful post-operative course and recovery on her follow-up after 6 months.

CONCLUSION

Angioleiomyoma, a rare variant of uterine leiomyoma is a benign mesenchymal tumor amenable to surgical excision. It has to be differentiated from the other mesenchymal neoplasms with prominent vascular components.



Figure 1: Uterocervix with bilateral adnexae and a mass in the left sided broad ligament



Figure 2: Cut surface of broad ligament mass - Gray-white, firm with whorling patterns, areas of hemorrhage and multiple tiny cysts

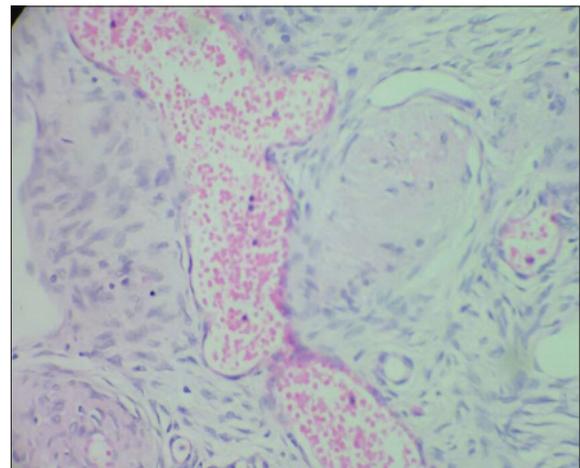


Figure 3: Benign mesenchymal tumor with prominent vascular channels lined by flattened endothelium surrounded by swirls of spindle cells having oval and bland nuclei

ACKNOWLEDGMENT

We wish to acknowledge Dr. M G Shivaramu, Principal Adichunchanagiri Institute of Medical Sciences for his constant support and encouragement.

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How to cite this article: Hemalatha AL, Nanjundaswamy DN, Sahni S, Kumari A. Angioleiomyoma of Broad Ligament: A Rare Variant of Leiomyoma. *Int J Sci Stud* 2016;3(11):290-292.

Source of Support: Nil, **Conflict of Interest:** None declared.

Meckel's Diverticulum as Bleeding Per Rectum in Adult Male: A Rare Presentation

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Abstract

Meckel's diverticulum results from an incomplete closure of the vitello-intestinal duct and generally arises from the antimesenteric border of the ileum. It is present in 2% of the population, 2 inches long and 2 feet proximal from the ileocecal junction. Meckel's diverticulum was named after a German anatomist in 1809. A 24-year-old male presented with a history of bleeding per rectum for the last 15 days to Goyal Surgical, Lapro, and Endoscopic Research Center, Kota, Rajasthan, India. The bleeding was sudden in onset. Each episode had around 250-300 ml of blood loss. It was bright red in color mixed with stools initially and later with clots. No symptom of vomiting in blood, fever, loose stool, history of abdominal trauma, no history of analgesic or any other drugs taken. No previous history of such bleeding. The patient had pallor and was in shock. Resection of Meckel's diverticulum and part of the ileum was done with end-to-end anastomosis. The patient had uneventful recovery.

Key words: Bleeding per rectum, Meckel's diverticulum, Vitello-intestinal duct

INTRODUCTION

Meckel's diverticulum results from an incomplete closure of the vitello-intestinal (omphalo-mesenteric duct).^{1,2} It arises from the antimesenteric border of the ileum. It is present in 2% of the population, 2 inches long and 2 feet proximal from the ileocecal valve.³ Meckel's diverticulum was named after a German anatomist in 1809. Some time it may be asymptomatic and found as incidental finding in cadaveric dissection. Common complications due to Meckel's diverticulum are inflammation, intestinal obstruction, intussusception, hernia, torsion, umbilical sinus or fistula, neoplasm and hemorrhage.⁴⁻¹¹

Meckel's diverticulum is often overlooked as a possible cause of lower gastrointestinal (GI) bleed in adults.^{3,4,5,9} Painless GI bleed is a common symptom of Meckel's diverticulum in children, and it is relatively rare in adults.^{3,9}

Hemorrhage from a Meckel's diverticulum is a very rare in the adult age group.^{4,5,9} The bleeding is almost always associated with peptic ulceration from the heterotopic gastric mucosa located within the diverticulum.⁷ The hemorrhage can be slow and occult or massive. Mucosa is found in almost 100% of patients with GI bleeding due to Meckel's diverticulum.³ We report a rare case of Meckel's diverticulum presenting as massive bleeding per rectum in an adult male.

CASE REPORT

A 24-year-old male presented with history of bleeding per rectum for the last 15 days to Goyal Surgery, Endoscopic and Research Medical Center, Kota, Rajasthan, India. The bleeding was sudden in onset. Each episode had around 250-300 ml of blood loss. It was bright red in color mixed with stools initially and later with clots. No symptom of blood in vomiting, fever, loose stool, history of abdominal trauma, intake of analgesic or any other drugs in the last few days.^{5,12} No previous history of such bleeding or bleeding disorder.

On general examination, he had pallor, with a pulse of 124/min, respiratory rate of 26/min and blood pressure of 90/60 mmHg at admission.^{4,5,10,11}

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www.ijss-sn.com

Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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His abdomen was soft with mild tenderness in the umbilical region. No mass was palpable in the abdomen. Per rectal and proctoscopy were normal. All investigation was within normal limit.

In view of hemodynamic instability, he was admitted to the ICU and resuscitation done. Investigations were done. Few hours later, the patient passed about 200-250 ml of blood mixed with clots per rectally. An urgent colonoscopy was done to identify the cause of the bleeding as his upper GI endoscopy was normal. Colonoscopy revealed active GI bleeding proximal to the ileocecal junction with fresh blood and clots in the colon.

