



General Information

About The Journal

International Journal of Scientific Study (IJSS) is a monthly journal publishing research articles after full peer review and aims to publish scientifically sound research articles in across all science like Medicine, Dentistry, Genetics, Pharmacy, etc.

Each article submitted to us would be undergoing review in three stages: Initial Review, Peer Review & Final Review.

All rights are reserved with journal owner. Without the prior permission from Editor, no part of the publication can be reproduced, stored or transmitted in any form or by any means.

Abstracting & Indexing Information

Index Medicus (IMSEAR), Global Index Medicus, Index Copernicus, Directory of Open Access Journals(DOAJ), Google Scholar, WorldCat, SafetyLit, WHO Hinari, Genamics Journal Seek Ulrichsweb Serials Solutions , International Committee of Medical Journal Editors(ICJME) Geneva Foundation for Medical Education & Research(GFMER), Socolar, Bielefeld Academic Search Engine(BASE) , Research Bible , Academic Journals Database, J-Gate, Jour Informatics, Directory of Research Journal Indexing(DRJI), Scientific Indexing Services(SIS) Rubriq-Beta, SHERPA RoMEO, New Jour, EIJASR), IndianScience.in, CiteFactor, Scientific Journal Impact Factor (SJIF), Journal Index.net, ROAD, Global Impact Factor(GIF) , International Society for Research Activity (ISRA), Advanced Science Index, OpenAccessArticles.com, etc

Information for Authors

The authors should follow “Instructions to Authors” which is available on website <http://www.ijss-sn.com/instructions-to-authors.html>. Authors should fill the Copyright Transfer form & Conflict of Interest

form. Manuscripts should be submitted directly to: editor@ijss-sn.com.

Publication Charges

International Journal of Scientific Study aims to encourage research among all the students, professionals, etc. But due to costs towards article processing, maintenance of paper in secured data storage system, databases and other financial constraints, authors are required to pay. However discount will be provided for the non-funding quality research work upon request. Details about publication charges are mentioned on journal website at: <http://www.ijss-sn.com/publication-charges.html>.

Advertising Policy

The journal accepts display and classified advertising. Frequency discounts and special positions are available. Inquiries about advertising should be sent to editor@ijss-sn.com.

Publishing Details

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)

Disclaimer

The views and opinions published in International Journal of Scientific Study (IJSS) are those of authors and do not necessarily reflect the policy or position of publisher, editors or members of editorial board. Though the every care has been taken to ensure the accuracy and authenticity of Information, IJSS is however not responsible for damages caused by misinterpretation of information expressed and implied within the pages of this issue. No part of this publication may be reproduced without the express written permission of the publisher.



Editorial Board

Founder & Editor In Chief

Dr. Swapnil S. Bumb – India (BDS, MDS, MPH, MSc, PGDHA, PDCR)

Assistant Professor, ACPM Dental College, Dhule, Maharashtra, India

Founder Editor

Dr. Dhairya Lakhani, India

Senior Editorial Board Member

Dr. Stephen Cohen – *United States of America (MA, DDS, FACD, FICD)*

Diplomate of the American Board of Endodontics

Senior editor for nine Editions of the definitive Endodontics Textbook - Pathways of the Pulp, and a Co-editor of the renamed 10 edition Cohen's Pathways of the Pulp.

Dr. Abdel Latif Mohamed – *Australia (MBBS, FRACP, MRCPC, MPaed, MPH, AFRACMA, MScEpi, MD)*

Professor in Neonatology, The Clinical School, Australian National University Medical School, Australia

Open Researcher and Contributor ID (ORCID): 0000-0003-4306-2933, Scopus ID: 13610882200

Dr. Bipin N. Savani – *United States of America (M.D)*

Professor of Medicine Director, Vanderbilt University Medical Center and Veterans Affairs Medical Center, Vanderbilt- Ingram Cancer Center, Nashville, TN, USA.

Associate Editor (previously co-editor) of the journal "Bone Marrow Transplantation" (official journal of the European Group for Blood and Marrow Transplantation- EBMT).

Editorial advisory board: Biology of Blood and Marrow Transplantation (official journal of the American Society of Blood and Marrow Transplantation).

Dr. Yousef Saleh Khader Al-Gaud, Jordan – *(BDS, MSc, MSPH, MHPE, FFFPH, ScD)*

Professor (Full) - Department of Community Medicine

Jordan University of Science and Technology, Jordan, Irbid

Dr. P. Satyanarayana Murthy – *India (MBBS, MS, DLO)*

Professor and Head, Department of ENT and Head & Neck Surgery, Dr.Pinnamaneni Siddhartha Institute of Medical Sciences and Research Center, Chinnaautapalli, Gannavaram

Editor - Indian journal of Otolaryngology (1991),

Editorial Chairman, Indian Journal of Otolaryngology and Head & Neck Surgery 2006-2009 & 2009-2012

Editor, International Journal of Phonosurgery and Laryngology

Editor in Chief designate, International Journal of Sleep Science and Surgery

Editor in Chief Designate, Journal of Indian Academy of Otorhinolaryngology and Head & Neck Surgery

Dr. Sidakpal S. Panaich – *United States of America (M.D)*

Interventional Cardiology Fellow, Department of Cardiology, Michigan State University/Borgess Medical Center

Cardiology Fellow, Department of Internal Medicine/Cardiology, Wayne State University/Detroit Medical Center

Associate Editors

Dr. Silvana Beraj, Albania
Dr. João Malta Barbosa, United States of America
Dr. Anastasia M. Ledyeva, Russia
Dr. Asfandyar Sheikh, Pakistan
Dr. John Park, Scotland

Dr. Mohannad Saleh Kiswani, Jordan
Dr. Safalya Kadthane, India
Dr. Dorcas Naa Dedei Aryeetey, Kumasi, Ghana
Dr. Animasahun Victor Jide, Sagamu, Nigeria
Dr. Hingi Marko C., Mwanza City, Tanzania

Contents

ORIGINAL ARTICLES

- Risk Factors in ABO Blood Group for Coronary Artery Disease
P. Manimekalai, S. Suresh Kanna 1
- Comprehensive Skin Care Regimen of Moisturizer with Broad-Spectrum Sunscreen as an Adjuvant in Management of Acne (CHARISMA)
Shabir Ahmed Bhat, Gaurav A. Deshmukh, Dhiraj S. Dhoot, Hanmant Barkate 5
- Role of Magnetic Resonance Venography, Diffusion-Weighted Imaging, and Gradient-Recalled Echo in Cerebral Sinovenous Thrombosis
Nadeem Ahmed, Alle Praveen Kumar, Swapna Chouhan, Shaik Ismail, Uzma Afreen 10
- Combined Spinal- Epidural in Labor Analgesia: Comparison of Fentanyl Bupivacaine Mixture versus Sufentanil - Bupivacaine Mixture
S Vijay Anand, T Kabila Rajee, Saranya Nagalingam 15
- Prevalence and Etiological Profile of Patients with Acute Confusional State
Sajad Sumji, Mohd Iqbal Wani, Muzzafar Mohi-ud-Din 24
- Translating Phenytoin Therapeutic Drug Monitoring for Potential Utilities to Pharmacovigilance: Capacity Raking an Established Tertiary Care Service
Shazia Kousar, Fayaz Ahmad Wani, Zaid Ahmad Wani, Arjumand Nazir, Ahmad Tauqeer Zahid, Z A Wafai 30
- Epidemiological Study of Childhood Dermatitis in Eastern Uttar Pradesh
Anil K Gupta, Ali Mohammad, Lalit Mohan, S K Singh, Snehlata, Amit Kumar Soni, Sushantika, Naveen Kumar 35
- Breast Cancer Awareness in South India
Lalitha Subramanian, V U Salini, Heber Anandan, U Insuvai 39
- Study on Clinical Profile of Dengue Fever in a Tertiary Care Centre of Bihar
Amit Kumar Mishra, Sudhir Kumar, Praveen Kumar, Arshad Ahmad, Shailesh KumarKalyan Kumar Saha, Manoj Kumar Choudhary, Naresh Kumar 43
- Adult Attention Deficit Hyperactivity Disorder in Health Science Students of India
Bhushan Shashi, Piplani Shobhit, Tekkalaki Bheemsain 47

- Knowledge of Cervical Cancer and Uptake of Pap Smear Test and Human Papillomavirus Vaccination among Gynecologic Clinic Attendees in Sokoto, Nigeria
Kehinde J Awosan, Mairo Hassan, Buhari M Ibrahim 52
- An Insight in Sexual Behavior of Married Women
Shashi Prateek, Himani Goyal, Yamini Verma, Geetika Nain 59
- Knowledge of Human Papillomavirus Infection and Vaccination, and Practices Regarding Human Papillomavirus Vaccination among Female Health-care Professionals in Sokoto, Nigeria
Mairo Hassan, Kehinde Joseph Awosan 62
- Transvaginal Sonographic Measurement of Cervical Length during Midtrimester in Predicting Preterm Labor in Asymptomatic Singleton Pregnancies
Mahalakshmi Aravazhi, Madhumitha Chandrasekaran, Deepak Chandrasekaran 71
- Clinical Profile and Visual Outcome of Ocular Injuries Presenting to Tertiary Care Hospital Located on a State Highway
M Sunil Kumar, D Vishwas 76
- Prevalence of Thrombophilia in Patients with Adverse Pregnancy Outcome
S Sooraj 82
- Predictors of Visual Acuity in Traumatic Cataract
Shilpi Aggarwal, Sapan Phalod 93
- Parents' Management of Acute Upper Respiratory Tract Infections in Children, Al Ahsa, Saudi Arabia
Zainab Al Shuhayb, Sukainah Al Haddad, Khalid Al Yahya, Rabel Khawaja 99
- Clinical Study on Prophylactic and Therapeutic Management of Thrombophilia in Adverse Pregnancy Outcome Patients
S Sooraj 105
- A Comparative Study of Equi-concentration of Bupivacaine-Fentanyl and Ropivacaine-Fentanyl for Epidural Labor Analgesia
Gunda Shravan Kumar, B Srinivas Rao, U Mahesh Kumar 112

- Effect of Audio and Audiovisual Aids on Anxiety Level of Patients during First Appointment of Root Canal Treatment: An *In Vivo* Study
Sadashiv Daokar, Snehashree Pophli, Kalpana Pawar, Kapil Wahane, Rohit Tambake, Laxmikant Late 121
- A Comparative Study between Bupivacaine 0.5% and Ropivacaine 0.75% in Epidural Analgesia in Patients Undergoing Elective Lower Abdominal and Lower Limb Surgeries
G Shravan Kumar, R Shanthan Kumar, Laxmi Kanth, M Srinath 127
- Clinical and Epidemiological Evaluation and Assessment of Various Modes of Therapeutic Management of Locally Advanced Carcinoma of Breast in a Tertiary Care Hospital: An Observational Study
Gaddam Padmasree 136
- To study Incidence of Coronary Artery Disease in Asymptomatic Chronic Smokers by Using Exercise Stress Test
Mohd Suhel Siddiqui, Lalit Jain, Arpita Shrivastav, Shivesh Thakur 147
- A Clinical Study of the Different Types of Inguinoscrotal Swellings and Their Management in a Tertiary Care Referral Center
Radha Verma, Chirag Vaja, Swarup Anand, Kiran Gaikwad, Aditya Tripathi, Rutuja Narvekar 152
- CASE REPORT**
- A Rare Case of Leiomyosarcoma with Hemoperitoneum in Pregnancy
Ragini Agrawal, Pallavi Vasal, Bijal Bhati, Charu Dutt Arora 170

Risk Factors in ABO Blood Group for Coronary Artery Disease

P. Manimekalai, S. Suresh Kanna

Assistant Professor, Department of General Medicine, Sree Balaji Medical College and Hospital, Chennai, Tamil Nadu, India

Abstract

Introduction: There are many reports regarding the association between ABO and Rhesus blood groups and coronary artery disease. ABO blood groups, in particular non-O blood groups, have been suggested to be associated with several cardiovascular risk factors, and even higher risk of ischemic heart disease, cerebral ischemia of arterial origin, and of developing severe manifestations of atherosclerosis.

Aim: The aim of this study was to study the prevalence of risk factors in ABO blood group of coronary artery disease and to study immediate prognosis and mortality.

Materials and Methods: This study was conducted in the Department of Cardiology and Medicine, Government Rajaji Hospital, Madurai. Patients admitted with clinical features of acute myocardial infarction confirmed by electrocardiogram and patients admitted with angina pectoris clinically were included in the study. Detailed history, general examination, cardiovascular examination, and relevant investigations were done in all patients.

Results: The incidence of coronary artery disease is predominant in "A" Group. The incidence of diabetes mellitus (DM) and hypertension (HT) is 40% and 30% in "A" Group which constitutes about 21.2% among the population. In female population, menopause is the main risk factor. Here, also the incidence of DM, HT, and hypercholesterolemia is most commonly found in "A" Group individuals. About 66% contribution is from the smoker. DM contributes to 22%.

Conclusion: The type of ABO blood group seems to have an impact on the risk of coronary artery involvement and the type of blood group effects on the severity of CAD. Smoking affects the prognosis whichever blood group they belong. About 66% incidence of left ventricular clot is seen among smokers.

Key words: ABO blood group, Association, Ischemic heart disease

INTRODUCTION

Coronary artery disease is also known as ischemic heart disease (IHD) is a common cause of death in the adults. It may present as sudden death, but more usually causes angina pectoris, myocardial infarction (MI) (heart attack), or heart failure. It can also lead to the change of heart rhythm. Factors associated with an increased risk of developing

coronary artery disease include diabetes, cigarette smoking, high blood pressure, obesity, and a raised concentration of cholesterol in the blood.^[1] Compared to other illnesses, IHD causes more deaths and disabilities and incurs greater economic costs in our modern world. IHD is the common, serious, chronic, and life-threatening disease in the United States, where more than 12 million people have IHD, more than 6 million have angina pectoris, and more than 7 million have a sustained MI.^[2]

The ABO blood group system consists of three main alleles (two codominant [A and B] and one recessive [O]).^[3,4] The A and B alleles of the ABO locus encode A and B glycosyltransferase activities, which convert precursor H antigen into either A or B determinants, the A and B antigens having an extra saccharide unit to the O

Access this article online



www.ijss-sn.com

Month of Submission : 06-2018
Month of Peer Review : 07-2018
Month of Acceptance : 08-2018
Month of Publishing : 08-2018

Corresponding Author:

Dr. S. Suresh Kanna, Department of General Medicine, Sree Balaji Medical College and Hospital, Chennai, Tamil Nadu, India
E-mail: mekalap32@gmail.com

unit (N-acetylgalactosamine and galactose, respectively). Group O individuals lack such transferase enzymes and express basic unchanged H antigen.^[5] Notably, the ABO antigens are expressed not only on the surface of red blood cells but also on a variety of human cells and tissues including epithelia, platelets, vascular endothelia, and neurons.^[6]

Aim

The aim of this study was to study the prevalence of risk factors in ABO blood group and to study immediate prognosis and mortality.

MATERIALS AND METHODS

This study was conducted in the Department of Cardiology and Medicine, Government Rajaji Hospital, Madurai. The patients for the study were taken from those admitted as inpatients or those attending outpatient departments of Medicine and cardiology.

Inclusion Criteria

Patients admitted with clinical features of acute MI with electrocardiogram (ECG) confirmation, patients admitted with angina pectoris clinically also ECG wise, and patients getting drugs for IHD from the Department of Medicine and cardiology were included in the study.

Exclusion Criteria

Those patients having congenital heart disease and rheumatic heart disease were excluded from the study. Detailed history, general examination, and cardiovascular examination were done in all patients.

RESULTS

Our study group consisted of males 84% (97 patients) and females 16% (18 patients). This shows male dominance in the prevalence of coronary artery disease.

The age group of patients ranged from 28 years to 75 years. Majority of patients were in the age group above 50, and they contributed 64% of the total. The prevalence of young IHD patients was 11% that is 13 patients out of 75.

MI forms the major part of our study group. They contribute 74% of the total with 86 patients. Other patients included were clinical angina 15.6%, asymptomatic but with ECG evidence of IHD 5%, and symptomatic but normal ECG five patients [Table 1].

In the total of 115 patients, 40 patients were of ‘B’ Group among that 36 were male, and 4 were female. Group B

is the common blood group in our part of the country. Next was the ‘O’ Group which constituted 37 patients in total. ‘A’ Group and ‘AB’ Group contributed 28 and 10 patients, respectively.

Anterior and inferior walls MI were common in four groups of patients. The clot was found in only one patient who belonged to A Group with diabetes mellitus (DM) as the risk factor in postmenopausal stage. Her ejection fraction (EF) was 34%. In O Group, two patients had the EF <40 [Tables 2 and 3].

The incidence of DM and hypertension (HT) is 40% and 30% in ‘A’ Group which constitutes about 21.2% among population. In female population, menopause is the main risk factors. Here, also the incidence of DM, HT, and hypercholesteremia is most commonly found in ‘A’ Group individuals [Table 4].

Among the 18 patients, 12 patients are smokers. Six patients, who are smokers, are found to have EF 40%–42%, two patients presented with NYHA Class III symptoms are diagnosed to have postinfarction angina, and they are detected to have left ventricular (LV) apical clot. One belongs to ‘O’ Group who is a smoker. Other belongs to ‘B’ Group in whom except age and sex no other risk factors are made out. Among the seven patients, who belong to ‘B’ Group, three are found to have ischemia of right coronary artery territory, and one patient is detected to have left anterior descending artery territory [Figures 1 and 2].

Out of 86 MI cases, eight patients expired – they were male patients. They belong to various blood groups. Among the

Table 1: Acute coronary syndrome

Acute coronary syndrome	Number of patients (%)
MI	86 (74)
Clinical angina	18 (15.6)
Asymptomatic but with ECG evidence of IHD	6 (5)

IHD: Ischemic heart disease, ECG: Electrocardiogram, MI: Myocardial infarction

Table 2: Blood group and region of infarct

Region of infarct	A	AB	B	O
Anterior wall MI	2	1	1	1
Inferior wall MI	3	1	1	1

MI: Myocardial infarction

Table 3: Analysis of myocardial infarction

Type of infarction	A1+ve	B+ve	A1B+ve	O+ve
Anterior wall MI	11	1	5	19
Inferior wall MI	9	11	4	10

MI: Myocardial infarction

Table 4: LV clot in relation to blood group

Risk factors	A1+ve		B+ve		A1B+ve		O+ve	
	Male	Female	Male	Female	Male	Female	Male	Female
Smoking	12	-	28	-	6	-	18	-
Alcoholism	4	-	7	-	1	-	7	-
Obesity	5	-	10	-	5	-	6	-
DM	8	2	6	2	2	-	7	-
HT	6	2	5	-	-	-	2	-
Family history	4	1	4	-	2	-	2	1
Hypercholesterolemia	7	1	11	1	2	-	3	-

LV: Left ventricular, HT: Hypertension, DM: Diabetes mellitus

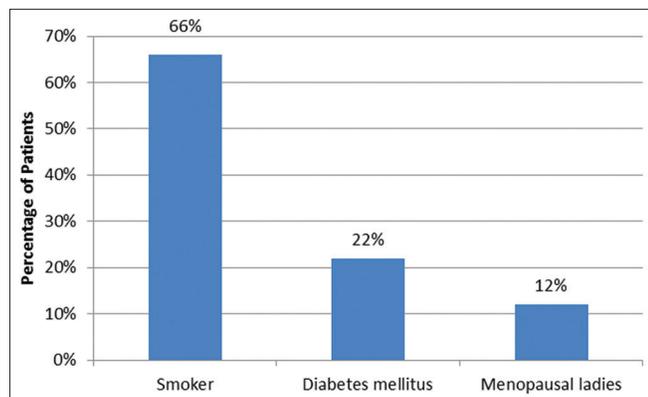


Figure 1: Left ventricular clot in relation to risk factor

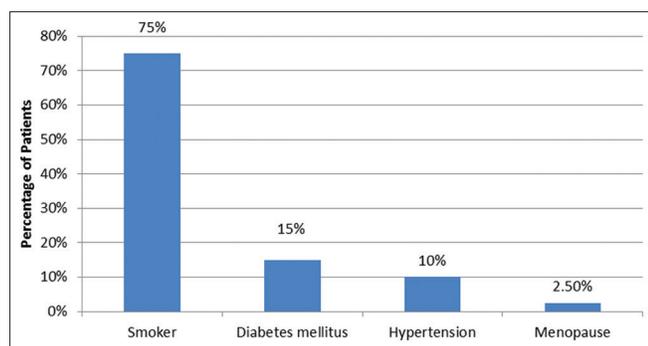


Figure 2: Left ventricular dysfunctions (EF <40%) in relation to risk factors

eight patients, three belong to “O” Group, two belong to “B” Group, 1 belongs to “AB” Group, and two belong to “A” Group.