His hemoglobin was 5 g%, total count 8000; platelets 145,000, all the other investigation were with normal limit. Five units were transfused and patient taken for emergency exploratory laparotomy.

On exploration of abdomen, the entire jejunum was collapsed, and distal ileum was distended with blood in it. Enterostomy was done proximal to ileocecal junction and endoscope passed proximally to see the site of bleeding. There was no external finding except Meckel's diverticulum found on the external surface of gut. Active bleeding about 2 inches proximal to ileocecal junction at Meckel's diverticulum site (Figure 1) was seen. We confirmed that Meckel's diverticulum was the source of the bleed. Resection of Meckel's diverticulum and part of the ileum was done with end-to-end anastomosis. The patient recovered uneventfully. He was discharged on 10 post-operative days after removing the sutures.

Histopathology revealed heterotropic gastric mucosa in Meckel's diverticulum (Figure 2).

DISCUSSION

The anatomic variant was initially identified by Fabricius Hildanus in 1598; however, Johann Meckel was the first to publish a detailed description of this not uncommon finding.¹ Meckel's diverticulum results from an incomplete closure of the vitello-intestinal duct (Omphalomesenteric duct) and arises from the antimesenteric border of the ileum.² It is present in 2% of the population, 2 inches long and 2 feet from the ileocecal valve.² Meckel's diverticulum is often overlooked as a possible cause of lower GI hemorrhage in adults.¹⁰⁻¹² Hemorrhage from a Meckel's diverticulum is very rare in the adult age group.^{10,11} The hemorrhage can be slow and occult or massive. Gastric mucosa is found in almost 100% of patients with GI bleeding due to Meckel's diverticulum.⁷

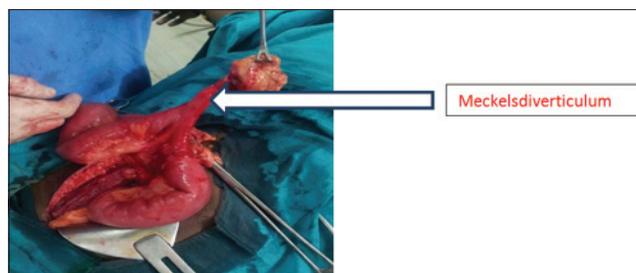


Figure 1: Resected specimen showing Meckel's diverticulum

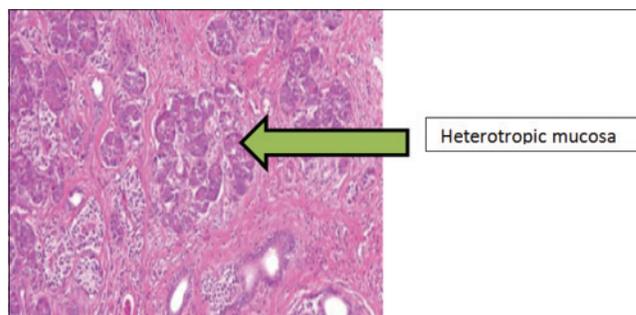


Figure 2: Heterotropic mucosa

Meckel's diverticula are lined with heterotropic mucosa in up to 60% of cases with 62% with gastric mucosa, 6% pancreatic, 2% jejunal, 2% Brunner's glands, 5% have both gastric and pancreatic and 2% have both gastric and duodenal.^{8,11} Tc-99m pertechnetate scanning is known to be the most useful diagnostic method for the diagnosis of Meckel's diverticulum, with heterotropic gastric mucosa with diagnostic accuracy in more than 90% in children and 50-65% in adults.¹³ This, however, cannot be done in emergency situations, as in this case. This was emergency case, so Tc-99m could not be performed. Upper GI endoscopy cannot diagnose the bleeding from Meckel's diverticulum. Colonoscopy will show only bleeding until ileocecal junction.

In this case, after laparotomy scope was passed through enterostomy proximal to ileocecal junction and directed proximally to see the site of bleeding. Active bleeding was seen at Meckel's diverticulum mucosa. Surgical resection of Meckel's diverticulum with part of ileum is the treatment of choice for symptomatic Meckel's diverticulum.¹²

CONCLUSION

Massive bleeding from Meckel's diverticulum is rare in adult patients. Possibility of Meckel's diverticulum should be kept in mind. Resection of Meckel's diverticulum and part of the ileum is the treatment of choice.

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How to cite this article: Rathore KB, Masih WF, Goyal SK. Meckel's Diverticulum as Bleeding Per Rectum in Adult Male: A Rare Presentation. *Int J Sci Stud* 2016;3(11):293-295.

Source of Support: Nil, **Conflict of Interest:** None declared.

Chondroid Syringoma: A Rare Case Series of Cutaneous Adnexal Neoplasm

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Abstract

Chondroid syringomas (CSs) are rare, mixed tumors of the skin arising from the eccrine sweat glands with tumor differentiation in the epithelial and mesenchymal tissues. The most common sites are head and neck, although they may be also found in the axilla, trunk, limbs, and genitalia. It is more frequent in male adults and is usually benign. It is treated surgically and its diagnosis is histological. It can be classified as eccrine and apocrine according to its pathological characteristics. The incidence of CS is <0.01% of all primary skin tumors. Malignant CSs are rare. We report four cases of CSs occurring at different sites over a period of 2-year.

Key words: Benign, Chondroid syringoma, Eccrine glands, Histology, Neoplasms

INTRODUCTION

A chondroid syringoma (CS), also known as mixed tumors of the skin, are composed of both epithelial and mesenchymal components. Lesions are typically located on head and neck, and are non-ulcerating, slow growing, subcutaneous, or dermal nodules. Incidence of CS has been reported as <0.01% of primary tumors of the skin.¹ CS usually affects middle-aged or older male patients. Headington divided CSs into apocrine and eccrine variants based on histological differences in the luminal morphology, but there remains debate as to their exact origin. The term "CS" was introduced by Hirsch and Helwig in 1961. They proposed the following microscopic diagnostic criteria: (a) Nests of cuboidal or polygonal cells; (b) intercommunicating tubuloalveolar structures lined with two or more rows of cuboidal cells; (c) ductal structures composed of one or two rows of cuboidal cells; (d) occasional keratinous cysts; and (e) a matrix of varying composition in hematoxylin and

eosin stain.² On samples from fine-needle aspiration biopsy, there is a usually mesenchymal tissue with a chondroid appearance and an epithelial component. Diagnosis of CS is mainly histological. The treatment of choice for CS is a wide surgical excision.

CASE REPORTS

Case 1

A 40-year-old male presented with a subcutaneous gradually increasing swelling measuring 2 cm × 2 cm over right cheek from last 2 years. Fine-needle aspiration cytology (FNAC) of the swelling revealed benign adnexal neoplasm. Histopathology revealed a nodular lesion with differentiation toward the adnexal ductal epithelium with chondromyxoid and adipocytic differentiation in the stroma (Figure 1).

Case 2

A 15-year-old male presented with swelling over bilateral foot. One of the swellings was 3 cm × 2.5 cm from last 3 months and the other swelling was 1.5 cm × 1 cm presented since last 1½ months. FNAC of lesion was not done. Grossly both the lesions were well encapsulated and gray-brown with no areas of hemorrhage and necrosis. After excision, both the lesions showed similar histology (Figure 2).

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www.ijss-sn.com

Month of Submission : 12-2015

Month of Peer Review : 01-2016

Month of Acceptance : 01-2016

Month of Publishing : 02-2016

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Case 3

A 55-year-old female presented with a swelling measuring 6 cm × 3 cm over left arm. The swelling was gradually increasing from last 1.5 months and was clinically suspicious of some infective pathology. FNAC showed the presence of mesenchymal tissue with a chondroid appearance and an epithelial component and was reported as benign neoplasm. On microscopy, similar histology was noted.

Case 4

A 48-year-old male presented with a left thigh swelling of size 4 cm × 3 cm from last 6 months. FNAC of the lesion was inconclusive. After excision, the lesion showed similar histology (Figures 3 and 4).

DISCUSSION

The CS is a rarely mixed tumor of sweat gland origin that has both a benign and malignant form.^{3,4} In 1961, Headington divided CS into two groups, including apocrine type and eccrine type, based on their histopathological

appearance.⁵ CSs share similarities with pleomorphic adenomas, which are mixed tumors arising from the salivary gland.⁶ In contrast to pleomorphic adenomas, CSs are thought to arise from sweat glands.

CSs most commonly occur in the head and neck and usually present with solitary, solid, painless, non-ulcerative, subcutaneous, or intracutaneous slow growing nodule.^{7,8} However, Sungur *et al.*, reported a benign case where rapid growth, ulceration, and necrosis was evident at tumor site.⁹ Less commonly, this tumor can develop on the scalp, eyelid, hand, foot, forehead, axillary region, abdomen, penis, vulva, and scrotum.¹⁰⁻¹²

Radiological features of CS are not as suggestive as the histological findings. The MRI features are non-specific, but can accurately depict the anatomic extent and identify tissue of origin, depth of invasion and relation to adjacent structures, such as muscles and bones.¹³ Treatment of choice is excision of the tumor.

CS is a benign tumor. However, rare cases of malignant CS have been reported. These malignant forms occur more commonly in younger female patients and have a predilection for occurring on the trunk or extremities.^{4,9}



Figure 1: Subcutaneous swelling over cheek



Figure 2: Bilateral swelling over foot

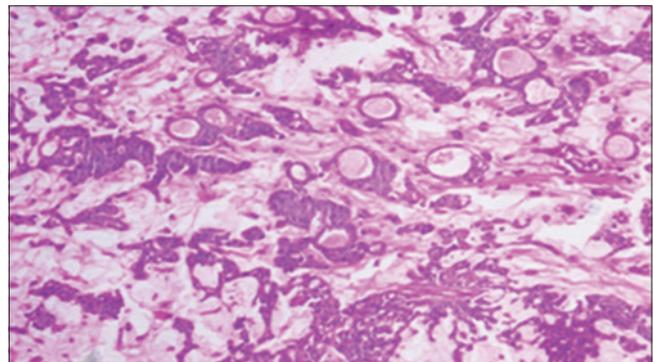


Figure 3: Photomicrograph of H and E stained section showing chondromyxoid matrix and tubular ducts (x200)

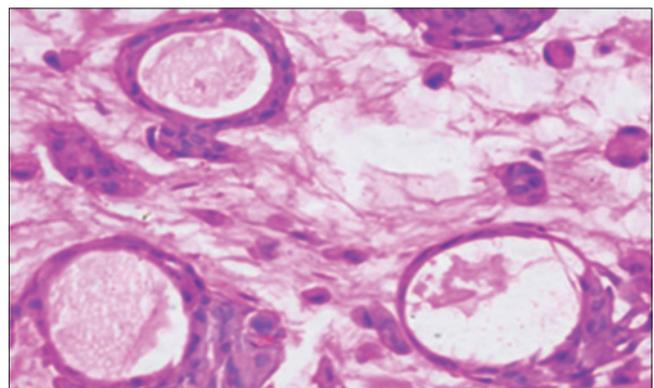


Figure 4: Photomicrograph of H and E stained section showing tubular ducts lined by single row of cuboidal cells

These tumors often are larger than 3 cm and are locally invasive. Histological findings such as cytologic atypia, infiltrative margins, satellite tumor nodules, tumor necrosis, and involvement of deep structures are considered as signs of malignant transformation.¹⁴ Close follow-up of these tumors is recommended because of the risk of malignancy and recurrence.