DISCUSSION

The association between ABO blood groups and the development of atherosclerosis is still unclear, despite several studies addressing this topic. There is a very distinct difference among the blood types with regard to the incidence of heart disease. Platt *et al.* studied the correlation between blood group and cardiac infarction in two different age groups. The patients were divided into two groups as follows: those who were older than 65 years

and younger. The predominance of blood group A in patients with cardiac infarction was highly significant in both age groups ($P < 0.005$).^[7]

The association between ABO blood group and coronary heart disease (CHD) risk was not significantly modified by other known risk factors for CHD including age, sex, alcohol consumption, smoking, physical activity, or DM history. The mechanisms underlying the associations between ABO blood group and CHD risk remain unclear. However, several lines of evidence support its potential cardiovascular effects. In the analyses of the relationship between the ABO blood group and major cardiovascular risk factors, the only association of note was that O blood group, probably by association with lower HDL-c levels, smoking habit, and family history, significantly increases the risk of CHD, and contributes substantially to the incidence of CHD in the studied populations, in the two previous reports.^[8,9]

CONCLUSION

Controversies between the association of blood group and CAD can be due to several confounding factors such as DM, HT, and smoking. Another important factor is of race and genetics which may have different impact on relationship between blood groups and coronary artery involvement among the Asian population. In addition, socioeconomic condition, environmental, and lifestyle may have some effect on the correlation of ABO blood group and CAD.

REFERENCES

- Marcovitch H. Black's's Medical Dictionary. 41st ed. Lanham, Md.: Scarecrow Press; 2005.
- Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J, *et al.* Harrison's Principles of Internal Medicine. 18th ed., Vol. 2. USA, New York: Mc Graw-Hill; 2011.
- Yamamoto F, Clausen H, White T, Marken J, Hakomori S. Molecular genetic basis of the histo-blood group ABO system. *Nature* 1990;345:229-33.
- Storry JR, Olsson ML. The ABO blood group system revisited: A review

Manimekalai and Kanna: Risk Factors in ABO Blood Group of Coronary Artery Disease

- and update. *Immunohematology* 2009;25:48-59.
5. Lowe JB. The blood group-specific human glycosyltransferases. *Baillieres Clin Haematol* 1993;6:465-92.
 6. Franchini M, Liumbruno GM. ABO blood group: Old dogma, new perspectives. *Clin Chem Lab Med* 2013;51:1545-53.
 7. Platt D, Muhlberg W, Kiehl L, Schmitt-Ruth R. ABO blood group system, age, sex, risk factors and cardiac infarction. *Arch Gerontol Geriatr* 1985;4:241-9.
 8. Langman MJ, Elwood PC, Foote J, Ryrie DR. ABO and Lewis blood-groups and serum-cholesterol. *Lancet* 1969;2:607-9.
 9. Oliver MF, Geizerova H, Cumming RA, Heady JA. Serum-cholesterol and ABO and rhesus blood-groups. *Lancet* 1969;2:605-7.

How to cite this article: Manimekalai P, Kanna SS. Risk Factors in ABO Blood Group for Coronary Artery Disease. *Int J Sci Stud* 2018;6(5):1-4.

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

Comprehensive Skin Care Regimen of Moisturizer with Broad-Spectrum Sunscreen as an Adjuvant in Management of Acne (CHARISMA)

Shabir Ahmed Bhat¹, Gaurav A. Deshmukh², Dhiraj S. Dhoot³, Hanmant Barkate⁴

¹Consultant Dermatologist, Department of Dermatology and Venereal Diseases, JK Health Services, Anantnag, Jammu and Kashmir, India, ²Medical Advisor, Department of Pharmacology, Medical Services Glenmark Pharmaceuticals Ltd., Mumbai, Maharashtra, India, ³Senior Manager, Department of Paediatrics, Medical Services Glenmark Pharmaceuticals Ltd., Mumbai, Maharashtra, India, ⁴Vice-President, Department of Pharmacology, Medical Services Glenmark Pharmaceuticals Ltd., Mumbai, Maharashtra, India

Abstract

Introduction: Both acne and topical anti-acne therapies are associated with cutaneous reactions, thereby jeopardizing patient adherence, and thus compromising treatment efficacy. In addition, many acne therapies are associated with thinning of skin and predispose to ultraviolet damage which has been implicated in acne flares. Use of photoprotecting moisturizer may help to alleviate these reactions thus benefiting the patients.

Methods: This was a multicenter, open-label retrospective questionnaire-based survey designed primarily to assess the cutaneous tolerability, overall performance, and cosmetic acceptability of Episoft AC, a moisturizer with broad-spectrum sunscreen activity as an adjuvant in the management of acne. Each doctor was given a survey questionnaire booklet containing survey forms. Patients were evaluated for their skin tolerability by analyzing the responses from both patients (subjective assessment) and investigator (objective assessment).

Results: A total of 100 doctors participated in a survey involving 340 patients. There was a significant improvement in all the parameters of facial skin tolerability (subjective assessment), i.e., itching, burning, stinging, and tightness at day 28 compared to a baseline which was maintained until day 56 with continued therapy with Episoft AC. Similarly, objective facial skin tolerability assessments determined by the investigator showed significant improvement in dryness and erythema at day 28 relative to a baseline which was maintained until day 56 with continued use of Episoft AC. Majority of patients felt that the treatment regimen was easy to use, were satisfied with the treatment regimen, and would continue to use it.

Conclusion: The results of this survey signify that incorporating a comprehensive skin care regimen of moisturizer with broad-spectrum sunscreen in the overall management plan of acne may help in improvement of cutaneous tolerability and overall patient satisfaction with acne treatment.

Key words: Moisturizer, Sunscreen, Acne

INTRODUCTION

Acne is a chronic inflammatory disease of the pilosebaceous unit that affects almost all teenagers between the ages of 15 and 17 years.^[1] Clinical features include

open and closed comedones, papules, and pustules.^[2] Increased sebum production, follicular hyperkeratinization, propionibacterium acnes proliferation, and inflammation are four main processes in the pathogenesis of the disease.^[3]

Multiple therapies, both topical and systemic are available for the treatment of acne vulgaris (AV).^[4,5] Even though anti-acne therapies are efficacious and safe in the management of acne, one of the major limitations of topical therapies for AV is the relatively high potential for cutaneous reactions characterized by signs (erythema, dryness, roughness, etc.) and symptoms (stinging, burning, etc.).^[6-9] These reactions can result from direct effects of

Access this article online



www.ijss-sn.com

Month of Submission : 06-2018
Month of Peer Review : 07-2018
Month of Acceptance : 08-2018
Month of Publishing : 08-2018

Corresponding Author: Dr. Gaurav A. Deshmukh, Corporate Enclave, Glenmark Pharmaceutical Ltd, B. D. Sawant Road, Andheri East, Mumbai - 400 099, Maharashtra, India. Phone: 7977659978. E-mail: dr.gaurav.deshmukh@glenmarkpharma.com

active ingredient or acne itself leading to epidermal barrier damage.^[10-13] In addition, many acne therapies are associated with thinning of the skin and predispose to ultraviolet (UV) damage which has been implicated in acne flares.^[14]

Non-adherence to the treatment regimen is most common problem associated with these undesirable effects of acne and acne therapies leading to suboptimal therapeutic outcomes. Many patients lose follow-up with dermatologists after experiencing skin irritation which further reduces the efficacy of treatment regimen and recurrence of acne.^[15]

These undesirable dermatological effects can be taken care by moisturizers and photoprotectants which may be beneficial for AV patients.^[14-16] These moisturizers and photoprotectants should be non-comedogenic, devoid of skin irritants and compatible with therapeutic regimens.^[16] However, many acne patients neither find it intuitive nor consider it necessary to use a moisturizer or photoprotection as part of their skin care regimen, because of conventional beliefs. Therefore, it is crucial to counsel acne patients regarding both moisturization and sun protection.^[16]

Numerous skin care moisturizers are available in the market; however, there is a paucity of studies that have evaluated their efficacy and compatibility specifically in AV patients especially in a country like India. Consequently, AV patients are left with multiple over-the-counter skin care products to complement their treatment, but in many cases, these products may magnify the side effects of treatment regimens exacerbating the patient's AV.

Hence, considering these scenarios, we conducted this survey with the aim to assess the cutaneous tolerability, overall performance, and cosmetic acceptability of Episoft AC, a photoprotecting moisturizer specifically designed for acne-prone skin as an adjuvant skin care regimen in management acne.

MATERIALS AND METHODS

This was a multicenter, open-label retrospective questionnaire-based survey designed primarily to assess the cutaneous tolerability, overall performance, and cosmetic acceptability of Episoft AC, a moisturizer with broad-spectrum sunscreen activity as an adjuvant in the management of acne. The survey was conducted in compliance with the Declaration of Helsinki and current Good Clinical Practice guidelines.

Dermatologists involved in the management of AV were identified through "SCRIP intelligence" database. Among these 100 doctors who were maintaining the patients' clinical record including the sensorial profile of cosmetic

products were selected across 4 zones (east, south, west, and north) each by convenient sampling to have a uniform representation of population across the country.

Each doctor was given a survey questionnaire booklet containing survey forms. The questionnaires' booklets were collected after the end of survey period, and data from all the patients were assessed to evaluate cutaneous tolerability, overall performance, and cosmetic acceptability of Episoft AC. Each patient was evaluated at baseline (day 0), day 28, and day 56. The total survey period was from July 2017 to December 2017.

Patients more than 12 years of age with mild to moderate acne on stable anti-acne therapy along with Episoft AC, with facial skin symptoms (itching, burning, erythema, dryness, etc.) and keeping monthly follow-up with dermatologists were included in the survey. Patients with severe acne (presence of nodules and cysts) were excluded from the survey. Patients who changed their anti-acne therapy or who underwent any dermatological procedures (e.g., chemical peeling, and lasers) during the survey period were also excluded from the final analysis. Individuals with any visible dermatological disorder or abnormal skin pigmentation that may have interfered with subjective or objective assessments were also excluded from the final analysis.

Skin Tolerability Assessment

Skin tolerability assessment was done by analyzing the responses from both patients (subjective assessment) and investigator (objective assessment). For subjective assessment, data regarding various symptoms such as itching, burning, stinging, and skin tightness experienced by the patients during the previous 8 weeks were analyzed. Similarly for objective assessment, data regarding visible signs such as erythema, dark spots, dryness, and roughness evaluated by the investigators during the previous 8 weeks were analyzed. Each parameter was measured on 4 points Likert Scale (0–3) ranging from no evidence of any facial skin symptom to severe facial skin symptom. The parameters were evaluated at baseline, on days 28 and 56. All the patients were further evaluated for satisfaction with the treatment regime by analyzing the questionnaires regarding sensorial parameters at the end of 8 weeks of therapy.

Safety Assessment

Safety assessment was done by analyzing all the reported adverse events during the survey period.

RESULTS

A total of 120 doctors participated in the survey, from whom a total of 480 completed survey forms were collected at the end of 6 months period. Out of 480 forms collected, 340 forms fulfilling all the inclusion criteria were

considered for further evaluation. The average age of the population was 17.6 years. Out of total 340 patients evaluated, 56% ($n = 190$) were male while 44% ($n = 150$) were female patients. All the patients were taking some form of topical therapy for management of their acne. In this survey, combination of adapalene and benzoyl peroxide was most commonly prescribed anti-acne therapy (43% $n = 146$) followed by a combination of adapalene and clindamycin which was prescribed to 37% ($n = 129$) patients. Less commonly prescribed anti-acne therapies were combination of clindamycin and nicotinamide, monotherapy with either tretinoin or adapalene.

Subjective Assessment

Improvement in mean facial tolerability score was reported by each patient during each visit relative to baseline. There was a significant improvement in all the parameters of facial skin tolerability, i.e., itching, burning, stinging, and tightness at day 28 compared to baseline which was maintained until day 56 with continued therapy with Episoft AC [Figure 1].

Objective Assessment

Objective facial skin tolerability assessments determined by the investigator showed improvement in mean scores relative to baseline for erythema, dark spots, dryness, and roughness during each visit. There was a significant improvement in dryness and erythema at day 28 relative to a baseline which was maintained until day 56 with continued use of Episoft AC [Figure 2].

Subject Satisfaction

Patients satisfaction with the treatment regime was assessed by analyzing the data regarding sensorial parameters evaluated by the investigators. Majority of patients felt that the treatment regimen was easy to use, were satisfied with the treatment regimen, and would continue to use it. Figure 3 depicts the data from subject satisfaction questionnaire.

In this survey, more than 90% of patients reported very good or excellent adherence to treatment. None of the patient reported any adverse event related to survey drug. There were no discontinuations from the survey related to adverse events including skin tolerability reactions.

DISCUSSION

One of the major limitations of topical therapies for AV is the relatively high potential for cutaneous reactions characterized by signs (erythema, dryness, roughness, etc.) and symptoms (stinging, burning, etc.).^[6-9] These reactions can result from direct effects of active ingredient or acne itself leading to epidermal barrier damage.^[10-13] Thiboutot *et al.* in their review highlighted

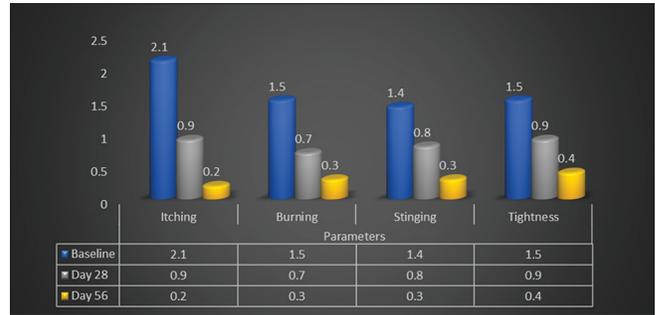


Figure 1: Mean facial skin tolerability assessment (subjective)

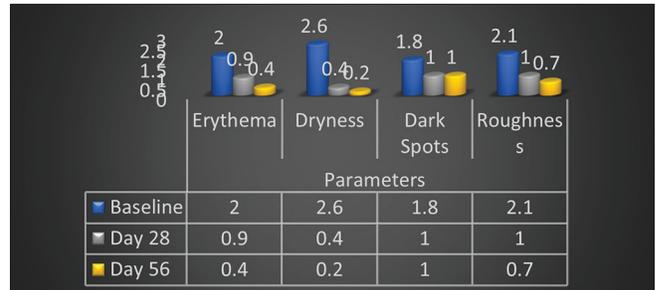


Figure 2: Mean facial skin tolerability assessment (objective)

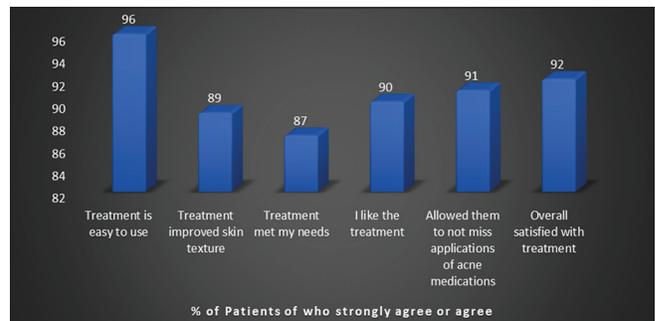


Figure 3: Subject satisfaction questionnaire at week 8: Regimen satisfaction

that AV itself is associated with some inherent epidermal barrier impairments.^[10] Similarly, Thiboutot and Del Rosso,^[10] Del Rosso and Brandt^[17] highlighted the role of anti-acne therapy in epidermal barrier damage. Trautinger *et al.* in their review reported that many acne therapies are associated with phototoxicity and increased risk of UV damage.^[18]

Hence, focusing on photoprotection and moisturization are very important adjuvant skin care strategies to a complete anti-acne regimen that serves to optimize therapeutic outcomes for the patient. This is especially true in those using topical AV therapy and in those treated with oral antibiotics associated with increased risk of photosensitivity. Various clinical trials have shown the effectiveness of photoprotection and moisturizers to mitigate the cutaneous reactions associated with acne.^[14,15,19,20]

The moisturizer component assists in mitigating epidermal barrier impairment and its related skin sensitivity and irritation.^[21-23] Both the moisturizer and sunscreen components can assist in the prevention of residual hyperpigmentation, which can result from skin irritation and inflammation, especially in individuals with darker skin.^[23,24] The sunscreen component may also protect against photosensitivity induced by UV radiation in patients using certain Rx medications for AV.^[23-25]

It must be noted that both moisturizers and sunscreen can cause irritation and can be comedogenic leading to flare up of acne in some patients, hence while choosing these components dermatologist must be sure that the adjuvant therapy should be non-comedogenic.^[17,23,26,27] Episoft AC is one such novel photoprotecting moisturizer which has shown to be non-comedogenic and did not exacerbate or worsen AV with continued use, including in subjects using a variety of Rx products for AV.

We conducted this survey to find out cutaneous tolerability, overall performance, and cosmetic acceptability of Episoft AC as adjuvant skin care in the management of acne. In this survey continued use of Episoft AC was associated with improvement in mean facial skin tolerability scores as determined by both patients and dermatologists. There was a significant improvement in both signs such as erythema, dryness, and symptoms such as itching and burning associated with anti-acne treatment during the survey.

These results were in accordance with earlier results reported by various authors. Bowe and Kircik in their study highlighted the importance of photoprotection and moisturization in the management of acne. Authors concluded that moisturizer with broad-spectrum sunscreen was associated with better therapeutic outcomes in the management of acne.^[14] Laquieze *et al.* reported that Retinoid-induced skin irritation can be relieved by the regular use of a gentle moisturizing cream as an adjunctive treatment.^[19] Kircik *et al.* highlighted that a comprehensive skin care regimen of moisturizer and sunscreen may maximize efficacy and tolerability and contribute to the armamentarium for treating both photodamage and acne at the same time.^[20]

All the patients participated in the survey were highly satisfied with the treatment regimen, with the following percent of subjects noting specific observations with Episoft AC. 96% - easy to use, 89% - improvement in skin texture, 87% - treatment met their need, 91% - allowed them to not to miss their acne medication, and 92% - overall satisfied with Episoft AC as an adjuvant. These results were also in accordance with published reports from various investigators.^[17,23]

Another important observation seen in this survey was very good or excellent adherence to entire treatment regimen over a period of 8 weeks which is very important since poor adherence to treatment is one of the most common problems associated with acne management. Multiple clinical trials by Gollnick *et al.*,^[28] Yentzer *et al.*,^[29] Koo *et al.*,^[30] and Tan *et al.*^[31] reported that one of the central reasons for nonadherence is dryness and irritation associated with topical acne treatment. In our survey, Episoft AC was associated with improvement in signs and symptoms of cutaneous irritation which may have resulted in increased adherence to treatment. Hayashi *et al.* reported similar results and concluded that “the concomitant use of a moisturizer with adapalene from the beginning of treatment did not affect its therapeutic effects and helped to improve adherence to treatment with adapalene.”^[32]

In this survey Episoft AC was well tolerated by the patients, none of the patients reported any adverse event related to Episoft AC. There were no discontinuations from the survey because of adverse events including skin tolerability reactions.

This survey has certain limitations. Due to the observational and retrospective design of the survey, the possibility of selection bias cannot be ruled out. Long-term prospective comparative studies to address the shortcomings of the present survey are warranted.

CONCLUSION

The results of this survey signify that incorporating a comprehensive skin care regimen of moisturizer with broad-spectrum sunscreen in the overall management plan of acne may help in improvement of cutaneous tolerability and overall patient satisfaction with acne treatment.

ACKNOWLEDGMENTS

We would like to acknowledge the contribution of the doctors all over India who provided data for this survey.

REFERENCES

1. Williams HC, Dellavalle RP, Garner S. Acne vulgaris. *Lancet* 2012;379:361-72.
2. Katsambas A, Dessinioti C. New and emerging treatments in dermatology: Acne. *Dermatol Ther* 2008;21:86-95.
3. Kurokawa I, Danby FW, Ju Q, Wang X, Xiang LF, Xia L, *et al.* New developments in our understanding of acne pathogenesis and treatment. *Exp Dermatol* 2009;18:821-32.
4. Thiboutot DM, Dréno B, Abanmi A, Alexis AF, Araviiskaia E, Barona Cabal MI, *et al.* Practical management of acne for clinicians: An international consensus from the global alliance to improve outcomes in acne. *J Am Acad Dermatol* 2018;78:S1-S23.e1.
5. Zaenglein AL, Pathy AL, Schlosser BJ, Alikhan A, Baldwin HE, Berson DS,

- et al.* Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol* 2016;74:945-7.
6. Thielitz A, Gollnick H. Topical retinoids in acne vulgaris: Update on efficacy and safety. *Am J Clin Dermatol* 2008;9:369-81.
 7. Gold LS, Tan J, Cruz-Santana A, Papp K, Poulin Y, Schlessinger J, *et al.* A North American study of adapalene-benzoyl peroxide combination gel in the treatment of acne. *Cutis* 2009;84:110-6.
 8. Galvin SA, Gilbert R, Baker M, Guibal F, Tuley MR. Comparative tolerance of adapalene 0.1% gel and six different tretinoin formulations. *Br J Dermatol* 1998;139 Suppl 52:34-40.
 9. Kosmadaki M, Katsambas A. Topical treatments for acne. *Clin Dermatol* 2017;35:173-8.
 10. Thiboutot D, Del Rosso JQ. Acne vulgaris and the epidermal barrier: Is acne vulgaris associated with inherent epidermal abnormalities that cause impairment of barrier functions? Do any topical acne therapies alter the structural and/or functional integrity of the epidermal barrier? *J Clin Aesthet Dermatol* 2013;6:18-24.
 11. Del Rosso JQ, Levin J. The clinical relevance of maintaining the functional integrity of the stratum corneum in both healthy and disease-affected skin. *J Clin Aesthet Dermatol* 2011;4:22-42.
 12. Draelos ZD, Ertel KD, Berge CA. Facilitating facial retinization through barrier improvement. *Cutis* 2006;78:275-81.
 13. Yamamoto A, Takenouchi K, Ito M. Impaired water barrier function in acne vulgaris. *Arch Dermatol Res* 1995;287:214-8.
 14. Bowe WP, Kircik LH. The importance of photoprotection and moisturization in treating acne vulgaris. *J Drugs Dermatol* 2014;13:s89-94.
 15. Feldman SR, Chen DM. How patients experience and manage dryness and irritation from acne treatment. *J Drugs Dermatol* 2011;10:605-8.
 16. Bikowski J. The use of therapeutic moisturizers in various dermatologic disorders. *Cutis* 2001;68:3-11.
 17. Del Rosso JQ, Brandt S. The role of skin care as an integral component in the management of acne vulgaris: Part 2: Tolerability and performance of a designated skin care regimen using a foam wash and moisturizer SPF 30 in patients with acne vulgaris undergoing active treatment. *J Clin Aesthet Dermatol* 2013;6:28-36.
 18. Trautinger F, Passeron T, Moyal D. Useful photoprotection in dermatological practice. *EMJ Dermatol* 2016;4:32-8.
 19. Laquieze S, Czernielewski J, Rueda MJ. Beneficial effect of a moisturizing cream as adjunctive treatment to oral isotretinoin or topical tretinoin in the management of acne. *J Drugs Dermatol* 2006;5:985-90.
 20. Kircik LH, Dahl A, Yatskayer M, Raab S, Oresajo C. Safety and efficacy of two anti-acne/anti-aging treatments in subjects with photodamaged skin and mild to moderate acne vulgaris. *J Drugs Dermatol* 2012;11:737-40.
 21. Del Rosso JQ. The role of skin care as an integral component in the management of acne vulgaris: Part 1: The importance of cleanser and moisturizer ingredients, design, and product selection. *J Clin Aesthet Dermatol* 2013;6:19-27.
 22. Goodman G. Cleansing and moisturizing in acne patients. *Am J Clin Dermatol* 2009;10 Suppl 1:1-6.
 23. Del Rosso JQ, Gold M, Rueda MJ, Brandt S, Winkelman WJ. Efficacy, safety, and subject satisfaction of a specified skin care regimen to cleanse, medicate, moisturize, and protect the skin of patients under treatment for acne vulgaris. *J Clin Aesthet Dermatol* 2015;8:22-30.
 24. Drucker AM, Rosen CF. Drug-induced photosensitivity: Culprit drugs, management and prevention. *Drug Saf* 2011;34:821-37.
 25. Tashtoush BM, Jacobson EL, Jacobson MK. UVA is the major contributor to the photodegradation of tretinoin and isotretinoin: Implications for development of improved pharmaceutical formulations. *Int J Pharm* 2008;352:123-8.
 26. Dessinioti C, Antoniou C, Katsambas A. Acneiform eruptions. *Clin Dermatol* 2014;32:24-34.
 27. Chularojanamontri L, Tuchinda P, Kulthanan K, Pongparit K. Moisturizers for acne: What are their constituents? *J Clin Aesthet Dermatol* 2014;7:36-44.
 28. Gollnick H, Cunliffe W, Berson D, Dreno B, Finlay A, Leyden JJ, *et al.* Management of acne: A report from a global alliance to improve outcomes in acne. *J Am Acad Dermatol* 2003;49:S1-37.
 29. Yentzer BA, Ade RA, Fountain JM, Clark AR, Taylor SL, Fleischer AB Jr, *et al.* Simplifying regimens promotes greater adherence and outcomes with topical acne medications: A randomized controlled trial. *Cutis* 2010;86:103-8.
 30. Koo J. How do you foster medication adherence for better acne vulgaris management? *Skinmed* 2003;2:229-33.
 31. Tan JK, Balagurusamy M, Fung K, Gupta AK, Thomas DR, Sapra S, *et al.* Effect of quality of life impact and clinical severity on adherence to topical acne treatment. *J Cutan Med Surg* 2009;13:204-8.
 32. Hayashi N, Kawashima M. Study of the usefulness of moisturizers on adherence of acne patients treated with adapalene. *J Dermatol* 2014;41:592-7.

How to cite this article: Bhat SA, Deshmukh GA, Dhoot DS, Barkate H. Comprehensive Skin Care Regimen of Moisturizer with Broad-Spectrum Sunscreen as an Adjuvant in Management of Acne (CHARISMA). *Int J Sci Stud* 2018;6(5):5-9.

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

Role of Magnetic Resonance Venography, Diffusion-Weighted Imaging, and Gradient-Recalled Echo in Cerebral Sinovenous Thrombosis

Nadeem Ahmed¹, Alle Praveen Kumar², Swapna Chouhan³, Shaik Ismail⁴, Uzma Afreen⁴

¹Professor, Department of Radiology, Osmania General Hospital, Hyderabad, India, ²Assistant Professor, Department of Radiology, Mahatma Gandhi Memorial Hospital, Warangal, India, ³Associate Professor, Department of Radiology, Mahatma Gandhi Memorial Hospital, Warangal, India, ⁴Postgraduate, Department of Radiology, Mahatma Gandhi Memorial Hospital, Warangal, India

Abstract

Background: Cerebral venous thrombosis (CVT) is a cause of stroke with inconspicuous pathophysiological properties that differ from arterial stroke. It is an elusive diagnosis because of its non-specific presentation and its subtle imaging findings. Diagnosis is often missed on initial imaging. Patients with CVT often make dramatic recoveries after effective therapies including anticoagulants and intravenous thrombolysis. Accurate diagnosis is difficult as conventional magnetic resonance imaging (MRI) which cannot differentiate between cytotoxic and vasogenic edema. The use of magnetic resonance venography (MRV), diffusion-weighted imaging (DWI), and gradient echo (GRE) combines the strengths of individual imaging sequences in improving diagnostic yield. Accurate and timely imaging diagnosis is essential because it facilitates patient triage, guides clinical management, and helps determine patient prognosis. Diffusion-weighted MRI (DWI) has been reported to detect early ischemic damage (cytotoxic edema) as bright high-signal intensity (SI) and vasogenic edema as heterogeneous SI.

Aim: The aim of this study was as follows: (1) To study the extent of venous sinus involvement and associated cerebral parenchymal changes on MRV, (2) to study the pattern of diffusion-weighted images and apparent diffusion coefficient (ADC) mapping in patients with CVT, (3) to study the role of GRE in patients with CVT, and (4) to characterize the clinical applications of DWI in CVT.

Methods: A study was conducted on 20 patients diagnosed to have CVT on imaging, over the period of 6 months.

Results: Imaging analyses of 20 patients (9 males, 11 females, and age range 19–65 years) were done. Thrombus on MRV was seen as loss of high-flow signal from the sinus in cases of total occlusion of the sinus and frayed or patchy flow signal in the cases of non-occlusive thrombus. 10 patients with hemorrhagic infarct showed heterogeneous SI on DWI and blooming on GRE sequence. Five patients with non-hemorrhagic infarct showed multifocal high-signal intensities in DWI with variable ADC values and no blooming on GRE sequence. Two patients with intracerebral hematoma showed areas of heterogeneous signals on DWI with blooming on GRE sequence, corresponding ADC values were variable. Two patients with no parenchymal changes and one patient with chronic venous thrombosis presented with benign intracranial hypertension.

Conclusions: MRV, DWI, and GRE can be used to evaluate the extent of thrombus, differentiate between types of edema, detect intracerebral hematoma, hemorrhagic and non-hemorrhagic infarcts, and give time-saving information for early diagnosis of CVT.

Key words: Cerebral venous thrombosis, Diffusion-weighted imaging, Gradient echo, Magnetic resonance venography

INTRODUCTION

Cerebral venous thrombosis (CVT) differs from arterial infarction in several ways. First, the clinical presentation

is variable and ranging from headache, raised intracranial pressure to severe multifocal deficits, seizures, and coma.^[1] Headache is the most common presentation, occurring in nearly 90% of cases. The headache is usually non-focal, often slowly increasing in severity over several days to weeks. Its main mechanisms of pathophysiology are the breakdown of the blood–brain barrier and the coexistence of cytotoxic and vasogenic edema. Rother *et al.*^[2] summarized the mechanisms: (1) Increased pressure in superior sagittal sinus results in reduced capillary perfusion pressure^[3] and increased cerebral blood volume,^[4] (2) obstruction of venous flow leads to increased intracranial

Access this article online



www.ijss-sn.com

Month of Submission : 06-2018
Month of Peer Review : 07-2018
Month of Acceptance : 08-2018
Month of Publishing : 08-2018

Corresponding Author: Dr. Alle Praveen Kumar, Assistant Professor, Department of Radiology, Mahatma Gandhi Memorial Hospital, Mattewada, Warangal, Telangana 506007, India. Phone: 9666060506, E-mail: allepravi@gmail.com.

pressure and blood–brain barrier disruption, resulting in decreased cerebral blood flow,^[5] (3) the net capillary filtration increases, leading to progressive cerebral edema, and (4) intracerebral and subarachnoid hemorrhage additionally compromising the brain tissue.^[6]

There have been a few case reports on the application of diffusion-weighted imaging (DWI) in patients with CVT.^[7-9] These reports revealed that the most striking feature of DWI findings was that reversible apparent diffusion coefficient (ADC) changes (decrease^[7,8] or increase^[9]) were evident during the acute period of CVT. More recently, various DWI results have been reported^[10,11] such as heterogeneous findings and the possibility that cytotoxic edema is a feature of CVT. We report various DWI findings in CVT and evaluate the prognostic value of DWI. Furthermore, the mechanisms of venous stroke were characterized by analyzing ADC maps.

MATERIALS AND METHODS

This prospective study was performed on 20 patients diagnosed to have CVT over the period of 6 months, from January to June 2018, in the Department of Radiodiagnosis of MGM Hospital, Warangal, Telangana, India.

After an informed consent was taken, patients in this study were scanned with 1.5 T *magnetic resonance imaging* (MRI) (GE 1.5T) in the department of radiodiagnosis and examined with the following sequences:

- T1- and T2-weighted sequence.
- Fluid-attenuated inversion recovery (FLAIR) sequence.
- DWI sequence with corresponding ADC mapping.
- Gradient echo (GRE) sequence.
- 3D time-of-flight imaging sequence.

ADC values were calculated by the software and then displayed as a parametric map that reflected the degree of diffusion of water molecules through different tissues. Then, ADC measurements were recorded for a specified region by drawing regions of interest on the ADC map. ADC values of the region of interest were compared with ADC values of the normal brain parenchyma.

Role of DWI with ADC mapping is to distinguish the type of edema, GRE to diagnose the presence of any bleed and MR venography (MRV) to determine the extent of thrombus are also evaluated.

Inclusion Criteria

Any patient diagnosed to have CVT on computed tomography or MRI.

Exclusion Criteria

All patients with metallic implants and pacemakers and claustrophobic patients are excluded from the study.

RESULTS

A total of 20 patients who were diagnosed with CVT on imaging are included in the present study [Table 1].

In the present study, the female: male ratio is 1.2:1.

The peak incidence of CVT is seen in the age group of 21–40 years in both males and females (55.5% and 45.4%, respectively) [Table 2].

Headache was the most common symptom seen in 6 patients (30%), the next common clinical feature being seizures in 5 patients (25%) followed by hemiparesis in 4 patients (20%) [Table 3].

Hemorrhagic infarct was the most common associated manifestation seen in 10 patients (50%) followed by non-hemorrhagic infarct in 5 patients (25%), intracerebral

Table 1: Sex-wise distribution in patients with CVT

Sex	Number of cases (%)
Male	9 (45)
Female	11 (55)
Total	20 (100)

CVT: Cerebral venous thrombosis

Table 2: Sex-wise and age-wise distribution in patients with CVT

Age (years)	Males	Cases %	Females	Cases %	Total number of cases
0–20	0	0	2	18.1	2
21–40	5	55.5	5	45.4	10
41–60	2	22.2	3	27.2	5
>61	2	22.2	1	9.0	3
Total	9	100	11	100	20

CVT: Cerebral venous thrombosis

Table 3: Distribution of patients based on clinical history in patients with CVT

Clinical feature	Cases (%)
Headache	6 (30)
Hemiparesis	4 (20)
Giddiness	2 (10)
Seizures	5 (25)
Vomiting	1 (5)
Coma	1 (5)
Raised ICT	1 (5)
Total	20 (100)

CVT: Cerebral venous thrombosis, ICT: Intracranial tension

hematoma in 2 patients (10%), without parenchymal changes in 2 patients (10%), and chronic venous thrombosis with benign intracranial hypertension in 1 patient (5%) [Table 4].

Transverse sinus is most commonly involved in dural venous thrombosis which is seen in 6 patients (30%). The next most common sinus involved is superior sagittal sinus in 4 patients (20%) followed by straight sinus in 2 patients (10%) [Table 5].

Coexistence of cytotoxic and vasogenic edema was seen in 10 patients (50%), vasogenic edema in 4 patients (20%), and cytotoxic edema in 3 patients (15%); no edema was seen in 3 patients (15%) [Table 6].

DISCUSSION

Cerebral venous infarction is uncommon form of stroke, secondary to CVT. CVT is the occlusion of venous channels in the cranial cavity including dural venous thrombosis, superficial vein thrombosis, and deep cerebral vein thrombosis. They often exist together and

Table 4: Distribution of patients with CVT depending on associated manifestations

Associated manifestation	Number of cases (%)
Hemorrhagic infarct	10 (50)
Non-hemorrhagic infarct	5 (25)
Intracerebral hematoma	2 (10)
Without parenchymal changes	2 (10)
Chronic venous thrombosis with benign intracranial hypertension	1 (5)

CVT: Cerebral venous thrombosis

Table 5: Distribution of sinuses involvement in patients with CVT

Sinus	Number of cases (%)
Superior sagittal sinus	4 (20)
Inferior sagittal sinus	1 (5)
Straight sinus	2 (10)
Transverse sinus	6 (30)
Cortical veins	1 (5)
Cavernous sinus	2 (10)
Vein of Galen	2 (10)
Sigmoid sinus	1 (5)
Internal jugular vein	1 (5)

CVT: Cerebral venous thrombosis

Table 6: Distribution of pattern of edema in patients with CVT (Cerebral venous thrombosis)

Types of edema	Number of cases (%)
Cytotoxic edema	3 (15)
Vasogenic edema	4 (20)
Cytotoxic and vasogenic edema	10 (50)
No edema	3 (15)

the clinical presentation among them is very similar and nonspecific.

Correct diagnosis depends on neuroimaging. The diagnostic imaging features can be subtle.^[12] This disorder is potentially lethal but treatable, often underdiagnosed in both clinical and radiologic in routine practice. MRV, GRE, and DWI with ADC mapping are a useful method to establish the diagnosis.

These images may reveal either direct sign (visualization of intraluminal clot) or indirect signs (parenchymatous change and intracranial hemorrhage). Early diagnosis and effective treatment will improve the prognosis of the patient.

Parenchymal hemorrhages were seen in 17 patients with CVT. James *et al.* concluded in a study in 2006 that the mechanism of hemorrhage is multifactorial. Hemorrhage may be because of continued arterial perfusion in areas of cell death, as can be seen at reperfusion in arterial ischemia. Elevation of venous pressure beyond the limit of venous wall is also believed to be a cause.^[13]

Favrole *et al.* found that the movements of water molecules are restricted within the venous clot according to the stage of thrombus formation in CVT. Some authors have suggested that the migration of fibroblasts into the clot and incorporation of collagen may render the fibrin less accessible to fibrinolytic enzymes.^[14] Others say that this resistance may be related mainly to an abnormal fibrin polymerization.^[15]

DWI and ADC measurement of intraparenchymal hematoma were reported by Atlas *et al.*, but in our study, ADC values of hematoma were avoided because the determining factors of ADC values in hematoma may be due to paramagnetic effect of the methemoglobin rather than the true restriction of water movement.^[16]

CVT is more common in women than in men. In a study of 110 cases, Ameri and Bousser reported a female-to-male ratio of 1.29:1.

Ferro *et al.* made the same observations in a prospective study from 1995 to 1998. This females preponderance is probably due to specific causes such as oral contraceptives, pregnancy, and puerperium.^[17] This preponderance of females did not exist before the era of the oral contraceptive pills. Female predominance was also seen in our study where female-to-male ratio was 1.2:1.

Carrol *et al.* reported seizures in 29.83% of patients, Srinivasan and Natarajan found seizures in 66% of patients.^[18,19] Mehta *et al.* found seizures in 26.6%. In our study, 25% of patients had convulsion of which generalized tonic-clonic type

was the most common. Our study had 20% of patients with hemiplegia. Hemiplegia was the most common form noticed in various series.^[20] Headache was the most common symptom seen in our study which was seen in 6 patients (30%) Khaladkar *et al.* found that the most common sinus involved was superior sagittal sinus with almost equal involvement of transverse and sigmoid sinuses, and the deep venous system was affected in 17.5% of patients, and superficial venous system affected in 2.5% of cases. Most of the patients had involvement of more than one sinus.^[21]

The most common association was noticed between superior sagittal sinus and transverse sinuses. Greiner *et al.* found that in veno-occlusive stroke, the superior sagittal sinus followed by transverse, sigmoid, and straight was generally involved.^[22] In our study, transverse sinus was the most common sinus involved in 30% of cases followed by superior sagittal sinus in 20% of cases, straight sinus in 10%, and sigmoid sinus in 5% of cases.

CONCLUSION

Cerebral venous sinus thrombosis is a frequently misdiagnosed condition because of its variability of clinical symptoms and signs. It is very often missed on initial imaging. All age groups can be affected. The prognosis of cerebral venous sinus thrombosis depends on early and accurate diagnosis of CVT.

Our study shows the importance of role of MRI with MRV, DWI with ADC mapping, and gradient-recalled echo in early and precise diagnosis of CVT.

Thrombus on MRV was seen either as loss of high-flow signals from the sinus in cases of total occlusion of the sinus or frayed or patchy flow signal in non-occlusive thrombus. MRV is also useful for demonstrating the extent of cerebral venous system involvement, recanalization of thrombosis in venous sinuses.

DWI with ADC maps can be used to differentiate between vasogenic and cytotoxic edema for tissue viability and to gives information about stages and diagnostic clues in CVT.

Although both vasogenic and cytotoxic edema are identified in the early phase of CVT, vasogenic edema develops more frequently. Our study showed coexistence of increased and decreased ADCs in hemorrhagic infarcts. Increase in ADC suggests predominance of vasogenic edema and decrease in ADC suggests cytotoxic edema.

Gradient-recalled echo is an important technique that detects early hemorrhagic transformations within

acute infarctions accurately. It also detects chronic microbleeds and intracerebral hematomas, thus warning the treating physician about the devastating complication of anticoagulant and revascularization therapies.

Case 1

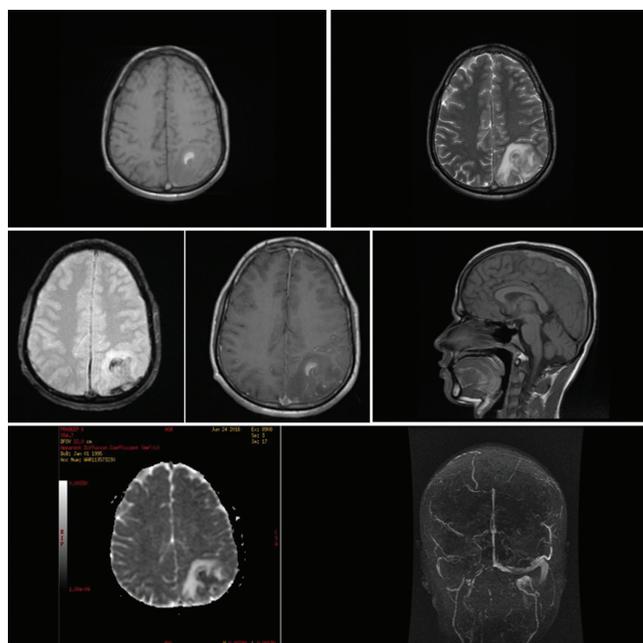
T1, T2, GRE, T1+C, T1 SAGGITAL, DWI, ADC, and MRV

Heterogeneous signal lesion with hyperintense areas in it, which shows blooming on GRE, restricted diffusion on DWI in the left posterior parietal region suggestive of hemorrhagic infarct with vasogenic edema.