CONCLUSION

The CS is a rare subcutaneous tumor composed of mesenchymal and sweat gland elements that are usually found in the head and neck. This tumor is most often benign and is usually seen in men, however, malignant forms do occur. Excision is the treatment of choice, thereby making early identification advantageous. Importantly, the histology does not always predict the clinical behavior of the tumor, and benign-appearing lesions have been known to metastasize.

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How to cite this article: Goel S, Bairwa S, Sharma M, Kanwat P. Chondroid Syringoma: A Rare Case Series of Cutaneous Adnexal Neoplasm. *Int J Sci Stud* 2016;3(11):296-298.

Source of Support: Nil, **Conflict of Interest:** None declared.

Management of Ruptured Hepatic Subcapsular Hematoma in Hemolysis, Elevated Liver Enzymes, Low Platelets Syndrome: A Case Report

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Abstract

Regular antenatal checkup and early detection of hypertension can lead to better maternal and perinatal outcome. Surgeons as well as obstetrician have to be vigilant to prevent rare complications like subcapsular hematoma. Every patient of gestational hypertension being operated should also undergo examination of liver to preclude these complications in future. 30-year-old female admitted in Government Medical College, Nagpur as a case of G3P0A2 at 34 weeks of gestation with impending eclampsia with severe intrauterine growth restriction with severe oligohydramnios. An emergency cesarean section was performed. The patient went in shock 1½ h of the cesarean section so she was explored for hemoperitoneum. There was subcapsular liver hematoma with rupture intraoperatively. A external compression was done and drains were kept. Postoperatively, patient was managed conservatively with blood and blood products. The patient was discharged after 5 weeks of hospital stay in stable condition.

Key words: Hematoma, Hepatic subcapsular, Operative management, Rupture

INTRODUCTION

The hemolysis, elevated liver enzymes, low platelets (HELLP) syndrome is associated with preeclampsia. Subcapsular liver hematoma has been reported in <2% of pregnancies complicated by HELLP syndrome. Subcapsular liver hematoma may result in hepatic rupture. The incidence of subcapsular liver hematoma with rupture in pregnancies varies from 1/40000 to 1/250000. Moreover, this significantly increases both maternal and perinatal morbidity and mortality. In this case, we report a subcapsular liver hematoma managed by both operative and conservative measures.

CASE REPORT

A 30-year-old female referred to Government Medical College and Hospital, Nagpur, on 4th August 2015 as a case of gravida 3 abortion 2 at 34 weeks gestation with impending eclampsia with severe intrauterine growth restriction and severe oligohydramnios. An emergency cesarean section was performed in view of fetal distress and delivered a female child of 1.7 kg at 12.47 p.m. Intra-operative findings were hemorrhagic peritoneal fluid of around 100 cc and liquor was thick meconium. The patient was shifted to post-operative ward at around 2.00 p.m. Laboratory investigations were as follows¹:

On 4.8.15 (on admission)
 Hemoglobin (Hb): 9.4 g% (12.00 p.m.) - Around (8.00 p.m.)
 Hb: 6.8 g%
 International normalized ratio: 1.4
 Platelet: 600,000/cumm
 Bilirubin: 1.4 mg%
 Urinary protein: -3+
 Kidney function test:
 Blood urea: 50 mg%

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Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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Serum creatinine: 1.2 mg%

Liver function test:

Serum glutamic oxaloacetic transaminase: 247 U/UL

Serum glutamate pyruvate transaminase: 212 U/UL

Alkaline phosphatase: 24 kau

Suddenly at 3.30 p.m. patient went in shock, her pulse became feeble, blood pressure was non recordable and patient was not maintaining oxygen saturation. Furthermore, there was abdominal distension so hemoperitoneum was suspected and an urgent transabdominal ultrasound (USG) guided tapping was performed (Figures 1 and 2). Hemorrhagic fluid on tapping was confirmatory and an urgent decision of exploration was taken.

Immediately, patient was shifted to operation theater for exploration. Intraoperatively there was collection of around 700 cc frank blood with large blood clot adherent to liver surface seen, hence surgeons were called (Figure 3). There was also evidence of active blood oozing from capsular breach on liver surface of size 10 cm × 5 cm suggestive of subcapsular hematoma with spontaneous rupture.

External compression was done for 10 min and hemostatic material, surgiseal was kept over the hematoma. Meanwhile, the uterus became flabby so prophylactic B-lynch sutures were taken. Sub-hepatic drain on the right side and drain in pelvic space on the left side was kept.

The patient received 3 units of red packed cells, 3 units of fresh frozen plasma, 2 units of platelet concentrate. Anti-hypertensive treatment was started to the patient along with antibiotics.

On the seventh post-operative day patient had continuous spikes of fever of 103°F, the patient was thoroughly investigated. USG was suggestive of ill-defined hyperechoic area in superior border of right and left lobe of liver in supcapsular region but the decision was taken to manage the hematoma conservatively.