Loss of flow void noted in superior sagittal sinus suggestive of superior sagittal sinus thrombosis.

MRV shows superior sagittal sinus and right transverse sinus thrombosis.

On contrast, mild gyral enhancement noted.



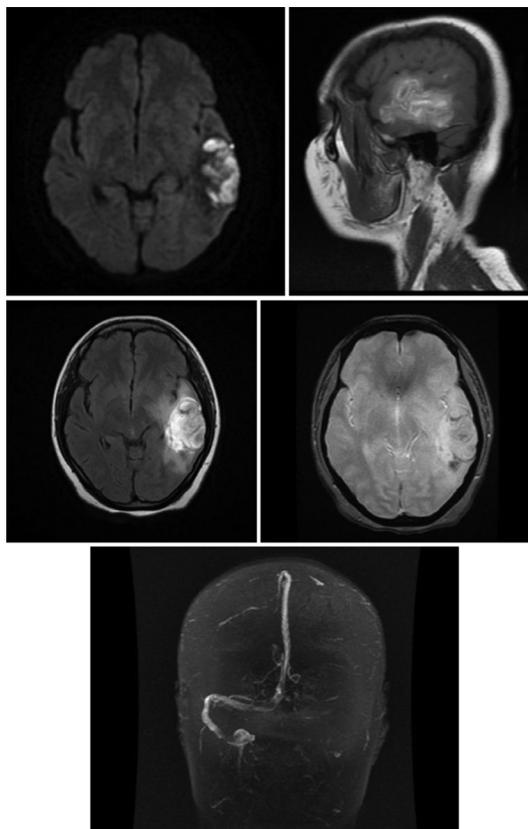
Case 2

T1, T2, FLAIR, GRE, T1 SAGGITAL, DWI, and MRV

T1, T2, and FLAIR hyperintense lesion showing restriction on DWI and blooming areas on GRE in the left temporoparietal convexity noted.

MRV shows the left transverse and sigmoid sinus thrombosis.

Hemorrhagic infarct with vasogenic edema.



REFERENCES

1. Benamer HT, Bone I. Cerebral venous thrombosis: Anticoagulants or thrombolytic therapy. *J Neurol Neurosurg Psychiatry* 2000;69:427-30.
2. Rother J, Waggie K, Van Bruggen N, De crispigny AJ, Moseley ME. Experimental cerebral venous thrombosis: Evaluation using magnetic resonance imaging. *J Cereb Blood Flow Metab* 1996;16:1353-61.
3. Wagner E, Traystman R. Effects of cerebral venous and cerebrospinal fluid pressure on cerebral flow. In: Auer L, Low F, editors. *The Cerebral Veins*. New York: Springer; 1983. p. 223-30.
4. Gotoh M, Ohmoto T, Kuyama H. Experimental study of venous circulatory disturbance by dural sinus occlusion. *Acta Neurochir* 1993;124:120-6.
5. Kurokawa Y, Hashi K, Okuyama T, Uede T. Regional venous ischemia in cerebral venous hypertension due to embolic occlusion of superior sagittal sinus in the rat. *Surg Neurol* 1990;34:390-5.
6. Garcia J. Thrombosis of cerebral veins and sinuses: Brain parenchymal effects. In: Einhaupl K, Kempfski O, Baethmann A, editors. *Cerebral Sinus Thrombosis*. New York: Plenum Press; 1990. p. 27-37.
7. Corvol JC, Oppenheim C, Manai R, Logak M, Dormont D, Samson Y, *et al.* Diffusion-weighted magnetic resonance imaging in a case of cerebral venous thrombosis. *Stroke* 1998;29:2649-52.
8. Manzione J, Newman GC, Shapiro A, Santo-Ocampo R. Diffusion-and perfusion-weighted MR imagings of dural sinus thrombosis. *AJNR Am J Neuroradiol* 2000;21:68-73.
9. Keller E, Flacke S, Urbach H, Schild HH. Diffusion-and perfusion-weighted magnetic resonance imaging in deep cerebral venous thrombosis. *Stroke* 1999;30:1144-6.
10. Ducreux D, Oppenheim C, Vandamme X, Dormont D, Samson Y, Rancurel G, *et al.* Diffusion-weighted imaging patterns of brain damage associated with cerebral venous thrombosis. *AJNR Am J Neuroradiol* 2001;22:261-8.
11. Forbes KP, Pipe JG, Heiserman JE. Evidence for cytotoxic edema in the pathogenesis of cerebral venous infarction. *AJNR Am J Neuroradiol* 2001;22:450-5.
12. Van Gijn J. Cerebral venous thrombosis: Pathogenesis, presentation and prognosis. *J R Soc Med* 2000;93:230-3.
13. Hermier M, Nighoghossian N. Contribution of susceptibility-weighted imaging to acute stroke assessment. *Stroke* 2004;35:1989-94.
14. Favrole P, Guichar JM, Crassard I, Bousser MG, Chabriat H. Diffusion weighted imaging of intravascular clots in cerebral venous thrombosis. *Stroke* 2004;35:199-203.
15. Soria C, Soria J, Mirshahi M, Desvignes P, Bonnet P, Caen JP. Importance of the structure of the clot in thrombolysis. *Ann Biol Clin* 1987;45:207-11.
16. Atlas SW, Dubois P, Singer MB, Lu D. Diffusion measurement in intracranial hematoma: Implications of MR imaging in acute stroke. *Am J Neuroradiol* 2000;21:1190-4.
17. Ferro JM, Lopes MG, Rosas MJ, Femo MA, Fontes J. Long-term prognosis of cerebral vein and dural sinus thrombosis. Results of the venoport study. *Cerebrovasc Dis* 2002;13:272.
18. Carrol JD, Lead D, Lee HA. Cerebral thrombo phlebitis in pregnancy and puerperium. *QJ Med* 1966;35:347-8.
19. Srinivasan K, Natarajan M. Cerebral venous and arterial thrombosis in pregnancy and puerperium. *Neurol India* 1974;22:131-40.
20. Nagaraja D, Taly AB. Puerperal cerebral venous thrombosis. *Prog Clin Neurosci* 1986;16:165-177.
21. Khaladkar SM, Thakkar DK, Thakkar DK, Shrotri H, Kulkarni VM. Cerebral venous sinus thrombosis on MRI: A case series analysis. *Med J DY Patil Univ* 2014;7:296-303.
22. Greiner FG, Takhtani D. *Neuroradiology case of the day*. Superior sagittal sinus thrombosis and infarcts. *Radiographics* 1999;19:1098-101.

How to cite this article: Ahmed N, Kumar AP, Chouhan S, Ismail S, Afreen U. Role of Magnetic Resonance Venography, Diffusion-Weighted Imaging, and Gradient-Recalled Echo in Cerebral Sinovenous Thrombosis. *Int J Sci Stud* 2018;6(5):1-5.

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

Combined Spinal- Epidural in Labor Analgesia: Comparison of Fentanyl Bupivacaine Mixture versus Sufentanil - Bupivacaine Mixture

S Vijay Anand¹, T Kabila Rajee², Saranya Nagalingam³

¹Assistant Professor, Department of Anaesthesiology, Velammal Medical College Hospital and Research Institute, Anuppanadi, Madurai, Tamil Nadu, India, ²Senior Resident, Department of Obstetrics and Gynaecology, Velammal Medical College Hospital and Research Institute, Anuppanadi, Madurai, Tamil Nadu, India, ³Junior Resident, Intensive Care Unit, Velammal Medical College Hospital and Research Institute, Anuppanadi, Madurai, Tamil Nadu, India

Abstract

Background: We conducted a prospective randomized control trial on labor analgesia involving 30 parturient. We evaluated and compared the efficacy of bupivacaine fentanyl (BF) and bupivacaine-sufentanil (BS) administered in combined spinal-epidural for labor analgesia. The time required to achieve fitness for ambulation after intrathecal drug administration was also assessed. 30 parturients who voluntarily opted for labor analgesia were randomly divided into two groups to receive either BF or BS.

Methods: The intrathecal drug solution was bupivacaine (2.5 mg) with either fentanyl (25 µg) or sufentanil (5 µg). This was followed by continuous infusion of 10 ml/h 0.0625% bupivacaine with either fentanyl 2.5 µg/ml or sufentanil 0.5 µg/ml when the intrathecal drug effect wore off. Ambulation was assessed at 30, 45, and 60 min after intrathecal drug administration.

Results: Demographic data and labor characteristics were comparable between the groups, all parturient in both the group had rapid onset of analgesia (3.25 ± 0.29 min in group BF vs. 3.23 ± 0.19 min in group BS). There was motor block following intrathecal drug administration (Modified Bromage score of 1 or 2) in all parturients. The duration of analgesia following intrathecal drug administration was comparable between the two groups (89.29 ± 15.78 min in group BF vs. 87.60 ± 14.47 min in group BS). The epidural drug solution was started when visual analog scale (VAS) pain score exceeded 40. After negative aspiration, bolus of 10 ml of drug solution was given in increments. VAS score, maternal heart rate (HR), blood pressure, saturation, and fetal HR were observed at 5, 10, 20, and 30 min after intrathecal drug administration and every 30 min until epidural was initiated. The duration of the first stage of labor was 218.56 ± 69.56 min in group BF and 211.56 ± 58.96 min in group BS. The duration of the second stage of labor was 54.90 ± 32.27 min in group BF and 51.78 ± 16.71 min in group BS.

Conclusion: Both the combination provided equally efficacious analgesia. The numbers of breakthrough pain episodes were comparable between the groups. The VAS score was comparable between the groups at all intervals during epidural drug infusion. The duration for which epidural drug was administered and the amount of bupivacaine consumed was similar between the two groups. 11 parturient in group BF and 13 in parturient in group BS rated their pain relief as excellent

Key words: Fentanyl, Intrathecal drug, Spinal-epidural anesthesia, Sufentanil, Visual analog scale score

INTRODUCTION

Labor is a physiologic process but associated with the severest form of pain.^[1] Some parturients have rated

pain as severe as amputation of the digit without anesthesia.^[2] Unrelieved labor pain is associated with maternal hyperventilation during uterine contractions and increased oxygen consumption^[3] and excess stress with increased plasma epinephrine and norepinephrine concentration.^[4,5] ACOG and ASA jointly opined that maternal request is sufficient enough indication for the provision of labor analgesia.^[6] Labor analgesia is being provided by various techniques. Nonpharmacological method of providing labor analgesia was comforting but do not provide adequate pain relief.^[7] Pharmacological method of providing labor analgesia depends on

Access this article online



www.ijss-sn.com

Month of Submission : 06-2018
Month of Peer Review : 07-2018
Month of Acceptance : 08-2018
Month of Publishing : 08-2018

Corresponding Author: Dr. Saranya Nagalingam, No. 14, Shanumganathan Visithravanitha Illam, S.K.S. Nagar, Uthangudi, Madurai - 625 107, Tamil Nadu, India. Phone: +91-9787789524. E-mail: dr.n.saranya@gmail.com

the usage of inhalational agents, opioid, and local anesthetics. Inhalational agents provide some analgesia but were associated with uterine relaxation and maternal hypoxemia.^[8] Opioid are used parenterally for providing labor analgesia but associated with maternal and fetal adverse effect such as maternal sedation and neonatal respiratory depression.^[9,10] Regional analgesia is widely used for providing labor analgesia. They include both peripheral and central neuraxial block. Bilateral cervical and bilateral paravertebral block provide analgesia only during the first stage of labor bilateral pudendal block provides effective analgesia only during the second stage of labor. Central neuraxial block is the only method of providing effective analgesia during both stages of labor.^[11] Spinal analgesia provides the short duration of action. This technique will not be able to provide adequate analgesia for the whole duration of labor.^[12] Caudal epidural is lone of oldest method for providing labor analgesia, but the success rate is low.^[13] Lumbar epidural analgesia is the most widely used technique for providing labor analgesia. This is considered gold standard in providing labor analgesia. It can provide analgesia for both the stages of labor and can be extended to provide anesthesia for cesarean section or instrumental delivery if the need arises. The drawback with this technique includes delayed onset of analgesia^[14] and failure rate of 1.5–5% despite correct identification of epidural space.^[15] Combined spinal epidural (CSE) is a relatively new technique which combines the advantage of both spinal (rapid onset) and epidural (prolonged duration of action). The analgesia in the intrathecal component can be provided by opioid only^[12] or local anesthetic only.^[16] However, the combination of opioid helps in reduction of the local anesthetics requirement and prolongation of the duration local anesthetic action. These also help in decreasing the incidence of maternal hypotension and motor block.^[17] This reduced motor block allows maternal ambulation throughout labor. Ambulation during labor increases maternal satisfaction. Ambulation also observed to decrease the incidence of instrumental delivery,^[18] decreased oxytocin requirement, and duration of labor.^[19]

The combination of local anesthetic and opioid used in epidural delivered by include intermittent boluses, continuous infusion, and patient-controlled epidural analgesia (PCEA). Studies comparing the different modes of epidural drug administration found increased drug consumption and motor block with continuous infusion technique.^[20,21,22] These studies were refuted by other authors who observed no difference in the drug consumption or motor block with continuous infusion compared to intermittent boluses or PCEA.^[24] Fentanyl and sufentanil most commonly used in combination with local anesthetics were found to be effective in providing labor analgesia. Studies comparing fentanyl and

sufentanil in labor analgesia are few and give conflicting results. Some studies observed sufentanil had a prolonged duration of action than fentanyl^[25] while others did not find any difference in the duration of action between the two drugs. Hence, we did a study to compare the efficacy between fentanyl and sufentanil combined with low dose bupivacaine intrathecally and low concentration bupivacaine by continuous infusion in the epidural route using CSE technique.

Aims and Objectives

The objectives are as follows:

1. To compare the efficacy of intrathecal bupivacaine fentanyl (BF) mixture with bupivacaine sufentanil (BS) mixture for providing labor analgesia.
2. To compare the efficacy of continuous epidural infusion of BF mixture and BS mixture following intrathecal analgesia when used to alleviate labor pain by CSE.
3. To compare the time required to achieve fitness criteria for ambulation after intrathecal BF mixture and BS mixture administration.

MATERIALS AND METHODS

The study was prospective, double-blind, and randomized control study. The parturients who opted for labor analgesia were randomly divided into two groups. The parturients were explained about the CSE procedure and visual analog scale (VAS) score for pain. 30 ASA I and II, singleton primigravidae with vertex presentation were divided randomly into two groups after obtaining informed written consent. One group received CSE with fentanyl and bupivacaine (Group BF), while the other group received sufentanil and bupivacaine (Group BS) intrathecally followed by continuous epidural infusion of the same combination of drugs when the intrathecal analgesia wore off. Both the parturient and observer were blinded to the study solution.

Exclusion Criteria

The following criteria were excluded from the study:

1. Parturient refusal
2. Parturients with any contraindication to neuraxial block
3. With multiple pregnancies
4. Parturient with obstetrics complication
5. Parturient who had received opioid by another route during previous 4 h.

Labor analgesia was initiated when cervix dilatation reached 3–5 cm. The baseline maternal heart rate (HR), blood pressure (BP), and oxygen saturation (SPO₂) were recorded. All parturients were preloaded with 10 ml/kg of Ringer

lactate intravenously. The CSE was administered in the operation theater with parturients in left lateral position at the level of L2₃/L_{3,4} space under all aseptic precautions.

Study Design

The technique of cse was the same in both groups. The CSE comprised of an 18G Tuohy needle, a 27G spinal pencil point needle and an epidural catheter with filter (Portex). The study drug solutions for intrathecal drug administration and epidural infusion were prepared by one of the investigators who did not participate further in the study observations. A needle through needle technique was followed for CSE. The parturients were randomly divided into two groups to receive one of the following study solutions.

Intrathecal

Group I (BF): 0.5 ml	}
Bupivacaine 0.5% heavy 2.5 mg bupivacaine	
± ±	}
Fentanyl 25 µg 0.5 ml of fentanyl	
Total volume of injectate = 1 ml	
Group II (BS): 0.5 ml of 0.5%	}
Bupivacaine bupivacaine 2.5 mg	
± ±	}
Sufentanil 5 µg 0.1 ml sufentanil ± 0.4 ml of NS	

Total volume of injectate= 1 ml
The time of intrathecal injection of the above study solution was noted, the spinal needle removed, and epidural catheter was placed about 4 cm toward cephalic end inside epidural space and secured. After intrathecal drug administration, the parturient was made to lie in the supine position. The maternal HR, BP, SPO₂, motor power, sensory block level, VAS score for pain, the fetal heart rate (FHR), the time for onset of analgesia, and intrathecal duration of action were monitored.

When intrathecal analgesia weaned off and VAS > 40, an epidural bolus and continuous epidural infusion were initiated. No test dose was given, but bolus dose was given in increments, injected slowly after negative aspiration test to rule out intrathecal intravascular placement of the catheter.

Epidural

Group I (BF): 0.0625% bupivacaine ± 2.5 µg/ml fentanyl.
Group II(BS): 0.0625% bupivacaine ± 0.5 µg/ml sufentanil.

The 10 ml of the above study solution was given as a bolus. Initially, 4 ml of study solution was injected slowly,

and maternal non-invasive BP, HR, SpO₂, VAS, motor block, and sedation were recorded for 10 min. If no sign suggestive of intrathecal or intravascular placement of the catheter, remaining 6 ml was injected slowly again after negative aspiration test, and the maternal and fetal vitals were monitored for another 20 minutes before initiating infusion. The infusion rates were as follow:

Group I (BF): 0.0625% bupivacaine ± fentanyl 2.5 µg ml at 10 ml/h.

Group II (BS): 0.0625% bupivacaine ± sufentanil 0.5 µg ml at 10 ml/h.

Preparation of Epidural Drug Solution

Group I (BF)

6.25 ml of 0.5% heavy bupivacaine	}	Total volume of 50 ml
± 2.5 ml (125 µg) of fentanyl		
± 41.25 ml of NS	}	Total volume of 50 ml
± 43.25 ml of NS		

Group II (BS)

6.25 ml of 0.5% heavy bupivacaine	}	Total volume of 50 ml
± 0.5 ml (25 µg) of sufentanil		
± 43.25 ml of NS	}	Total volume of 50 ml
± 43.25 ml of NS		

Whenever the VAS score was >40, a bolus of 5 ml of the above study solution was given and observed for 20 min. If pain relief is still inadequate another bolus of 2.5 ml of study solution was given and again observed for 20 min before the administration of another top-up if required. The same drug solution at the same rate was continued in the second stage of the labor until the fetus was delivered.

All women in both groups were allowed to ambulate, after meeting the fitness criteria for ambulation and under the supervision of a doctor or nurse. The parturient ambulated only if she wished to do so. If the women in any group suffered hypotension (≥20% fall in the baseline and systolic BP), it was treated by intravenous fluid, supplemented by 2, positioning patient in left lateral position, and incremental bolus dose of IV ephedrine. In both groups, in case of inadvertent dural puncture, the epidural needle was removed, and epidural analgesia was provided one space above with 0.25% bupivacaine as per standard departmental protocol. The parturient was taken out of the study, and

the same was noted as technique complication. Number of attempts in establishing CSE and difficulty in epidural catheter placement was noted. Nausea and vomiting were treated with ondansetron 4 mg IV. Pruritus was usually self-limiting. Hence, parturients were given reassurance and treated with chlorpheniramine maleate 12.5–25 mg intravenously if it was severe. In case of instrumentation delivery, a 8–10 ml of 0.5% bupivacaine was given through the epidural catheter. Occurrence of fetal bradycardia was dealt with relieving aortocaval compression by putting the mother in left lateral position, discontinuing IV oxytocin drip if any and 2 supplementations. Naloxone was kept ready to treat if any neonatal respiratory depression occurs. The epidural catheter was removed 12–24 h after the delivery.

Observations and Assessment

The pain was assessed by 0–100 mm, VAS scale taking 0 as no pain and 100 as maximum pain. VAS score was measured at the peak of uterine contractions. After intrathecal drug administration, the VAS was assessed at 5, 10, 20, and 30 min and then every 30 min until the requirement of epidural analgesia.

Onset of Analgesia

From time of intrathecal drug administration to time of VAS < 40.

Duration of Analgesia

From VAS <40 to time for requirement of epidural analgesia.

After epidural bolus and starting of infusion, VAS was recorded every 10 min for first 30 min and every 30 min thereafter until the end of delivery. Maternal HR, noninvasive BP, SPO₂, and FHR were recorded as per the same interval. Upper level of sensory block was determined in the midclavicular line using bilateral pinprick testing. Motor block was assessed by straight leg rising against resistance using a modified Bromage scale. Both these parameters were monitored at 10, 20, and 30 min after intrathecal drug administration and every 30 min, until the end of intrathecal analgesia. After epidural analgesia, the motor and sensory block was monitored initially at 10, 20, and 30 min and every 30 min later, until the delivery of the baby. The criteria for fitness of ambulation were assessed at 30, 45, and 60 min after intrathecal analgesia. Sedation was assessed by four-point scale at every 15 min intervals after intrathecal analgesia. Pruritus and nausea were rated subjectively as none, mild, moderate, or severe. Hypotension and bradycardia were treated and documented. Similarly, urinary retention, if it occurs, was treated by catheterization and documented. Neonatal APGAR at 1 and 5 min were recorded. At postpartum each

study participant was asked to rate overall satisfaction on 3 point scale. The patients were followed for post-dural puncture headache until she was in a hospital stay.

Duration of First Stage of Labor

Time of onset of labor to full cervical dilatation.

The Duration of Second Stage of Labor

Time of full cervical dilatation to the delivery of the baby.

The mode of delivery, the need for instrumentation with its cause and type of instrument used, need for cesarean section with its cause, was recorded. The total amount of bupivacaine in each group individually; fentanyl and sufentanil required in corresponding groups were recorded. Numbers of top-up required in each group were noted. All the data collected were analyzed statistically with the appropriate test.

RESULTS AND OBSERVATION

The study was a randomized, double-blind control study on 30 primiparous parturients. CSE procedure was done, and cerebrospinal fluid (CSF) was identified in all parturient. 15 parturient in each group received intrathecal BF or BS followed by continuous infusion of the same drug solution till the end of delivery. In one parturient CSF was identified, and intrathecal drug was given, but there was technical difficulty in threading the epidural catheter. Hence, this parturient was excluded from the study, and one more parturient was included in her place to complete the study for further statistical analysis.

Demographic Characters

The demographic characters (age, weight, and height) were comparable in both the groups [Table 1].

Onset of Action

Onset of action was defined as the time of intrathecal drug administration to the VAS score to become <40. In Group BF, the onset of action was 3.25 ± 0.29 min and in group BS the onset of action was 3.23 ± 0.19 min. All parturient had no pain on the first contraction after intrathecal drug administration which usually occurred within 2–4 min of drug administration [Table 2].

Duration of Action

Duration of action was the duration from the time of onset of action (VAS < 40) to the time for the requirement of epidural analgesia. 1 parturient in group BF and five parturient in group BS were taken for the emergency cesarean section before the request for additional analgesia. In group BF another parturient delivered before initiation of epidural. In both the groups, the duration of action

Table 1: Demographic characteristics

Variable	Group BF (n=15)	Group BS (n=15)	P
Age (year)	25.87±2.59	26.87±3.07	NS
Weight (kg)	67.10±9.75	63.05±6.80	NS
Height (cm)	160.33±4.92	160.80±6.80	NS

P<0.05 is considered significant. BF: Bupivacaine fentanyl, BS: Bupivacaine sufentanil

Table 2: Onset and duration of intrathecal drug action

Variables	Group BF (n=15)	Group BS (n=15)	P value
Onset of action (min)	3.25±0.29	3.23±0.19	NS
Duration of action (min)	89.29±15.78	87.60±14.47	NS

P<0.05 is considered significant. BF: Bupivacaine fentanyl, BS: Bupivacaine sufentanil

was comparable (89.29 ± 15.78 min in BF and 87.60 ± 14.47 min in BS group) [Table 2]. The minimum duration was 65 min in BF group and BS group it was 64 min. The maximum duration was 114 min in BF group and 110 min in BS group (65–114 min in BF group and 64–110 min in BS group).

Fitness Criteria for Ambulation Achieved

The fitness criteria for ambulation were achieved in 53.35 ± 5.77 min in BF group and 50.80 ± 8.11 min in BS group. Ambulation was assessed at 30, 45, and 60 min after intrathecal drug administration. No parturient achieved fitness criteria for ambulation at 30 min. All parturient fulfilled the criteria for ambulation within 45–60 mm.

VAS Score

After intrathecal analgesia

VAS score reached 0 within 5 min of intrathecal drug administration in all parturients. The score persisted at 0 at 30 min in all except 2 parturients. One parturient in group BF had a score of 18, and another parturient in group BS had score of 10 at 30 min [Table 3].

After epidural analgesia

VAS score was comparable between two groups at any interval during epidural infusion. The baseline VAS score recorded before initiating epidural was 42.93 ± 12.45 in the BF group and in BS group it was 44.24 ± 10.47. VAS score was higher (39.46 ± 16.99 in BF group and 33.71 ± 5.79 in BS group) at 10 min after initiating epidural. It remained at a higher level for next 20 min [Table 4].

Labor characteristics and obstetric outcome

The cervical dilatation at which CSE initiated was 3.471 ± 0.40 cm in BF group and 3.80 ± 0.41 min BS group. The gestational age was 37.86 ± 0.74 weeks in BF group

Table 3: Pain score (VAS) after intrathecal drug injection

Interval (min)	Group BF (n=15)	Group BS (n=15)	P value
0	83.00±11.48	82.93±10.97	NS
5	0.00±0.00	0.00±0.00	-
10	0.00±0.00	0.00±0.00	-
20	0.00±0.00	0.00±0.00	-
30	1.28±4.81	0.60±2.58	NS
60	3.54±8.86	9.67±12.22	NS
90	27.46±11.08	27.78±14.46	NS

P<0.05 is considered significant. BF: Bupivacaine fentanyl, BS: Bupivacaine sufentanil, VAS: Visual analog scale

Table 4: Pain score (VAS) during epidural infusion

Interval (min)	Group BF (n=13)	Group BS (n=10)	P value
0	42.93±12.45	44.24±10.47	NS
10	39.83±17.99	34.13±5.49	NS
20	34.45±12.34	30.12±7.09	NS
30	31.18±8.72	29.99±6.34	NS
60	26.20±8.04	24.40±11.37	NS
90	28.78±15.64	26.80±6.83	NS
120	30.75±8.71	26.00±7.81	NS
150	27.83±6.97	31.00±11.86	NS
180	28.00±15.39	29.00±10.89	NS
210	32.87±12.76	31.97±12.93	NS
240	35.00	-	-
270	27.00	-	-
300	36.00	-	-

P<0.05 is considered significant. BF: Bupivacaine fentanyl, BS: Bupivacaine sufentanil, VAS: Visual analog scale

(37–40 weeks) and 38.73 ± 0.70 weeks (38–40 weeks) in BS group. Both these labor characters were similar and statistically insignificant. Labor was induced with dinoprostone (cerviprime) in 20 parturients (11 in BF group and 9 in BS group). 10 parturient had spontaneous onset of labor (4 parturient in BF group and 6 parturient in BS group). Oxytocin augmentation for labor was done in 25 parturients (12 in BF group and 13 in BS group). Oxytocin augmentation was done at the discretion of attending obstetrician [Table 5].

Duration of Labor

The average duration of the first stage of labor was 218.56 ± 69.56 min in group BF and 211.56 ± 58.96 min in group BS, the range being 69–320n: In BF group and 135–235 min in group BS. The average duration of the second stage of labor was 54.90 ± 32.27 min in BF group versus 51.78 ± 16.71 min in BS group. This difference was not statistically significant [Table 6] (n=9 after excluding parturients who underwent cesarean section).

Mode of Delivery

14 parturients had spontaneous vaginal delivery (6/15 in BF group and 8/15 in BS group). 3 in group BF and 1 in group BS had forceps-assisted delivery. In all the four Parturients, the indication was poor maternal effort. Six

Table 5: Labor characteristics

Interval (min)	Group BF (n=15)	Group BS (n=15)	P
Cervical dilatation (cm)	3.471±0.40	3.80±0.41	NS
Estimated gestational age (week)	37.86±0.74	38.73±0.70	NS
Induction (%)			
Yes	11 (73.3)	9 (60)	NS
No	4 (26.7)	6 (40)	NS
Augmentation (%)			
Yes	12 (80)	13 (8.7)	NS
No	3 (20)	2 (13.3)	NS

P<0.05 is considered significant. BF: Bupivacaine fentanyl, BS: Bupivacaine sufentanil

Table 6: Duration of labor

Stage of labor	Group BF (n=9)	Group BS (n=9)	p value
First stage (min)	218.56±69.56	211.56±58.96	NS
Second stage (min)	54.90±32.27	51.78±16.71	NS

P<0.05 is considered significant. BF: Bupivacaine fentanyl, BS: Bupivacaine sufentanil

parturient in each group underwent emergency cesarean section [Table 7]. Fetal bradycardia was the indication for cesarean section in 6 parturients in group BF and 6 parturient in group BS. In one parturient in group BF, the indication was fetal tachycardia, and in another, the indication was nonprogression of labor. None of the parturients in group BS had nonprogression of labor or fetal tachycardia.

Number of Breakthrough Pain Episodes

15 parturients (8 in SF group and 7 in BS group) had no breakthrough pain during epidural continuous infusion. 7 parturient had I episode of breakthrough pain (4 in BF group and 3 in BS group). 6 parturients had 2 episodes of breakthrough pain (3 parturient in each group). The breakthrough pain episode usually occurred as the labor progressed. These differences were statistically not significant [Table 8].^[23]

Epidural Bupivacaine Consumption

Bupivacaine consumption was 23.89 ± 12.77 mg in BF group as compared to 22.84 ± 9.96 mg in group BS. This was not statistically significant. In both groups, the same concentration of bupivacaine was used, and rescue analgesia for breakthrough pain during epidural analgesia was managed with same amount of bupivacaine in both the groups. Hence, the difference in the amount bupivacaine used was related to the difference in the duration of labor, duration of epidural drug administered and the number of breakthrough pain episodes. We did not perform statistical analysis for the epidural opioid since the potency of fentanyl and sufentanil is not same. Hence, the amount of fentanyl would be high [Table 9].

Table 7: Mode of delivery

Made of delivery	Group BF n=15 (%)	Group BS n=15 (%)	P value
Spontaneous vaginal	6 (40)	8 (53)	NS
Forceps application	3 (20)	1 (6.7)	NS
Cesarean section	6 (40)	6 (40)	NS

P<0.05 is considered significant. BF: Bupivacaine fentanyl, BS: Bupivacaine sufentanil

Table 8: Number of break through pain episode

	Group BF (n=15)				Group BS (n=15)				P value
	0	1	2	3	0	1	2	3	
Number of parturients	8	4	3	0	7	3	3	0	NS

P<0.05 is considered significant. BF: Bupivacaine fentanyl, BS: Bupivacaine sufentanil

Table 9: Epidural duration, bupivacaine, and opioid used

Variables	Group BF (n=13)	Group BS (n=10)	P value
Duration (min)	154.77±94.22	160.60±94.22	NS
Bupivacaine (mg)	23.89±12.77	22.84±9.96	NS
Opioid (µg)	92.05±54.09	35.50±39.30	-

P<0.05 is considered significant. BF: Bupivacaine fentanyl, BS: Bupivacaine sufentanil

DISCUSSION

The goal of labor analgesia is to provide adequate pain relief without causing any maternal or fetal jeopardy. Epidural analgesia is the common method of providing labor analgesia while CSE is gaining popularity in labor analgesia. Opioids are commonly being used in combination with local anesthetic drugs through central neuraxial route for labor analgesia. Opioids help in reducing the minimum analgesic dose of the intrathecal local anesthetic drug^[26] and the concentration of local anesthetic agent given epidurally.^[27] This helps in preserving maternal ambulation throughout the process of labor by avoiding motor block CSE technique provides rapid onset of action similar to spinal analgesia, and the analgesic duration can be prolonged by activating the epidural. In our study, we used either 25 µg fentanyl or 5 µg sufentanil added to 2.5 mg bupivacaine in the intrathecal component of CSE. Addition of opioid to local anesthetic epidurally helps to reduce the local anesthetic concentration. Both fentanyl^[28] and sufentanil^[27] were found to have dose-sparing effect on bupivacaine when coadministered epidural. Chestnut *et al.* in their study found both 0.0625% bupivacaine and 0.125% bupivacaine produced similar quality of analgesia. In both

groups, fentanyl 2 µg/ml was added to the local anesthetic drug solution.^[29] In another study by Chestnut *et al.* found that a combination of 0.0625% bupivacaine with 2 µg/ml of fentanyl provided adequate analgesia during both stages of labor including the second stage of labor.^[30] Bernard *et al.* in their study compared two different concentrations of ropivacaine 0.1% and 0.2% in 6 different volumes. 3 groups received diluted solution in both stages of labor analgesia while the other 3 groups received concentrated solutions for the second stage of labor. They found no difference between the two groups in terms of adequate pain relief in the second stage of labor. This led them to conclude that there was no role for increasing the concentration of local anesthetic drug during the second stage of labor to improve analgesia. Rather increasing the volume of drug solution is sufficient.^[31] Similarly sufentanil at 0.5 µg/ml added to local anesthetic drug solution epidurally observed to produce adequate analgesia and helps in the reduction of local anesthetic concentration.^[32] Herman *et al.* in their study found that the potency ratio of epidural fentanyl and sufentanil, when coadministered along with 0.125% bupivacaine, was 5:1.^[33] In our study, we compared the efficacy of 0.0625% bupivacaine with either 2.5 µg 1 ml fentanyl or 0.5 µg ml of sufentanil as a continuous epidural infusion. The concentration of bupivacaine remained the same in both stages of labor and rescue analgesia for breakthrough pain was provided by boluses of the same drug solution. One of the advantages of using a low concentration of a local anesthetic opioid combination is limited to absent motor block. This helps the parturient to ambulate or move about in their bed on their own. There is a general agreement that ambulation provides better maternal satisfaction as parturients can carry out their self-requirements. In our study, we used a low dose of and low concentration of bupivacaine epidurally. We allowed parturients to ambulate under supervision after achieving the criteria for fitness of ambulation.

Pain Score after Intrathecal Analgesia

In our study, we planned to assess the VAS score 5 min after intrathecal drug administration. However, we noticed initially that the VAS score was 0 within 5 min of intrathecal drug administration and all the parturients had no pain on the first contraction after intrathecal drug administration, which usually occurred within 2–4 min. We found the onset of action was comparable in both groups (3.25 ± 0.29 min vs. 3.23 ± 0.19 min). All parturients had a VAS score of 0 within 5 min of intrathecal drug injection. The score was 0 in all parturients until 20 min after intrathecal analgesia. After half hour still, the VAS score remained 0 in all parturients except parturients in BF group and one parturient in the BS group. They had a VAS score of 18 and 10 at 30 min, respectively. The duration of intrathecal analgesia was comparable in both the groups. 5 parturients

in BS group and one in the BF group were taken for emergency cesarean section due to fetal bradycardia before intrathecal effect had worn off. One parturient in BF group delivered before intrathecal analgesia wore off. After excluding these parturients, the subgroup analysis showed the duration of action to be 89.29 ± 15.78 min in the BF group and 87.60 ± 14.47 min in the BS group. Buvanendra *et al.* in their study found the duration of 25 µg of fentanyl added to 2.5 mg bupivacaine was 94.5 min.^[34] Wong *et al.* found that the duration of 5 µg sufentanil added to 2.5 mg bupivacaine was 93 ± 45 min.^[35] Cheng *et al.* in their study compared the duration of action of intrathecally administered 25 µg fentanyl and 5 µg sufentanil added to 1.25 mg of bupivacaine. They found that the duration of action was 109 ± 49 min in fentanyl group and 18 ± 54 min in sufentanil group.^[24] Stocks *et al.* they found the minimum local analgesic dose of intrathecal bupivacaine to be 1.99 mg when coadministered with 25 µg fentanyl.^[36] The bupivacaine dose used by Cheng *et al.* was lower than the minimum local analgesic dose.^[24] Despite this the duration of action in both fentanyl and sufentanil groups was more than in our study.

VAS Score after Epidural Drug Administration

In epidural route, after negative aspiration for blood or CSF, a bolus of 10 ml of analgesic drug solution as given as a slow bolus over 30 min (4 ml in 10 min ± 6 ml in 20 min) when the intrathecal analgesia wore off. After bolus dose, the epidural drug solution of 0.0625% bupivacaine with either 2.5 µg/ml of fentanyl or 0.5 µg/ml of sufentanil started as an infusion at the rate of 10 ml/h. In our study, we did not use the traditional epidural test dose. D'Angelo *et al.* similarly administered the epidural drug in increments without any test dose and did not have any case of accidental intrathecal or intravascular drug injection.^[37] Rawal *et al.* described that the possibility of serious sequelae was avoided when low dose local anesthetic drug and opioid mixture was accidentally administered through a catheter either intravascularly or intrathecally. If intravascular injection occurs that the result would be minimal analgesia with regressing sensory level and maternal or fetal effects were absent or minimal. If the drug solution was administered accidentally by the intrathecal route, the possible worst scenario may be a slowly increasing motor blockade with minimal loss of sympathetic tone.^[38] Morgan *et al.* described that they administered 1200 CSE at Queen Charlotte's hospital in labor analgesia without administering test dose and they did not have any serious adverse event such as intravascular or intrathecal placement or migration.^[39] We wished to avoid the test dose because the high concentration of local anesthetic drug used in test dose may preclude ambulation.^[40] VAS pain score was comparable at varying intervals in both groups during epidural infusion [Table 5]. Number of breakthrough

pain episodes requiring interventions were similar in both the groups. 4 parturient in BF group and parturient in BS group required 1 intervention. 3 parturient in each group required 2 interventions. This was statistically insignificant. All the interventions were required for breakthrough pain. No interventions were required for any untoward effects such as slow increase in motor block or loss of analgesic effect with regressing sensory level. Most of the breakthrough pain episodes occurred in one of the two following occasions. First when intrathecal analgesia effect wore off and epidural analgesia was just initiated. The reason was that we started epidural infusion only when the intrathecal analgesic effect wore off. The epidural effect took time to come and required 1 or 2 additional boluses to achieve adequate analgesia. Second occasion in which more interventions were required was advanced stage of labor. Connelly *et al.* compared the efficacy of fentanyl and sufentanil when administered by the epidural route for labor analgesia. They found that the duration of action and pain scores was comparable between the groups.^[41] We also found that both sufentanil and fentanyl were equally efficacious in reducing the local anesthetic drug concentration when coadministered with low concentration bupivacaine.

Ambulation

Fitness criteria for ambulation were assessed at varying intervals starting from 30 min after intrathecal drug administration. The fitness criteria for ambulation included the absence of maternal hypotension, straight leg rising possible, able to perform partial knee bending, and negative Romberg's sign. In both groups, parturients achieved fitness criteria for ambulation at 53.35 ± 5.77 min in BF group (range 45–60 min) and 50.80 ± 8.11 min in BS group (range 45–60 min) [Table 3]. All parturients in our study were able to perform partial knee bending test. Some parturients expressed displeasure in performing partial knee bending test or uncomfortable in performing partial knee bending test. Cohen *et al.* in their study described that 37% of the parturients were not able to perform partial knee bending despite they were able to ambulate. In the same study, they had noticed some parturients were not able to perform partial knee bending even before initiating labor analgesia. In our study, parturients were allowed to ambulate under supervision once fitness for ambulation is achieved. Many mothers expressed satisfaction when they were able to change their position from supine to sitting or vice versa on their own. Chapelle *et al.* in their case-control study that in women who ambulated for a mean duration of 60 min had lesser instrumental delivery compared to who did not ambulate. They also noticed that the duration of labor was prolonged in ambulation group.^[18] In contrast, Frenea *et al.* did not find any prolongation of labor duration or decreased incidence of instrumental delivery in parturients

who ambulated for a mean duration of 64 min when compared to women who did not ambulate.^[19] Despite all parturients fulfilling criteria for ambulation only one parturient wished to ambulate while others restricted themselves to bed. The reason was a senior member of their family accompanying them suggested not to ambulate. Hence, we were not able to assess the presence or absence of any benefit due to ambulation in terms of oxytocin requirement, bupivacaine consumption, or incidence of instrumental delivery.

Maternal Satisfaction

13 parturient in BF group and 11 parturient in BS group rated their pain relief as excellent. 4 parturient in BF group and 2 parturient in BS group had some pain relief. None of parturient rated their pain relief as no relief. The maternal satisfaction was assessed in the postpartum period irrespective of mode of delivery. The parturients were specifically asked to rate only their pain relief. This was done to rule out the influence of the impact of delivery outcome in rating pain relief. All parturients who underwent cesarean section before the spinal effect wore off rated their pain relief as excellent. This was obvious since all parturients had low VAS score during the spinal effect. All the parturients who rated their pain relief as some relief had received both spinal and epidural analgesia. They rated the spinal analgesia effect as excellent and pain relief with epidural as some relief. All these parturients had 1 or 2 episodes of breakthrough episodes. The maternal satisfaction was comparable between the groups. Both group parturients had equally efficacious analgesia both after intrathecal drug administration and during epidural drug infusion.