On 12th post-operative day, patient had sudden onset of breathlessness with tachycardia. Urgent electrocardiogram (ECG) and X-ray chest were done,

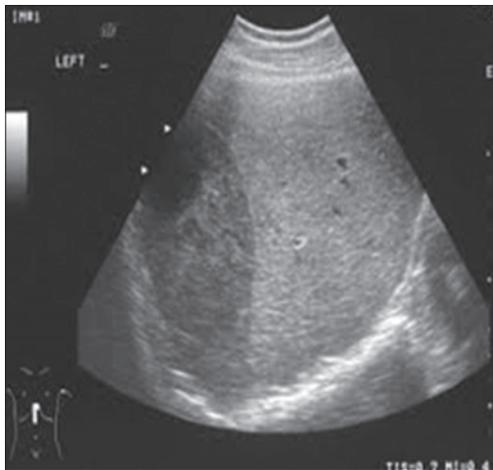


Figure 1: Free fluid in peritoneum



Figure 3: Subcapsular hematoma

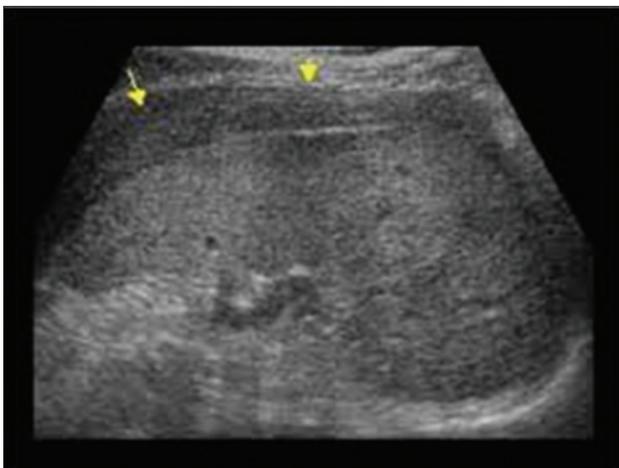


Figure 2: Subcapsular collection

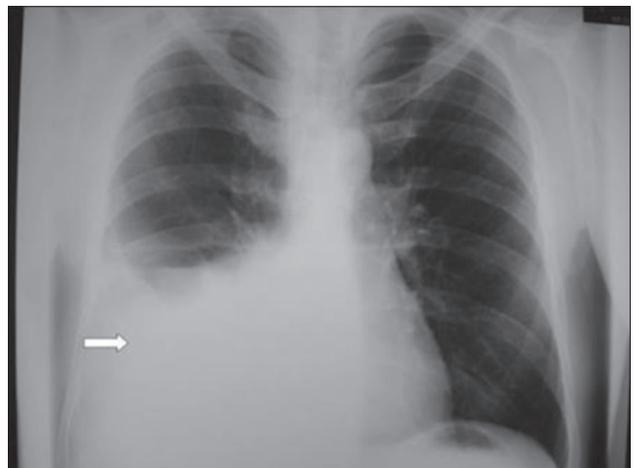


Figure 4: Right sided pleural effusion

ECG was suggestive of sinus tachycardia. X-ray chest was suggestive of right-sided pleural effusion (Figure 4). 2-dimensional echo suggestive of mild pericardial effusion, mild tricuspid regurgitation and mild pulmonary arterial hypertension and D-dimer was 16.3 and computed tomography (CT) pulmonary angiography was done which was suggestive of ground glass opacity in right lung.

The patient was shifted to intensive cardiac care unit and she was monitored. Patient was advised diagnostic pleural tapping. The fluid aspirated was hemorrhagic and was considered secondary to residual liver hematoma. Decision to manage the patient conservatively with a close observation was taken, and she was started on higher antibiotics with diuretics. As a result, effusion resolved gradually with time.² After the improvement in patient's condition drains were removed. 5 weeks postpartum patient had no complaints and was discharged on 13/9/15 from hospital in a stable state on dual hypertensive. During the entire hospital stay patient received 11 packed red cells; 10 fresh frozen plasma; 4 platelet concentrate. The patient is following up regularly; repeat scan was done after 3 months which was suggestive of no evidence of liver hematoma.

DISCUSSION

The HELLP syndrome and other hypertensive disorders are the main causes of maternal mortality. HELLP syndrome develops in about 70% of the cases before delivery and 30% in postpartum period.³ A mild and self-limited course to a fulminant process including multiple organ failure can be seen in HELLP syndrome. These major maternal complications include disseminated intravascular coagulation, abruptio placentae, acute renal failure pulmonary edema, and subcapsular liver hematoma.^{4,5} Liver hemorrhage and rupture are the most eccentric and critical complications of HELLP-associated disease. Maternal mortality occurs in about 18-86% cases of hepatic rupture. The causes of subcapsular and intraparenchymal hepatic hematomas in HELLP syndrome are unknown. Liver distention may occur with the obstruction of blood flow in the hepatic sinusoids.

This obstruction may lead to periportal necrosis and, in severe cases, intrahepatic hemorrhage, subcapsular hematoma formation or hepatic rupture. A fluorescent antibody technique has been used to demonstrate fibrin deposits in the hepatic sinusoids. Clinical symptoms and signs are non-specific and epigastric or right upper quadrant abdominal pain with shoulder irradiation to nausea, vomiting, and abdominal distension.

CONCLUSION

The cases of subcapsular liver hematomas must be treated in tertiary centers for prompt recognition and optimal treatment because the prognosis can be changed by the timely diagnosis and treatment. USG, CT, and magnetic resonance imaging (MRI) can be used for the diagnosis. Liver hematomas in pregnancy must be closely monitored by hemodynamic and coagulation parameters during the management of HELLP syndrome and other hypertensive disorders. Abdominal USG represents a useful first choice non-invasive tool for diagnosis and evaluation. Serial evaluation with imaging techniques, avoidance of the liver manipulation and immediately replacement of blood products are essential. Postpartum follow-up should include serial assessment with USG, CT or MRI until the defect resolves.