REFERENCES

1. Mezlack R, Schaffelberg D. Low back pain during labour. *Am J Obstet Gynecol* 1987;156:901-5.
2. Mezlack R. The myth of painless childbirth. *Pain* 1984;12:321-27.
3. Sangoul F, Fox GS, Houle GL. Effect of regional analgesia on maternal oxygen consumption during first stage of labor. *Am J Obstet Gynecol* 1975;121:1080-83.
4. Riffel HO, Nochimson OJ, Paul RH, Hon EH. Effects of meperidine and promethazine during labour. *Obstet Gynecol* 1973;42:738-45.
5. Casio M, Pygon B, Bernett C, Ramanathan S. Labour analgesia with intrathecal fentanyl decreases maternal stress. *Can J Anaesth* 1997;44:605-9.
6. ACOG Committee Opinion Number 269 February 2002. Analgesia and caesarean delivery rates. American college of obstetricians and gynecologists. *Obstet Gynecol* 2002;99:369-70.
7. Minnich ME. Childbirth preparation and non-pharmacological analgesia. In: Chestnut OH, editor. *Obstetric Anaesthesia: Principles and Practice*. Philadelphia, PA: Mosby; 2004. p. 302.
8. Lin OM, Reisner LS, Benumof J. Hypoxemia occurs intermittently and significantly with nitrous oxide analgesia (Abstract). *Anesth Analg* 1989;68:S167.
9. Way WL, Costley EC, Way EL. Respiratory sensitivity of the new born infant to meperidine and morphine. *Clin Pharm Ther* 1965;6:454-61.

10. Wilson CM, McClean E, Mooro J, Dundee JW. A double blind comparison of intramuscular petazocine and nalbuphine in labour. *Anaesthesia* 1986;41:1207-13.
11. Hepner DL, Datta S. Labour analgesia practices for the new millennium. In: Katz RL, editor. *Seminars in Anaesthesia, Perioperative Medicine and Pain*. Vol. 19. Philadelphia, PA: WB Saunders; 2000. p. 35-45.
12. Polley LS, Giosten B. Epidural and spinal analgesia/anesthesia: Local anesthetic technique. In: Chestnut DH, editor. *Obstetric Anaesthesia: Principles and Practice*. St. Louis: Mosby; 2004. p. 336.
13. Hinagson RA, Edwards WB. Continuous caudal anaesthesia during labor and delivery. *Anesth Analg* 1942;21:301.
14. Dawkins CJ. An analysis of the complications of extradural and caudal block. *Anaesthesia* 1969;24:554-63.
15. Crawford JS. The second thousand epidural blocks in an obstetric hospital practice. *Br J Anaesth* 1972;44:1277-87.
16. Stacey RG, Watt S, Kadim MY, Morgan BM. Single spacecombined spinal-extradural technique for analgesia in labour. *Br J Anaesth* 1993;71:499-502.
17. Wong CA, Scavone BM, Slavenas JP, Vidovich MI, Peaceman AM, Ganchiff JN, *et al.* Efficacy and side effect profile of varying doses of intrathecal fentanyl added to bupivacaine for labor analgesia. *Int J Obstet Anesth* 2004;13:19-24.
18. de la Chapelle A, Carles M, Gleize V, Dellamonica J, Lallia A, Bongain A, *et al.* Impact of walking epidural analgesia on obstetric outcome of nulliparous women in spontaneous labour. *Int J Obstet Anesth* 2006;15:104-8.
19. Frenea S, Chirossel C, Rodriguez R, Baguet JP, Racinet C, Payen JF, *et al.* The effects of prolonged ambulation on labor with epidural analgesia. *Anesth Analg* 2004;98:224-9.
20. Tan S, Reid J, Thorburn J. Extradural analgesia in labour: Complications of three techniques of administration. *Br J Anaesth* 1994;73:619-23.
21. Collis RE, Plaat FS, Morgan RM. Comparison of midwife top ups. Continuous infusions and patient controlled epidural analgesia for maintaining mobility after a low dose combined spinal. *Epidural Br J Anaesth* 1999;82:233-6.
22. Smedwig JP, Scoreide E, Gjessing L. Ropivacaine 1 mg/ml, plus fentanyl 2 µg/ml for epidural analgesia during labour. Is mode of administration important? *Acta Anaesthesiol Scand* 2001;45:545-99.
23. Nelson KE, Rauch T, Terebuh V, D'Angelo R. A comparison of intrathecal fentanyl and sufentanil for labor analgesia. *Anesthesiology* 2002;96:1070-3.
24. Cheng CJ, Sia AT, Lim EH, Loke GP, Tan HM. Either sufentanil or fentanyl, in addition to intrathecal bupivacaine, provide satisfactory early labour analgesia. *Can J Anaesth* 2001;48:570-4.
25. Javert CT, Hardy JD. Influence of analgesics on pain intensity during labour (with a note on natural childbirth). *Anesthesiology* 1951;12:189-215.
26. Campbell DC, Camann WR, Datta S. The addition of bupivacaine to intrathecal sufentanil for labor analgesia. *Anesth Analg* 1995;81:305-9.
27. Polley LS, Columb MO, Naughton NN, Wagner DS, Dorantes DM, van de Ven CJ, *et al.* Effect of intravenous versus epidural fentanyl on the minimum local analgesic concentration of epidural bupivacaine in labor. *Anesthesiology* 2000;93:122-8.
28. Lyons G, Columb M, Hawthorne L, Dresner M. Extradural pain relief in labour: Bupivacaine sparing by extradural fentanyl is dose dependent. *Br J Anaesth* 1997;78:493-7.
29. Chestnut DH, Owen CL, Bates JN, Ostman LG, Choi WW, Geiger MW, *et al.* Continuous infusion epidural analgesia during labor: A randomized, double-blind comparison of 0.0625% bupivacaine/0.0002% fentanyl versus 0.125% bupivacaine. *Anesthesiology* 1988;68:754-9.
30. Chestnut DH, Laszewski LJ, Pollack KL, Bates JN, Manago NK, Choi WW, *et al.* Continuous epidural infusion of 0.0625% bupivacaine-0.0002% fentanyl during the second stage of labor. *Anesthesiology* 1990;72:613-8.
31. Bernard JM, Le Roux D, Frouin J. Ropivacaine and fentanyl concentrations in patient-controlled epidural analgesia during labor: A volume-range study. *Anesth Analg* 2003;97:1800-7.
32. Eriksson SL, Frykholm P, Stenlund PM, Olofsson C. A comparison of three doses of sufentanil in combination with bupivacaine-adrenaline in continuous epidural analgesia during labour. *Acta Anaesthesiol Scand* 2000;44:919-23.
33. Herman NL, Sheu KL, Van Decar TK, Rubin JD, Gadalla F, Koff HD, *et al.* Determination of the analgesic dose-response relationship for epidural fentanyl and sufentanil with bupivacaine 0.125% in laboring patients. *J Clin Anesth* 1998;10:670-7.
34. Asokumar B, Newman LM, McCarthy RJ, Ivankovich AD, Tuman KJ. Intrathecal bupivacaine reduces pruritus and prolongs duration of fentanyl analgesia during labor: A prospective, randomized controlled trial. *Anesth Analg* 1998;87:1309-15.
35. Wong CA, Scavone BM, Loffredi M, Wang WY, Peaceman AM, Ganchiff JN, *et al.* The dose-response of intrathecal sufentanil added to bupivacaine for labor analgesia. *Anesthesiology* 2000;92:1553-8.
36. Stocks GM, Hallworth SP, Fernando R, England AJ, Columb MO, Lyons G, *et al.* Minimum local analgesic dose of intrathecal bupivacaine in labor and the effect of intrathecal fentanyl. *Anesthesiology* 2001;94:593-8.
37. D'Angelo R, Anderson MT, Philip J, Eisenach JC. Intrathecal sufentanil compared to epidural bupivacaine for labor analgesia. *Anesthesiology* 1994;80:1209-15.
38. Rawal N, Holmström B, Crowhurst JA, Van Zundert A. The combined spinal-epidural technique. *Anesthesiol Clin North America* 2000;18:267-95.
39. Morgan BM. Is an epidural test dose necessary. *Eur J Obst Gynecol* 1995;59:559-60.
40. Cohen SE, Yeh JY, Riley ET, Vogel TM. Walking with labor epidural analgesia: The impact of bupivacaine concentration and a lidocaine-epinephrine test dose. *Anesthesiology* 2000;92:387-92.
41. Connelly NR, Parker RK, Vallurupalli V, Bhopatkar S, Dunn S. Comparison of epidural fentanyl versus epidural sufentanil for analgesia in ambulatory patients in early labor. *Anesth Analg* 2000;91:374-8.

How to cite this article: Anand SV, Rajee TK, Nagalingam S. Combined Spinal - Epidural in Labor Analgesia: Comparison of Fentanyl Bupivacaine Mixture versus Sufentanil - Bupivacaine Mixture. *Int J Sci Stud* 2018;6(5):15-23.

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

Prevalence and Etiological Profile of Patients with Acute Confusional State

Sajad Sumji¹, Mohd Iqbal Wani¹, Muzzafar Mohi-ud-Din²

¹Senior Resident, Department of Endocrinology and Cardiology, SKIMS, Srinagar, Kashmir, India, ²Medical Officer, Health and Family Welfare, Government Medical College, Srinagar, Jammu and Kashmir, India

Abstract

Background: Confusion is a mental and behavioral state of reduced comprehension, coherence, and capacity to reason. Confused patient is usually subdued, not inclined to speak, and is physically inactive. A state of confusion that is accompanied by agitation, hallucination, tremor, and illusions (misperception of environmental sight and sound/touch) is termed delirium, as typified by delirium tremens from alcohol or drug withdrawal.

Objective: The objective of the study was to study the prevalence and etiological profile of patients with the acute confusional state.

Materials and Methods: All patients of acute confusional state admitted in the emergency wing of the Postgraduate Department of Medicine, Government Medical College, Srinagar, were enrolled prospectively in the study. Informed consent was taken from the attendants of the patients for participation in the study. A proper history was taken from attendants and other available sources. A thorough general physical and systemic examination was done.

Results: Prevalence of acute confusional state in total hospital admission in medical wards was 19.7%. Most of the patients were in the 6th decade of life. A good number of patients 74.2% received the correct working diagnosis assessment (history and examination). 71% of patients presented within 24 h of onset of acute confusional state.

Conclusion: This study emphasized the great importance of early accurate diagnosis of acute confusional state, as correct diagnosis can lead to judicious management and save many valuable lives.

Key words: Behavioral state, Confusional state, Hallucination, Mental

INTRODUCTION

Acute confusional state, synonyms: Acute brain failure, acute organic reaction, delirium, and post-operative psychosis are defined as a transient disorder of cognition and attention accompanied by disturbances of the sleep-wake cycle and psychomotor behavior.^[1] Confusion is a mental and behavioral state of reduced comprehension, coherence, and capacity to reason. Confused patient is usually subdued,

not inclined to speak, and is physically inactive. A state of confusion that is accompanied by agitation, hallucination, tremor, and illusions (misperception of environmental sight and sound/touch) is termed delirium, as typified by delirium tremens from alcohol or drug withdrawal. States of reduced alertness and responsiveness represent a continuum that in its severest form is called coma, a deep sleep-like state from which patient cannot be aroused.^[1] Acute brain failure, acute organic reaction, delirium, and post-operative psychosis are defined as a transient disorder of cognition and attention accompanied by disturbances of the sleep-wake cycle and psychomotor behavior.^[2] Delirious patients are distractible, often hypersensitive to stimuli, and they cannot prioritize important from irrelevant environmental sounds or sights. Today, it is still the most common mental health issue for the elderly, affecting 14–56% of elderly hospitalized medical patients and 6–24% of nursing home patients.^[3–5]

Access this article online



www.ijss-sn.com

Month of Submission : 06-2018

Month of Peer Review : 07-2018

Month of Acceptance : 08-2018

Month of Publishing : 08-2018

Corresponding Author: Dr. Sajad Sumji, Department of Endocrinology, Government Medical College, Srinagar, Jammu and Kashmir, India. Phone: +91-9797204113. E-mail: sajadsumji.endo@gmail.com

It is very common, especially in the elderly and many of these patients subsequently do not return to their baseline function, and some even require institutionalization. It can occur acutely or subacutely, and symptoms fluctuate. In to 1–3rd of cases, acute confusional state can be avoided, and the lack of awareness leads to a large amount of morbidity and mortality and a burden on NHS costs in the west.^[6] The role of medications may be suggested by a temporal relationship between onset of delirium and start of new medication. However, this is not always the case, and practitioners need to be aware of this. Medication lists should be thoroughly reviewed in delirium. The exact mechanism of delirium is unclear, but it is postulated that central cholinergic pathway blockade is a major factor.^[7] This may explain why anticholinergic medications readily lead to delirious states. It may be that this factor along with the pharmacokinetic changes that occur later in life and comorbidities increase the susceptibility of elderly patients to drug-induced delirium.

Making an accurate assessment relies on a collateral history to determine the patients pre-morbid level of function. There are very useful cognitive function screening tools, for example, abbreviated mental test score and confusion assessment method. The mental tests should be performed regularly and on all high-risk patients. However, it may not be appropriate or possible to do these tests on a sick patient.

Aim and Objective

The aim of the study was to study the prevalence and etiological profile of patients with the acute confusional state.

MATERIALS AND METHODS

All patients of acute confusion state admitted in the emergency wing of Postgraduate Department of Medicine Government Medical College, Srinagar, shall be enrolled prospectively in the study. Informed consent shall be taken from the attendants of the patients for participation in the study.

Inclusion Criteria

A patient is deemed to have an acute confusional state if the attending physician caring identifies any one of the following criteria for the patient at the time of initial presentation:

- Glasgow coma scale score <15
- Mini-mental state examination scores <24.
- Quick confusional score <15.^[8]
- Patient not alert and oriented to person, place, and or time.
- Diminished responsiveness to verbal or physical stimulation.

- Difficult to arouse, unable to remain awake, or conversant.
- Hallucinations, confusion, bizarre, or inappropriate behavior.

Exclusion Criteria

The following criteria were excluded from the study:

- Age <18.
- Any obvious evidence of trauma.
- Psychiatric disease.
- Patient with dementia.

A proper history was taken from attendants and other available sources. A thorough general physical and systemic examination was done. Baseline investigations (complete blood count, kidney function test, liver function test, blood sugar, arterial blood gas and electrolytes, chest X-ray, and electrocardiogram) were done routinely. Cranial computed tomography (CT) plain was done in every patient within 6 h of hospitalization. If required serum calcium, phosphorous, magnesium, blood, urine, and other relevant body fluid analysis were done in selected cases as and when required.

- The following were done as when required.
- EEG (awake record) were ever deemed necessary.
- MRI brain (1.5 Tesla) were ever deemed necessary.
- Cerebrospinal fluid analysis was done where deemed necessary.

Toxic screen was done in selected cases with a high index of suspicion of substance abuse or toxin exposure. Patients were assessed and followed up on a daily basis until he or she

- a. Was discharged from the hospital.
- b. Succumbs to illness.

OBSERVATIONS AND RESULTS

A total number of patients admitted during this period were 3202. Of these 631 patients were found to be in the acute confusional state. Hence, the prevalence of acute confusional state in our study was 19.7%.

Most of the patients were in the age group of 61–70 years (6th decade). Mean age was 60.0 years with standard deviation (SD) (17.80) for males with a maximum 105 years and minimum 18 years. For females, mean age was 61.8 years with SD (15.8) with a minimum of 18 years and maximum of 96 years. Median age was 62 years for males and 64 years for females. The distribution among sexes was fairly equal with 53.7% comprised by males and 46.3% comprised by female patients. However, there was more difference between the two sexes in the age group 71–80 years as shown in figure.

The mean Glasgow coma scale (GCS) was 10.5 (SD 2.45) with a minimum of 3 and maximum of 15 median GCS was 11. The frequency in various groups in descending order being 12–15 having 295 patients (46.8%), then 8–11 group having 230 patients (36.5%) followed by <8 group having 106 patients (16.8%).

Hypertension was seen in 242 patients (38%) of the subgroups. Hypertension was the highest in cerebrovascular accidents (CVA) (73.3%), diabetes mellitus was seen in 169 patients (26%). In various subgroups metabolic derangement group had 45.2% diabetes followed by sepsis (35.9%). The previous history of stroke was seen in 13% of CVA, history of similar episodes, i.e., history of similar type of acute confusional state in the past was present in 10% of patients. It was increasingly present in metabolic and seizure group patients in 19.1% and 15.6%, respectively. History of smoking was present in 127 patients (19%), i.e., 1 out of 5 patients was smoker. Out of various groups, smoking was present in 33.5% of CVA, 51.6% of CVS/shock, and 19.1% of the metabolic group.

On CT scan 224 patients reported normal. In 87 patients CT could not be done, either other diagnostic modalities took priority, or a therapeutic procedure precluded it from being done, and in other patients, consent could not be done after they had for example dramatic recovery, for example, hypoglycemia and poisoning.

The proportion of males in the CVA group is being 64.6% and females 35.4% and cardiovascular is being 71.0% in males and 29% in females. Conversely, the most common diagnosis in females was metabolic 85 patients (29.1%) followed by CVA 57 (19.5%) and sepsis/infections 63 (21.6%) and most common diagnosis in males was CVA (30.7%) and then metabolic 72 (21.2%). Moreover, poisoning was more common in female sex and seizures were relatively equally distributed in both sexes.

In 6.4% patient's diagnosis did not match, in 19.4% of patients it matches partially, and in 74.2% of patients, it matched completely. We grouped together the completely and partially matched groups we found that a good number of patients, 93.6% received the correct working diagnosis after initial assessment (history and examination).

The accuracy in diagnosis was in CVA 147 patients (82.2%), seizures 81 patients (90.0%) and poisoning 8 patients (100%). Among the patients were the diagnosis based on history and clinical examination matched with the final diagnosis. In metabolic group, 102 patients (70.8%) were diagnosed initially, similarly ICSOL Group 5 patients (50.0%) were diagnosed correctly and intracranial infection Group 21 patients (60.0%) were diagnosed correctly. If we

compare the proportions of correct diagnosis with CVA group most common group in our study, we find a significant difference in the correct diagnosis rate in the groups mentioned supra vide. Moreover, if we consider the initial diagnosis (based on history and examination) as benchmark, sepsis/infection was overdiagnosed, 144 patients were given label of infection/sepsis as against 102 as proven in the final diagnosis, *P* value significant (<0.0001).

CVA was seen in older age groups and was highest in the 6th decade of life in our study. 60 patients were in the age group 61–70 years of age and comprised 37.3% of the total. CVA was not seen below 30 years of age in our study, and 5 patients of 161 were young strokes in the age group of 31–40 years and comprised 3.1% of CVA group. Poisoning was exclusively seen in below 50 years of age group. In the age group, 18–30 years seizure disorder and poisoning were most common and comprised 61.3% and 12.3%, respectively. In 31–40 years age group seizure disorder was seen highest and was 53.4%. In the age group 51–60 years and 61–70 years, CVA constitutes 42.3% and 37.3%, respectively. Metabolic causes and sepsis were 29.0% and 27% in age group 71–80 years.

Time delay in presenting to hospital after developing acute confusional state historically had a large range between 1 h and 360 h with a mean of 35.40 h (SD 70.14). Median delay was 11.5 h. The distribution of patients on the basis of this delay “acute confusional state delay group” as seen in table and figure above showed most patients presented in 12–24 h group 32.2%, followed by >24 h group 28.3%, then 6–11 h group 21.6%, and then <6 h group 17.9%. Sepsis/infections, and intracranial infections and ICSOL group were relatively late to present 58.1% of infections/sepsis, 50% of intracranial infections, and 68.8% of ICSOL presented after 24 h. *P* = 0.0001 (significant).

GCS was grouped into 3 groups <8, 8–12, and 12–15. The <8 groups had 63% mortality 67 (out of 106), 8–11 had 11% mortality 25 (out of 230), and 12–15 group had 4% mortality 12 (out of 295). The individual components E, V, M were again seen to be individually having prognostic value.

Etiology of ACS: Etiology of ACS had an immense impact on the mortality. Poisoning, intracranial infections, and seizures all had decreased mortality, whereas CVS/shock, sepsis, and CVA groups had significantly increased mortality.

DISCUSSION

This was a hospital-based cross-sectional study. Consecutive patients were taken. The study was conducted between

April 2011 and March 2012. Seasonal distribution of 631 patients was that 290 patients were taken from winter, 341 from summer. The patients were taken on random days, a total number of days in which the patients were entered was 365 days, and 631 patients with acute confusional state were identified. Minimum of one and maximum of ten patients with acute confusional state were identified per day. A total number of patients seeking attention during these 365 days were 3202. Hence, the percentage of patients with acute confusional state presenting to the emergency department (ED) was calculated as 19.7%. Iqbal *et al.*^[9] and Holden *et al.*^[10] showed in their study the number of study patients represented 21% and 23% of total ED census. Our study showed that 19.7% of patients were in acute confusional state which are consistent with their data. The small difference can be explained by the fact that we had excluded from trauma, psychiatric disease, and dementia.