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How to cite this article: Ramteke S, Suresh S, Dharmale, Agrawal S. Management of Ruptured Hepatic Subcapsular Hematoma in Hemolysis, Elevated Liver Enzymes, Low Platelets Syndrome: A Case Report. *Int J Sci Stud* 2016;3(11):299-301.

Source of Support: Nil, **Conflict of Interest:** None declared.

Chronic Uterine Inversion Secondary to Submucous Fibroid: A Rare Case Report

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Abstract

Nonpuerperal uterine inversion is a rare condition. As nonpuerperal uterine inversion is rarely encountered by the gynecologist thus diagnosis and management could be challenging. We describe a case report of chronic inversion of nonpuerperal uterus secondary to submucous fibroid associated with severe anemia. A 45-year-old lady presented with menorrhagia and copious vaginal discharge followed by acute retention of urine. Diagnosis of partial inversion of the uterus was made, which was confirmed at laparotomy. Treatment of anemia was done and then she underwent abdominal hysterectomy with bilateral salpingo-oophorectomy after correction of inversion.

Key words: Fibroid, Inversion, Menorrhagia, Puerperal

INTRODUCTION

Uterine inversion refers to the descent of the uterine fundus to or through the cervix so that uterus is turned inside out. Uterine inversion is a rare condition that occurs usually as a complication of deliveries.¹ Nonpuerperal inversion is extremely rare representing about one-sixth of all inversion.² Prolapsed fibroids tend to be the most common inciting factors with an occasional report of inversion associated with uterine neoplasm and endometrial polyp. Three contributing factors proposed for uterine inversion are (1) sudden emptying of the uterus which was previously distended by a tumor (2) thinning of the uterine walls due to an intrauterine tumor and (3) dilatation of cervix.³⁻⁶ We report a case of chronic inversion of the nonpuerperal uterus due to large submucous fibroid with severe anemia.

CASE REPORT

A 45-year-old lady, P₃₊₀L₃ all vaginal deliveries (last child birth - 14 years back) presented to the RIMS gynecological

outpatient on 6 August 2015 with a complaint of menorrhagia and congestive dysmenorrhea for last 8 months followed by copious foul-smelling vaginal discharge for last 6 months. On general examination, she had severe pallor and tachycardia (pulse rate - 112/min), blood pressure was in normal range. On P/A examination nothing was remarkable. On P/S examination-cervix was not visualized. A pink colored polyp of 8 cm × 8 cm with few necrotic area was seen in vagina (Figure 1). On bimanual pelvic examination - A large polypoidal mass of 8 cm × 8 cm felt in upper part of vagina, firm in consistency, smooth surfaced with bleeds on touch. Cervical lip could not be felt with distinction, and uterine size could not be assessed properly. A clinical diagnosis of submucous fibroid polyp with severe anemia was made. After 2 days of admission, she suddenly developed acute retention of urine, for which was put on the indwelling catheter. Except of severe anemia (hemoglobin-6 g%), all routine pre-operative investigations were within normal range. Her ultrasound (USG) revealed inversion of uterus with a right simple ovarian cyst of 5 cm × 4 cm. Clinical diagnosis was revised to inversion of the uterus with fibroid polyp and was posted for abdominal hysterectomy after correction of anemia (4 unit of packed cell volume transfusion done). On laparotomy, there was the typical appearance of uterine inversion, i.e., broad ligament, round ligament, and other associated structures were stretched due to uterine inversion (Figure 2). Uterine reposition was done by giving a vertical incision into

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www.ijss-sn.com

Month of Submission : 12-2015
Month of Peer Review : 01-2016
Month of Acceptance : 01-2016
Month of Publishing : 02-2016

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posterior portion of the cervical ring and gentle traction on round ligaments (Haultain's method), with the simultaneous gentle pushing of fundus through vagina by an assistant (Figure 3). A sessile submucous fibroid of 8 cm × 8 cm size was attached to fundus which was

removed by enucleation. After correction of uterine inversion total abdominal hysterectomy and bilateral salpingo-oophorectomy done. Her post-operative period was uneventful and was discharged on 10th post-operative day in healthy condition. Histopathology of the excised polypoidal mass showed a picture of fibromyoma.



Figure 1: Perineal examination showing fibroid polyp



Figure 2: Laparotomy showing cupping of fundus of uterus



Figure 3: Repositioning of uterus

DISCUSSION

Uterine inversion can be classified into four stages as Stage 1: The inverted uterus remains in the uterine cavity, Stage 2: Complete inversion of the fundus through the cervix, Stage 3: The inverted fundus protrudes through vulva, and Stage 4: Inversion of the uterus and vaginal wall through the vulva.⁷ Inversion can also be classified as acute and chronic. With acute inversion, the patient may have severe pain in lower abdomen or excessive bleeding whereas chronic inversion may be insidious or patient may have lower abdominal discomfort, vaginal discharge, irregular vaginal bleeding, or anemia.⁸ In chronic inversion with sloughing of endometrium diagnosis, it is not very easy so detailed abdominal, and vaginal USG or Doppler may be required to confirm the diagnosis.^{9,10}

As nonpuerperal uterine inversion is rarely encountered by the gynecologist thus diagnosis and management could be challenging.¹¹ In our case, on clinical examination, the diagnosis was not clear, so detailed ultrasound of abdomen and pelvis was done to confirm the diagnosis. Repositioning of the uterus can be done manually in acute cases but in chronic nonpuerperal case, manual repositioning is not possible, especially in those cases associated with tumors. In chronic nonpuerperal cases, surgery is imperative. Considering patient's age, reproductive desire and associated conditions, surgical repositioning, or hysterectomy can be done.