Most of the entries were in the age group 61–70 years. Mean age was 60 years for males with SD 17.80 and for females it was 61.8 years with SD 15.8. The patients along with the respective percentages from a total of 631 patients in various age groups were 49 (7.8%) in 18–30 years age group, 45 (7.1%) in 31–40 years age group, 57 (9.0%) in 41–50 years age group, 116 (18.4%) in 51–60 years age group, 199 (31.5%) in 61–70 years age group, 107 (17.0%) in 71–80 years age group, 41 (6.5%) in 81–90 years age group, and 17 (2.7%) in >90 age group. In the study conducted by Kanich *et al.*,^[11] there was a bimodal distribution for the frequency of age occurrence, with one peak in the middle-aged adult about 45 years old and another peak in elderly adults nearly 78 years old. The mean age of all patients presenting in the study was 49 years. Possibly the reason for the higher mean age in our study is that the largest group CVA and metabolic group were constituted by elderly patients and we had excluded the pediatric age group. The sex distribution was males were 339 (53.7%) and females 292 (46.3%). In the study conducted by Kanich *et al.*,^[11] there were 57% males (180) and 43% females (137). In the study conducted by Nadeem *et al.*,^[12] the sex distribution was 312 male (60.35%) and 205 female (39.65%) patients. In the study conducted by Wofford *et al.*,^[13] which was done in elderly ED patients, the males were 32.2% (73) and females constituted 67.8% (154). Similarly, in a study conducted by George *et al.*^[14] in elderly patients, the females again predominated, females being 54.4% (93) and males 45.6% (73). Overall, males predominate than females in our study, but if we see the sex distribution in the age group 71–80 years out of 107 patients, 50 (46.7%) were males and 58 (53.3%) were females. In the study conducted by Bates *et al.*,^[15] males were 49.45% (153), females were 50.5% (157), but most comatose patients under 65 were men whereas women constituted the majority over the age

of 65. Thus, it is inferred that in the studies from the west in the older age group the relative percentage of females in altered mental status patients increase as compared from overall percentage while such relation could not be seen in our study except in the age group 71–80 years.

The average hospital stay in days was 8.5 days (range, 1–42 days) and the average time in which patient remained in acute confusional state was 5.56 days. In the study conducted by Kanich *et al.*, the average hospital stay was 7.6 days (range of 1–234 days), whereas the mean for critical care was 4.6 days (range, 1–109 days).

Of the 631 patients, there were 104 deaths, the mortality being 16.5%, 429 (68.0%) patients had good recovery, and 98 (15.5%) patients had partial recovery. In the study conducted by Nadeem *et al.*,^[12] 297 (57.4%) were discharged after recovery and 179 (34.6) died. 80 of 205 female patients died (39%) while 99 of 312 males had a fatal outcome (31.7%). In the study conducted by Nadeem *et al.*,^[12] the outcome of 248 patients (90.84%) was established. 152 (61.29%) were discharged after recovery and 96 (38.71%) died. The remaining 25 (9.16%) patients were lost to follow-up. In the study conducted by Kanich *et al.*,^[11] 91% of the patients lived, whereas 2% died in the ED and 7% died after admission to hospital.

In our study, the most common final diagnosis was CVA 161 patients (25.6%) followed by metabolic disturbances group 157 (24.9%), then Sepsis/infections 117 (18.5%), seizures 83 (13.0%), intracranial infections (meningitis, encephalitis, meningoencephalitis, and brain abscess) 32 patients (5.0%), then cardiovascular/shock group 31 (4.9%), ICSOL 16 (2.6%), poisoning 8 (1.3%), SDH 9 (1.5%), and unknown/miscellaneous 17 (2.7%).

In the study conducted by Kanich *et al.*,^[11] the most common diagnoses accounting for AMS were neurologic (28%) then toxicologic (21%) followed by trauma (14%), psychiatric (14%), infectious (10%), endocrine/metabolic (5%), pulmonary (3%), oncologic (3%), cardiovascular (1%), gastrointestinal (1%), and renal (1%).

In the study conducted by Nadeem *et al.*^[12] (17) 25.8% (30) had structural cause for coma. Nadeem *et al.* studied the etiology of coma with particular reference to the age and sex of patient, and the outcome. Their study revealed that metabolic coma was predominant cause in almost all age groups with structural coma progressively increasing with the age. Positioning were the common cause in patients under 30. The Leading causes among males were poisoning, hemorrhagic CVA, ischemic CVA, renal failure and hepatic coma. Among females casual distribution revealed renal failure followed by hepatic coma and hemorrhagic CVA.

Out of the patients whose outcome could be determined 57.4% were discharged after recovery and 34.6 % died. They concluded that coma etiology has insignificant effect on prognosis, while such significance could not be assigned to age or sex. Out of 14 patients having diffuse cerebral pathology, half were due to infectious diseases 6% of the total, i.e. pyogenic meningitis in 4 patients, 2 had tuberculous meningitis, and 1 had cerebral malaria, 3 heat stroke, 2 patients with post-cardiac arrest coma (hypoxic coma), and one patient had status epilepticus.

In the study conducted by Abdullah *et al.*,^[16] the causes were grouped into 12 categories, of which the leading cause of coma was found to be cerebrovascular disease followed by metabolic and infectious diseases. In our study, the most common diagnosis was CVA 161 (25.6%) followed by metabolic 157 (24.9%) and sepsis 117 (18.5%).

In the study by George *et al.*^[14] in elderly patients having confusion as a part of their complaints, the causes of delirium as in descending order were infection 35% (75), metabolic 15% (34), CVA 11% (24), drug-related 11% (24), carcinoma 5% (10), ICSOL 0.5% (1), SDH 1% (2), fractures 5% (10), and miscellaneous 6% (12).

In the study conducted by Bates *et al.*,^[15] various causes of coma out of 500 patients were hypoxia-ischemia in 210 (42%) patients, cardiac arrest in 150 (30%), brain infarct in 76 (15%), brain hemorrhage in 67 (13%), hepatic encephalopathy in 51 (10%), SAH in 38 (7.6%), other metabolic disturbances constituted 19 (3.8%), infection in 16 (3.2%), hypoglycemia in 12 (2.4%), and mass lesion in 11 (2.2%).

A much more contemporary review of coma by Huff^[17] reported that 25% of the patients had head trauma, 16% of these patients experienced multiple trauma, and 9% had isolated cranial trauma. Nontraumatic intracranial masses, primary spontaneous intracerebral hemorrhages, accounted for 21%, other neurologic disorders, predominantly seizures made up 16% of the patient population. Patients with a medical condition mainly resuscitated cardiac patients and patients with sepsis accounted for 13% and 12%, respectively. Toxicologic causes were encountered in 6% of the patients and psychiatric causes in 3%. No conclusive explanation of coma was determined in 3% at the time of death.

According to O'Keefe and Sanson *et al.*,^[18] the most common cause of AMS in elderly patients was metabolic/toxic (65%), structural (33%), and psychiatric (2%). In the study conducted by Wofford *et al.*,^[13] the most common cause of acute cognitive impairment in elderly was infection 26.1% (40), followed by decreasing order by metabolic/toxic group 22.9% (35), cerebrovascular 20.2% (31),

unknown 15.6% (24), miscellaneous 7.2% (11), trauma 6.5% (10), cardiac 6% (9), and medication-related 4.6% (2).

In the study conducted by Matuja *et al.*,^[19] to determine the causes and early prognosis in 150 patients admitted in a medical coma, 16 patients had cerebral malaria, 16 meningitis, 7 diabetic ketoacidosis, and 6 drug overdosage. Other causes were 20 (13%) with cerebrovascular diseases, 30 (20%) hepatic failure, and 11 (8%) were miscellaneous and obscure causes. The cause of coma was an important indicator of prognosis.

In our study, the various conditions under CVA were hemorrhagic stroke 98 of 161 patients, ischemic stroke 52, SAH 9, and TIA 2 of total 161 CVA patients. In the ICH subgroup, the various sites of bleed were putaminal 55.1%, thalamic 21.4%, pontine 7.3%, cortical 5.1%, cerebellar 5.1%, ventricular 3.0%, and lobar 3.0%. In the study conducted by Abdullah *et al.*, hemorrhagic lesions seen in 57.0% versus 37% infarcts.

In our study, 220 patients had other coexistent problems which could have contributed to the acute confusional state apart from primary. Some had one coexistent problem; others 2–3 problems. The metabolic group had the highest number of coexistent problems, in 83 patients of the metabolic group the number of comorbid problems being 70 in this group, followed by sepsis, 50 patients (40 problems), then CVA group 41 patients (36 problems) and then CVS 15 patients (18 problems). On the other hand, most common coexistent complicating problems were renal impairment 73 (out of 180) followed by sepsis then hypoglycemia, seizures, and then dehydration. In the study conducted by George *et al.*, 42 patients (25%) had two or more equally contributory causes.

CONCLUSION

The study was designed to work out the prevalence, important etiological factors and clinical correlates of acute confusional state in our population, so as to help in pointing out important and common causes with age and sex distribution of acute confusional state in our setup, thus helping to keep in mind different diseases while we are confronted with a patient of acute confusional state. This randomized cross-sectional study with a limited number of study population may not reflect the exact situation of the condition in the community, but its nearness to the reality cannot be underestimated. Age is an important predictor of the etiology of acute confusional state. In the older age group, the acute confusional state is mostly due to stroke, electrolytic imbalance, or systemic infection. In younger age group, acute poisoning, central nervous system infection or seizures are the common etiology of acute confusional

state. It is important to note that, many causes of altered consciousness are completely reversible with prompt diagnosis and proper management, like-infections and metabolic abnormalities. This finding emphasizes the great importance of early accurate diagnosis of acute confusional state, as correct diagnosis can lead to judicious management and save many valuable lives.

REFERENCES

1. Liposwki ZJ. Delirium (acute confusional states). JAMA 1987;258:1789-92.
2. Harrison TR. Acute confusional status and coma. In: Anthony SF, Longo DL, Braunwald E, Stephen LH, Jameson H. Principles of Internal Medicine. 16th Edition. New York: Mc Graw Hill Company; 2005. p. 1624-36.
3. Inouye SK. The dilemma of delirium: Clinical and research controversies regarding diagnosis and evaluation of delirium in hospitalized elderly medical patients. Am J Med 1994;97:278-88.
4. Rovner BW, Kafonek S, Filipp L, Lucas MJ, Folstein MF. Prevalence of mental illness in a community nursing home. Am J Psychiatry 1986;143:1446-9.
5. Sabin TD, Vitug AJ, Mark VH. Are nursing home diagnosis and treatment inadequate? J Am Med Assoc 1982;248:321-2.
6. Young J, Inouye SK. Delirium in older people. BMJ 2007;334:842-6.
7. Alagiakrishnan K, Wiens CA. An approach to drug induced delirium in the elderly. Postgrad Med J 2004;80:388-93.
8. Levy DE, Bates D, Caronna JJ, Cartlidge NE, Knill-Jones RP, Lapinski RH, *et al.* Prognosis in nontraumatic coma. Ann Intern Med 1981;94:293-301.
9. Iqbal F, Gul A, Hussain S. Predictive value of Glasgow coma scale(GCS) in cerebrovascular accidents. Proceeding Shaikh Zayed Postgrad Med Inst 2001;15:66-8.
10. Holden J, Jayathissa S, Young G. Delirium among elderly general medical patients in a New Zealand hospital. Intern Med J 2008;38:629-34.
11. Kanich W, Brady WJ, Huff JS, Perron AD, Holstege C, Lindbeck G, *et al.* Altered mental status: Evaluation and etiology in the ED. Am J Emerg Med 2002;20:613-7.
12. Nadeem MA, Irfan K, Waheed IA, Waseem T. Is there any relationship of age and sex to the etiology and outcome of medical coma? Ann King Edward Med Uni 2005;11:407-10.
13. Wofford JL, Loehr LR, Schwartz E. Acute cognitive impairment in elderly ED patients: Etiologies and outcomes. Am J Emerg Med 1996;14:649-53.
14. George J, Bleasdale S, Singleton SJ. Causes and prognosis of delirium in elderly patients admitted to a district general hospital. Age Ageing 1997;26:423-7.
15. Bates D, Caronna JJ, Cartlidge NE, Knill-Jones RP, Levy DE, Shaw DA, *et al.* A prospective study of nontraumatic coma: Methods and results in 310 patients. Ann Neurol 1977;2:211-20.
16. Abdullah M, Chandnal A, Khan AM. Etiology and outcome of coma –a hospital based study. J Coll Physicians Surg Pak 2001;11:572-5.
17. Huff JS. Altered mental status in coma. In: Tintinalli JE, Kelen GD, Stapczynski JS, editors. Emergency Medicine: A Comprehensive Study Guide. United States; 2000. p. 1440-9.
18. O’Keeffe S, Lavan J. The prognostic significance of delirium in older hospital patients. J Am Geriatr Soc 1997;45:174-8.
19. Matuja WB, Matekere NJ. Causes and early prognosis of non-traumatic coma in Tanzania. Muhimbili medical centre experience. Trop Geogr Med 1987;39:330-5.

How to cite this article: Sumji S, Wani MI, Mohi-ud-Din M. Prevalence and Etiological Profile of Patients with Acute Confusional State. J Sci Stud 2018. Int J Sci Stud 2018;6(5):24-29.

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

Translating Phenytoin Therapeutic Drug Monitoring for Potential Utilities to Pharmacovigilance: Capacity Raking an Established Tertiary Care Service

Shazia Kousar¹, Fayaz Ahmad Wani², Zaid Ahmad Wani³, Arjumand Nazir⁴, Ahmad Tauqeer Zahid⁵, Z A Wafai¹

¹Department of Clinical Pharmacology, Sheri Kashmir Institute of Medical Sciences, Srinagar, Jammu and Kashmir, India, ²Associate Professor, Department of Medicine, Government Medical College, Jammu, Jammu and Kashmir, India, ³Associate Professor, Department of Psychiatry, Government Medical College, Srinagar, ⁴Registrar Department of Ophthalmology GMC Srinagar, Jammu and Kashmir, India, ⁵Department of Management Studies, Kashmir University, Srinagar, Jammu and Kashmir, India

Abstract

Introduction: Properly applied therapeutic drug monitoring (TDM) is a proven method of reducing adverse drug events and hence health-care costs. It involves laboratory measurement of a chemical parameter of difficult to manage therapeutic drugs at the designated interval for optimization of therapy with these drugs.

Objectives: The objectives of the study were optimization of Pharmacodynamic responses by pharmacokinetic based adjustments in drug use taking phenytoin as a probe and investigation of the quality of requisitions made for TDM

Materials and Methods: This was a hospital-based prospective study done in cases of idiopathic epilepsy ($n = 90$). Pd analysis was performed by evaluating the clinical response to phenytoin therapy, adverse drug reaction monitoring, and causality categorization using the WHO-UMC causality categories and CDSCO criteria for the seriousness of adverse events. Phenytoin PK analysis was done by enzyme immunoassay technique. An audit of 135 requisitions for the quality of the information received was done by devising a scoring scale.

Results: Pd analysis of 90 patients revealed that 79% of patients responded positively to phenytoin after treatment optimization or could be tapered off phenytoin successfully after achieving seizure control and remained seizure free for the period of follow-up. A total of 8% of patients needed a second antiepileptic drug in addition to phenytoin and 13% of patients were discontinued from phenytoin either because of adverse effects or because phenytoin did not modify seizure activity in these patients. Gum hypertrophy was the most common adverse effect seen in this patient population. PK data for 87 patients revealed that mean serum phenytoin trough (C_{tr}) concentration was 12.105 ± 0.433 $\mu\text{g/ml}$, mean serum phenytoin peak (C_4) concentration was 16.895 ± 0.571 $\mu\text{g/ml}$, and mean area under plasma concentration-time curve was 57.99 ± 1.76 $\mu\text{g/ml/h}$. Audit of 135 TDM requisitions revealed that 40% requisitions were graded as unacceptable, 25% requisitions were of poor quality, 26% requisitions were incomplete, 9% requisitions were satisfactory, while none of the requisitions was complete.

Conclusion: TDM remains a largely underutilized tertiary care resource and best practice guidelines and professional standards of practice need to be adopted for optimum utilization of this resource.

Key words: Pharmacodynamics, Pharmacokinetics, Pharmacovigilance, Phenytoin, Therapeutic drug monitoring

Access this article online



www.ijss-sn.com

Month of Submission : 06-2018

Month of Peer Review : 07-2018

Month of Acceptance : 08-2018

Month of Publishing : 08-2018

INTRODUCTION

Monitoring is the essence of therapeutics. One may measure the desired therapeutic and undesired adverse outcomes clinically. Alternatively, a biomarker may be measured.^[1] Drug concentration measurement is needed when other measures of monitoring fail. Monitoring has more recently

Corresponding Author: Dr. Fayaz Ahmad Wani, Department of Medicine, Government Medical College Jammu, Jammu and Kashmir, India. Phone: +91-9205062319. E-mail: wanifayaz.a@gmail.com

extended to dosage adjustments on the basis of DNA sequencing of drug metabolizing enzyme genes.^[2] Although pharmacokinetic (PK)-based individualized therapy has been in use since 1970's, evidence is mounting that the current use is still suboptimal.^[3-5] Continuously escalating health-care costs and increasing consumer awareness have drawn attention toward laboratory test utilization as these have a significant share in health-care costs and therapeutic drug monitoring (TDM) has no exception in this regard.^[6,7]

The literature is scanty with regard to the quality of requests made for TDM although key inputs from requesting physicians are vital for meaningful interpretation of drug concentration measurements. While the quality of requests made for serum digoxin concentration has been reported to be generally unsatisfactory,^[8] no report is available regarding the quality of requests for antiepileptic drugs (AEDs) and non-AEDs other than digoxin.

With older opportunities existent for evaluating the definitive role of TDM for drugs whose patent lives have expired (e.g. aminoglycosides and digoxin) and opportunities continuing to arise with newer agents (such as mycophenolic acid and newer AEDs) that are likely to require TDM,^[9-11] strategies for quality improvement in TDM are needed. Further, the explosion in biotechnology, ease of genotyping, and intensive pharmacovigilance^[11] are taking therapeutic monitoring to newer horizons, and there is a need for translating such practices for clinical benefits. We investigated the PK and pharmacodynamic (Pd) (therapeutic and/or adverse) responses to phenytoin in a tertiary care setting in India.^[7] This study looks at existing deficiencies in the translation of TDM recommendations to bedside using phenytoin as a probe drug and is the first study to investigate the quality of requisitions made for TDM.

MATERIALS AND METHODS

This was a hospital-based prospective study conducted in the Department of Clinical Pharmacology at Sher-i-Kashmir Institute of Medical Sciences and Government Medical College, Srinagar, after obtaining the Ethical Approval. The study group constituted of cases of cryptogenic or idiopathic epilepsy ($n = 90$) who participated entirely on voluntary basis. Pd analysis was performed by evaluating clinical response to phenytoin therapy, adverse drug reaction (ADR) monitoring, and subsequent causality categorization. All ADRs were recorded and reported to National Coordination Centre, Indian Pharmacopoeia Commission (NCC-IPC) vide VigFlow. Causality assessment was done using WHO-UMC causality categories, for ADRs with objective evidence

either in the form of clinical signs on examination and/or lab investigation like nerve conduction velocity, serum phenytoin concentration. The same ADRs were subjected to categorization as serious or otherwise as per the CDSCO criteria for serious adverse events.

Phenytoin PK analysis was done by a validated immunoassay technique using Syva enzyme immunoassay (EMIT) 2000 phenytoin assay kit for the estimation of serum phenytoin trough, peak, or random levels as needed. The sensitivity level of the EMIT phenytoin assay is 0.5 µg/ml with a confidence level of 95%.

An audit of 174 requisitions for the quality of the information received was done exclusive of PK and Pd evaluation. Of the 174 requisitions, 39 requisitions were excluded from the audit on the basis of considering these situations as part of advocacy and sensitization of the prescribers on a rational approach to the TDM under the Information, Education, and communication activity of the Department of Clinical Pharmacology. The scoring scale was devised for quality assessment of remaining 135 requisitions with patient details written by the treating doctors, on the basis of their own pre-awareness level of knowledge and understanding of TDM, which are required for meaningful interpretation of drug concentration measurements [Table 1].

The software package SPSS version 22 was used for statistical analysis. Shapiro–Wilk test was used to check the sample for normal distribution of phenytoin PK parameters. The area under concentration-time curve (AUC_{0-4}) was derived numerically by linear trapezoidal method from peak and trough phenytoin concentrations using non-compartmental analysis. Results are presented as mean \pm standard deviation, median, or percentage as applicable. A $P < 0.05$ was taken as statistically significant.

RESULTS

An analysis of clinical response to phenytoin revealed that 79% of patients responded positively to phenytoin after treatment optimization or could be tapered off phenytoin successfully after achieving seizure control and remained seizure free for the period of follow-up. 8% of patients

Table 1: Quality assessment of requisitions received for therapeutic drug monitoring

Available detail	Score	Quality
Name, MRD No.	1	Unacceptable
I + Diagnosis	2	Poor
II + Dose of drug to be monitored	3	Incomplete
III + Indication for drug level monitoring	4	Satisfactory
IV + Timing of sampling relative to last dose	5	Desirable

could not achieve satisfactory therapeutic control with phenytoin alone and needed a second AED in addition to phenytoin. 13% of patients were discontinued from phenytoin either because of adverse effects or because phenytoin did not modify seizure activity in these patients. Figure 1 shows the distribution of patients on the basis of phenytoin response. An arbitrary categorization of patients into phenytoin response categories stands published.^[12]

Common adverse effects reported by patients are shown in Table 2. Gum Hypertrophy as an ADR in all cases fulfilled the criteria to be classified as certainly due to phenytoin. Peripheral neuropathy was detected in five cases, and in all the five cases, it fulfilled the criteria to be categorized as probably due to phenytoin. Morbilliform rash was likewise categorized to be certainly caused by phenytoin, and tremor was deemed to be possibly due to phenytoin. Irrespective of their severity, gum hypertrophy, peripheral neuropathy, morbilliform rash, and tremor were not serious adverse events as per CDSCO.