Surgical repositioning can be done vaginally or through abdominal route. In vaginal route approach (Spinelli's method), incision is given anteriorly in the constriction ring and bladder dissection is required; while in Kustner's method, posterior uterine wall incision is given which make it bit easier and safer.¹² Abdominal route repositioning can be done either using Huntington's procedure¹³ (cup of inversion is identified, dilating the cervical ring digitally and gently pulling out round ligaments) or by Haultain's method¹⁴ where a vertical incision is given in the posterior wall of the cervical ring, and gentle traction is given on round ligaments. We repositioned the uterus using Haultain's technique. Following that total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed. The other methods include laparoscopic reduction,¹⁵ the use of obstetrics ventouse at laparotomy¹⁶ and robotically assisted laparoscopic correction.¹⁷

CONCLUSION

Chronic uterine inversion is a rare condition that is difficult to diagnose even for the experienced gynecologists. Uterine inversion has a good prognosis when managed in timely correct manner. The treatment for chronic uterine inversion is surgical that includes both abdominal and vaginal approaches.

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How to cite this article: Kumari A, Vidhyarthi A, Salini KM. Chronic Uterine Inversion Secondary to Submucous Fibroid: A Rare Case Report. *Int J Sci Stud* 2016;3(11):302-304.

Source of Support: Nil, **Conflict of Interest:** None declared.

Rapid Intraventricular Clot Dissolution with Enoxaparin in Ischemic Cardiomyopathy

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A 50-year-old smoker and alcoholic male was admitted (03/01/2014) with 1 month history of progressive exertional dyspnea and paroxysmal nocturnal dyspnea, tender hepatomegaly, and anasarca. He had regular, feeble pulse at 100 a minute, blood pressure of 90/70 mm Hg, severe pedal edema, raised JVP, tender hepatomegaly with significant hepatojugular reflux and moderate ascites. Cardiopulmonary examination revealed biventricular enlargement, normal heart sounds, no murmur, a moderately large right sided pleural effusion, bilateral rhonchi, and crepitations. He was treated for ischemic dilated cardiomyopathy with congestive cardiac failure since past 2 weeks. Electrocardiogram showed QS complexes in the inferior and precordial leads suggestive of old inferior and extensive anterior wall myocardial infarction. The two-dimensional echocardiography 2 weeks back (18/12/13) showed globally hypokinetic ventricles, left ventricular ejection fraction (LVEF) 14%, moderate mitral regurgitation (MR) and grade IV tricuspid regurgitation (TR) but no intrachamber clots (Figure 1).

Though not themselves thrombolytic, use of high dose heparin or enoxaparin, relayed with warfarin, results in dissolution of cardiac clots.^{1,2} Our patient achieved rapid dissolution of big clots because they were recent and effective treatment of heart failure improved the ejection fraction thereby reducing stagnation. Such rapid ventricular clot dissolution with heparin is not reported very often. A case of antiphospholipid antibody syndrome had the disappearance of an intracardiac clot within 24 h³ of starting enoxaparin.

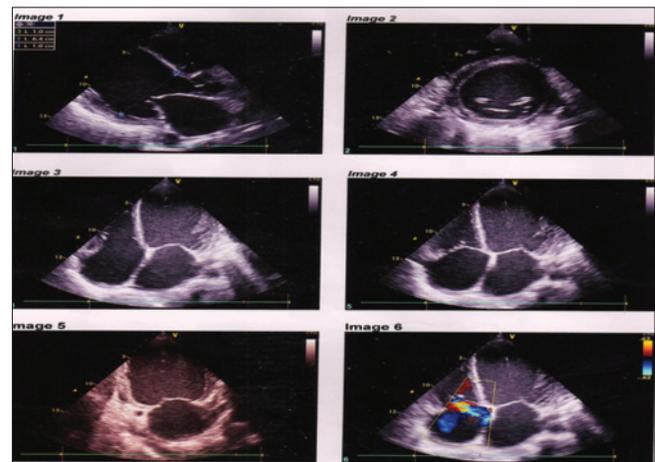


Figure 1: Echocardiogram 2 weeks before admission

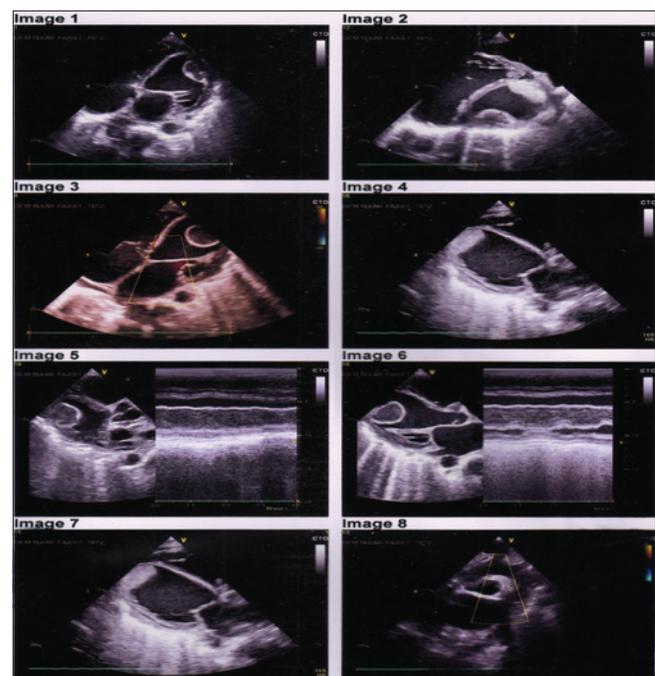


Figure 2: Echoardiogram at admission showing ventricular clots

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Month of Submission : 12-2015
 Month of Peer Review : 01-2016
 Month of Acceptance : 01-2016
 Month of Publishing : 02-2016

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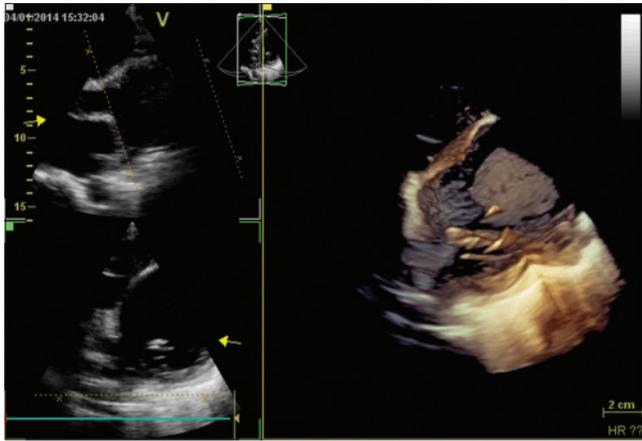


Figure 3: Four-dimensional echo showing ventricular clot

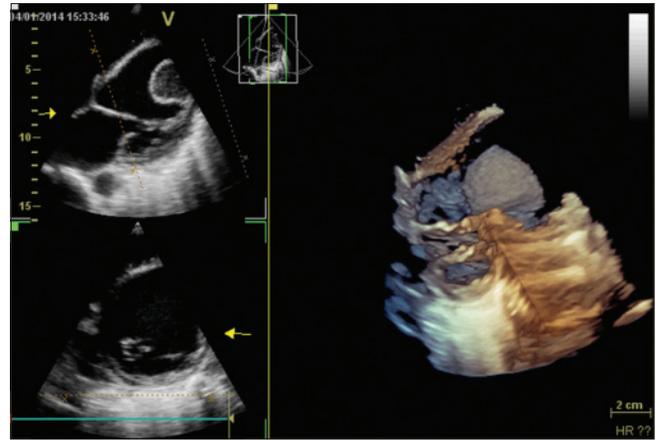


Figure 5: Four-dimensional echo showing ventricular clot

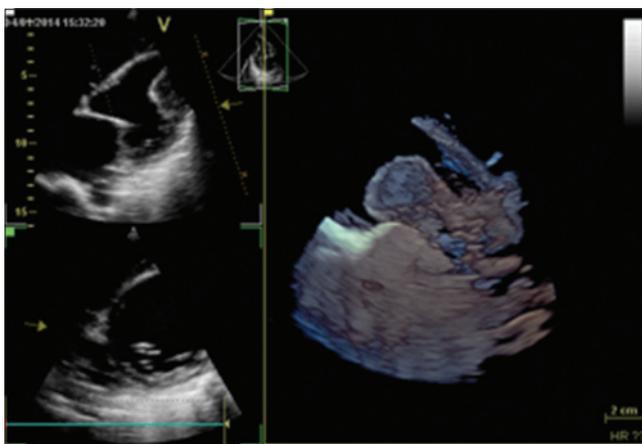


Figure 4: Four-dimensional echo showing ventricular clots

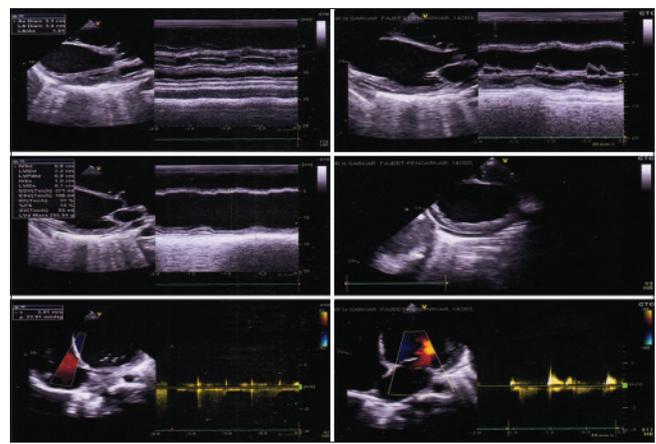


Figure 6: Echo after 1 week showing dissolution of clot

The two-dimensional (Figure 2) and four-dimensional (Figures 3-5) cardiac echocardiography and doppler on admission (4/1/14) revealed three large thrombi at the base of left atrium and both left and right ventricular apices along with biventricular dilatation and global hypokinesia with LVEF of 8-10%, mild MR, moderate TR, and pulmonary artery hypertension (PASP - 40 mmHg).

There was a significant improvement in cardiac failure with diuretics, subcutaneous enoxaparin (0.6 ml BD), warfarin, digoxin, aspirin, ramipril, antibiotics and therapeutic pleurocentesis of 750 ml fluid. A four-dimensional cardiac echocardiography a week later (11/1/14) revealed a LVEF of 25-30% with the disappearance of ventricular clots (Figure 6). The patient had experienced no clinical embolic or hemorrhagic complications during treatment.

Points to Ponder

1. Ventricular clots are sequelae of severe ventricular dysfunction.
2. Anticoagulants (injectable heparin relayed by oral warfarin) can effectively dissolve clots with minimal complications.

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How to cite this article: Ingle V, Dately A, Verma A, Gandhi Z. Rapid Intraventricular Clot Dissolution with Enoxaparin in Ischemic Cardiomyopathy. *Int J Sci Stud* 2016;3(11):305-306.

Source of Support: Nil, **Conflict of Interest:** None declared.