Ataxia was detected in three cases. Two patients recovered from ataxia due to phenytoin overdose (serum phenytoin concentration was above therapeutic range), and in both the cases, ataxia was assessed to be certainly caused by phenytoin. One patient persisted with ataxia for more than 2 years after discontinuation of phenytoin, and the causality of ataxia in this case was categorized to be possibly due to phenytoin as there was a strong possibility of cerebellar damage due to prolonged seizure. Nonetheless, ataxia in this patient was an AE associated with persistent significant disability or incapacity as the patient was unable to walk without support and hence a serious adverse event as per the CDSCO.

Pk data for 87 patients were subjected to final statistical analysis. Mean serum phenytoin trough (C_0) concentration was $12.105 \pm 0.433 \mu\text{g/ml}$. Mean serum phenytoin peak (C_4) concentration was $16.895 \pm 0.571 \mu\text{g/ml}$. Mean AUC_{0-4} was $57.99 \pm 1.76 \mu\text{g/ml/h}$. Shapiro–Wilk test revealed that the sample data for peak, trough, and AUC_{0-4} were normally distributed [Table 3].

Audit of 135 TDM requisitions revealed that 54 (40%) requisitions scored one and were graded as unacceptable; 34 (25%) requisitions scored two and were graded as of poor quality; 35 (26%) requisitions scored three and were graded as incomplete; 12 (9%) requisitions scored four and were graded as satisfactory; while none of the requisitions was found to have a score of five or complete.

DISCUSSION

PK monitoring commonly, though erroneously, known as “TDM” is considered useful in enhancing therapeutic

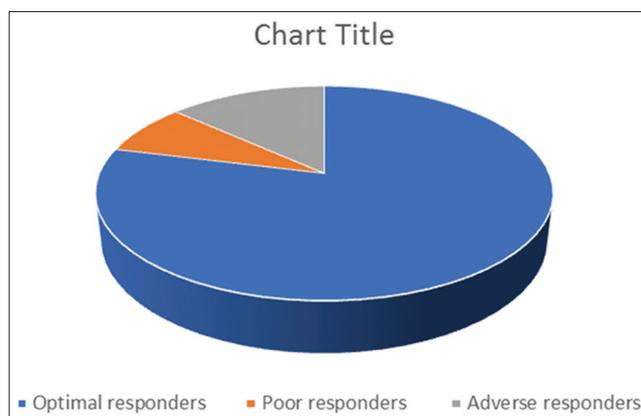


Figure 1: Case categorization of phenytoin pharmacodynamic response

Table 2: Common adverse effects reported by patients

Adverse effects	Number of instances
Gum hypertrophy	15
Forgetfulness	9
Generalized weakness	9
Headache	9
Tremor	7
Giddiness	5
Anxiety	5
Sleepiness	5
Peripheral neuropathy	5
Unsteadiness of Gait	3

Table 3: Average profile of phenytoin Pk parameters of participants (n=87)

Phenytoin Pk parameter	Mean±SD
C_0 ($\mu\text{g/ml}$)	12.10 ± 0.433
C_4 ($\mu\text{g/ml}$)	16.89 ± 0.57
AUC_{0-4} ($\mu\text{g/ml/hr}$)	57.99 ± 1.76

Pk: Pharmacokinetic, SD: Standard deviation

benefits and minimizing the incidence of adverse effects of narrow therapeutic index drugs. It begins with a determination of an initial dosage regimen appropriate for the clinical condition in the context of patient demographic characteristics as age, body weight, organ function, and concomitant drug therapy. Conventionally, drug concentration measurements are needed for reasons like dosage adjustments secondary to changes in clinical state, toxicity monitoring, lack of therapeutic response, differentiating noncompliance from metaboliser status, differentiation of disease state from toxicity, assessment for drug interactions or guiding withdrawal of therapy.^[13] Provision of appropriate information when requesting drug concentration measurement is essential to optimize interpretation of results and quality of feedback to the clinicians.^[14] Measuring plasma concentration of

all drugs is unnecessary, and it is prudent to employ drug concentration measurement only for drugs with narrow therapeutic range, marked PK variability, and when therapeutic and/or adverse effects are difficult to monitor. Conventionally, the best practice guidelines for TDM are ordering drug concentration measurements only when clearly indicated, conducting validated assays in appropriate biological matrices collected at recommended times relative to drug intake and finally providing assay results with meaningful interpretation on the basis of PK and clinical principles within useful time frames. As a rule biological matrix, essentially blood should be drawn at trough or just before the next dose (C_{\min} and C_{ps}) in routine drug level measurements as trough levels are less likely to be influenced by variations in absorption, distribution, and elimination. Two main exceptions to this rule are toxicity monitoring and poor therapeutic control requiring loading doses when random or immediate sampling might be done.^[15] Recently, the importance of incorporating pharmacovigilance and pharmacogenomic inputs to complement evidence generated by TDM has been underscored.^[12,16]

Phenytoin continues to be used by a large population in the developing countries. Although largely replaced by valproate or carbamazepine for use in partial and secondarily generalized seizures, it retains its rank in the treatment of status epilepticus.^[17-19] Classically a difficult to handle drug, due to changing kinetics at therapeutic doses, phenytoin therapy is further complicated by pathogenetically elusive adverse effects such as gum hypertrophy and cerebellar degeneration. The availability of CYP2C9, CYP2C19, and HLA B1507 gene sequencing, if at all helpful, is largely confined to few centers and not practiced routinely, especially in this part of the world. Besides, there is a lack of large prospective clinical trials to determine whether the use of genotyping improves clinical outcomes despite evidence of a link between adverse effects and polymorphisms specifically CYP2C9 *2 and *3 in this context.^[20] As such gene polymorphism-based recommendations might play a role in individualizing phenytoin therapy in newly diagnosed cases, these seem irrelevant in patients already maintained on phenytoin. In this backdrop, phenytoin seemed an ideal probe to reflect current practice and problems with TDM service. As phenytoin Pd analysis was done using an arbitrary scale, no study was available for the comparison of Pd analysis. The results of phenytoin Pk analysis were consistent with earlier results.^[21]

A review of the literature reveals the importance of HLAB * 1502 allele and CYP2C9 genotype to phenytoin treatment outcomes.^[22-26] Investigating these genes for personalization of phenytoin therapy can complement

phenytoin TDM, especially as regard adverse effects which cannot be correlated to serum phenytoin levels. It might seem wise to withhold implementation of these recommendations pending more evidence for mild or moderate ADRs; however, the same attitude as regard serious ADRs begs some questions. Expedited reporting for serious ADRs is already in place, and it is high time that such pharmacovigilance initiatives should be taken further by some sort of sentinel reporting and investigating serious ADRs on a priority basis.

Another issue that continues to plague TDM utilization is the lack of recent literature supporting its cost-effectiveness. A given dose of drug does not produce the same plasma concentration in all patients as there are considerable variations in absorption, distribution, and elimination among people. The polymorphism of drug metabolizing genes has, by far, the greatest impact for inter-individual differences in drug response. This issue was historically addressed by TDM, which developed in the 80's, an era when hospitals were considered mostly as non-profitable organizations contrary to the current era when hospitals in private and public sector both are trying to run on a no gain no loss economy so to say the least. In the current scenario especially in super specialties like clinical pharmacology, the borders between research and healthcare are blurred and so the argument of cost effectiveness seems unrealistic. Furthermore, with the availability of high throughput genome sequencing and nanotechnology, one is tempted to overlook the experience gained by this time-tested though tedious resource. Nonetheless, TDM remains an important milestone toward personalization of treatment, especially for drugs such as lithium and phenytoin.

Drug assay procedures have evolved from a variety of analytical methods ranging from spectrophotometry to high-performance liquid chromatography.^[27] Currently vast majority of drug assay procedures are some variant of immunobinding assay procedures such as fluorescence polarization immunoassay, EMIT, and enzyme-linked immunosorbent assay.^[28]

As such, TDM continues to be a tertiary care investigation provided by centralized laboratories having enormous equipment that can be handled by trained personnel only. This adds to the cost and time involved for TDM further compromising its application for personalization of medicine. Nanopharmacological techniques such as microfluidic electrochemical detection for *in vitro* continuous monitoring for doxorubicin/kanamycin and a portable device for monitoring methotrexate by surface plasma resonance have opened doors for the development of real-time point-of-care testing for some of the drugs requiring TDM.^[29] Extending such technological advances

to drugs such as lithium and phenytoin that classically required TDM and continue to be used by a large population remains the challenge to be taken up by medical and scientific communities.

An audit of TDM requisitions in our setting did not yield encouraging results. Authors propose a template which can be downloaded and modified for providing requisite information by or for TDM laboratories. Multidisciplinary educational approach, computerizing requesting methods, traditional and formal education for changing physician behavior, proactive approach on part of the clinical pharmacologists, and better advocacy are the need of the hour for optimum utilization of this underutilized health-care resource.

REFERENCES

- Aronson JK. Monitoring therapy. *Br J Clin Pharmacol* 2005;60:229-30.
- Caudle KE, Rettie AE, Whirl-Carrillo M, Smith LH, Mintzer S, Lee MT, *et al.* Clinical pharmacogenetics implementation consortium guidelines for CYP2C9 and HLA-B genotypes and phenytoin dosing. *Clin Pharmacol Ther* 2014;96:542-8.
- El Desoky DE, Klotz U. Value, limitations and clinical impact of therapeutic drug monitoring in adults. *Drug Invest* 1993;6:127-36.
- Pater C. Individualizing therapy—in search of approaches to maximize the benefit of drug treatment (II). *Curr Control Trials Cardiovasc Med* 2004;5:7.
- Paci A, Veal G, Bardin C, Levêque D, Widmer N, Beijnen J, *et al.* Review of therapeutic drug monitoring of anticancer drugs Part 1 – cytotoxics. *Eur J Cancer* 2014;50:2010-9.
- Bates DW, Soldin SJ, Rainey PM, Micelli JN. Strategies for physician education in therapeutic drug monitoring. *Clin Chem* 1998;44:401-7.
- Rao GG, Crook M, Tillyer ML. Pathology tests: Is the time for demand management ripe at last? *J Clin Pathol* 2003;56:243-8.
- Ellington C, Grgurinovich N, Miners JO, Mangoni AA. Quality of requests for serum digoxin concentrations: Experience from an Australian regional health service. *Br J Clin Pharmacol* 2007;63:623-7.
- Burton ME, editor. *Applied Pharmacokinetics and Pharmacodynamics: Principles of Therapeutic Drug Monitoring. A Critical Assessment of the Outcomes of Therapeutic Drug Monitoring.* Philadelphia, PA: Lippincott Williams & Wilkins; 2006. p. 867.
- Perucca E. Is there a role for therapeutic drug monitoring of new anticonvulsants? *Clin Pharm* 2000;38:191-204.
- Al-Essa RK, Al-Rubaie M, Walker S, Salek S. The Current Status of Drug Safety and Pharmacovigilance, in *Pharmaceutical Regulatory Environment: Challenges and Opportunities in the Gulf Region.* Cham: Springer International Publishing; 2015. p. 115-40.
- Kousar S, Wafai ZA, Wani MA, Jan TR, Andrabi KI. Clinical relevance of genetic polymorphism in CYP2C9 gene to pharmacodynamics and pharmacokinetics of phenytoin in epileptic patients: Validatory pharmacogenomic approach to pharmacovigilance. *Int J Clin Pharmacol Ther* 2015;53:504-16.
- Kang JS, Lee MH. Overview of therapeutic drug monitoring. *Korean J Intern Med* 2009;24:1-0.
- Sharpe PC, Morrow J, Trimble ER. An audit of therapeutic drug monitoring of anticonvulsants. *Ulster Med J* 1995;64:151-6.
- Gross AS. Best practice in therapeutic drug monitoring. *Br J Clin Pharmacol* 1998;46:95-9.
- Twardowschy CA, Werneck LC, Scola RH, De Paola L, Silvado CE. CYP2C9 polymorphism in patients with epilepsy: Genotypic frequency analyzes and phenytoin adverse reactions correlation. *Arq Neuropsiquiatr* 2011;69:153-8.
- Haroon A, Tripathi M, Khanam R, Vohora D. Antiepileptic drugs prescription utilization behavior and direct costs of treatment in a national hospital of India. *Ann Indian Acad Neurol* 2012;15:289-93.
- Rajshanker G. Recent trends in the management of status epilepticus. *Indian J Crit Care Med* 2005;9:52-63.
- Tudur Smith C, Marson AG, Williamson PR. Phenytoin versus valproate monotherapy for partial onset seizures and generalized onset tonic-clonic seizures. *Cochrane Database Syst Rev* 2001;4:CD001769.
- Ingelman-Sundberg M, Rodriguez-Antona C. Pharmacogenetics of drug-metabolizing enzymes: Implications for a safer and more effective drug therapy. *Philos Trans R Soc B Biol Sci* 2005;360:1563-70.
- Koch-Weser J. Serum drug concentrations in clinical perspective. *Ther Drug Monit* 1981;3:3-16.
- van der Weide J, Steijns LS, van Weelden MJ, de Haan K. The effect of genetic polymorphism of cytochrome P450 CYP2C9 on phenytoin dose requirement. *Pharmacogenetics* 2001;11:287-91.
- Thakkar AN, Bendkhale SR, Taur SR, Gogtay NJ, Thatte UM. Association of CYP2C9 polymorphisms with phenytoin toxicity in indian patients. *Neurol India* 2012;60:577-80.
- Man CB, Kwan P, Baum L, Yu E, Lau KM, Cheng AS, *et al.* Association between HLA-B*1502 allele and antiepileptic drug-induced cutaneous reactions in han chinese. *Epilepsia* 2007;48:1015-8.
- Li X, Yu K, Mei S, Huo J, Wang J, Zhu Y, *et al.* HLA-B*1502 increases the risk of phenytoin or lamotrigine induced stevens-johnson syndrome/toxic epidermal necrolysis: Evidence from a meta-analysis of nine case-control studies. *Drug Res (Stuttg)* 2015;65:107-11.
- Johnson JA, Caudle KE, Gong L, Whirl-Carrillo M, Stein CM, Scott SA, *et al.* Clinical pharmacogenetics implementation consortium (CPIC) guideline for pharmacogenetics-guided warfarin dosing: 2017 update. *Clin Pharmacol Ther* 2017;102:397-404.
- Dijkhuis IC. Quality control in therapeutic drug monitoring. *Pharm Weekblad* 1988;10:138-44.
- Waldman SA, Terzic A. In: Shaw M, editor. *Therapeutic Drug monitoring in Pharmacology and Therapeutics: Principles to Practice.* Philadelphia, PA: Saunders Elsevier; 2009. p. 275-87.
- Federico P, Giuseppe T. Point-of-care for therapeutic drug monitoring of antineoplastic drugs. *Med Chem* 2016;6:2.

How to cite this article: Kousar S, Wani FA, Wani ZA, Nazir A, Zahid AT, Wafai ZA. Translating Phenytoin Therapeutic Drug Monitoring for Potential Utilities to Pharmacovigilance: Capacity Raking an Established Tertiary Care Service. *Int J Sci Stud* 2018;6(5):30-34.

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

Epidemiological Study of Childhood Dermatoses in Eastern Uttar Pradesh

Anil K Gupta¹, Ali Mohammad², Lalit Mohan³, S K Singh¹, Snehlata², Amit Kumar Soni², Sushantika², Naveen Kumar²

¹Associate Professor, Department of Dermatology, BRD Medical College, Gorakhpur, Uttar Pradesh, India, ²Resident, Department of Dermatology, BRD Medical College, Gorakhpur, Uttar Pradesh, India, ³Professor, Department of Dermatology, BRD Medical College, Gorakhpur, Uttar Pradesh, India

Abstract

Background: Prevalence studies of skin disorders in children and adolescents are meager, in India few epidemiological data are available. Proper epidemiological data should be available to be familiar with a geographical area, compare data from other areas and to take steps for prevention of disease.

Aims: The purpose of this study was to evaluate the epidemiologic and clinical features of childhood dermatoses in Baba Raghav Das Medical College, Gorakhpur.

Materials and Methods: A retrospective investigation of a total of 3000 patients in the age group of 5-14 years visiting the Outpatient Department of Dermatology and Venereology of Baba Raghav Das Medical College, Gorakhpur was done. The parameters included were age at onset of disease, sex, type of disease, and distribution of lesions. Data and statistical analysis were done.

Results: Mean age was 7 years. M:F ratio was 1.5:1. Infectious disease(49%) were the most common followed by Eczematous disorders (18%). Among the infections dermatophytosis infections were the commonest followed by bacterial infections. Verruca vulgaris was commonest among viral diseases, and pityriasis alba was the commonest Eczema.

Conclusion: Superficial Dermatophytic infection was the commonest disease, followed by superficial pyodermas, viral warts followed by molluscum contagiosum were common viral infections, Vitiligo, keratosis pilaris, Nevi, Miliaria and Fordyce spots were other common diseases.

Key words: Childhood atopic infection, Childhood dermatoses, Clinical, Dermatologic, Fungal disease, Viral disease

INTRODUCTION

Disorders of the skin and its appendages, including the hair and nails, are frequently encountered in children, but prevalence studies of skin disorders in children and adolescents are meager. Low socioeconomic status, malnutrition, overcrowding, and poor standards of hygiene are important factors accounting for the difference of distribution of skin diseases in the developing and

developed countries, and reports from different parts of the world have revealed a wide variation in the prevalence of various skin disorders. Many epidemiological studies in India and parts of the world have been done to study the pattern of pediatric dermatoses.^[1-9] The epidemiological data in Indian studies are based on the pattern of pediatric dermatoses in school-going children in both urban and rural areas and in tertiary care hospitals (medical colleges).^[8,9] Moreover, the pattern of skin diseases in India is different across the states, rural and urban areas, and hilly areas.

Skin diseases in the pediatric age group can be transitory or chronic, and recurrent pediatric dermatoses require a separate view from adult dermatoses as there are important differences in clinical presentation, treatment, and prognosis. The chronic dermatoses are associated with

Access this article online



www.ijss-sn.com

Month of Submission : 06-2018
Month of Peer Review : 07-2018
Month of Acceptance : 08-2018
Month of Publishing : 08-2018

Corresponding Author: Dr. Ali Mohammad, Room no 146 Gautam Hostel, BRD Medical College, Gorakhpur, Uttar Pradesh, India.
Phone: +91-8933097079. E-mail: alimohammadabdiderma@gmail.com

significant morbidity and psychological impact. Cutaneous infections are common in children during school-going years. Most of the cutaneous diseases which result from intrinsic genetic abnormalities also have onset in the pediatric age group. A recent study done by Grills *et al.* in mountainous region of India (Uttarakhand) revealed that dermatological conditions were prevalent (45.3%) with 33% being of infectious etiology.^[1,10-12] In this study, atopic dermatitis (9.2%), scabies (4.4%), tinea corporis (4.1%), and pityriasis alba (3.6%) were common. We, hereby, try to find the epidemiological status in the northern part of India.

MATERIALS AND METHODS

The study was a retrospective study conducted on 3000 school-going children and adolescents in the age group of 5–14 years patients attending the Dermatology outpatient department of Baba Raghav Das Medical College, Gorakhpur, which is a 700-bedded multispecialty hospital in the urban area of Uttar Pradesh, India, and patients of eight districts visited our hospital (namely Gorakhpur, Maharajganj, Deoria, Kushinagar, Azamgarh, Mau, Basti, and Gopalganj). Most patients (40.2%) visited from Gorakhpur where the medical college is located. Their

Table 1: Age distribution of pediatric dermatoses (n=3000)

Age (in years)	Percentage
5–6	22
7–8	19
9–10	16
11–12	18
13–14	25

Table 2: Distribution of various dermatosis

Disease	Total number (%)
Infectious disease	1504 (49)
Eczema	533 (18)
Keratinization disorders	78 (2.6)
Photodisorders	48 (1.6)
Hair and nail disorders	135 (4.5)
Vesiculobullous disorders	19 (0.63)
Pigmentary disorders	507 (16.9)
Nutritional disorders	78 (2.6)
Sebaceous gland disorders	90 (3)
Miscellaneous disorders	34 (2)

Table 3: Prevalence of infections and infestations

Infections and infestations	Percentage
Dermatophytic	719
Bacterial	160
Viral	138
Scabies and pediculosis	652

records were reviewed retrospectively. Patients visiting from June 1, 2017, to June 1, 2018, were included in the study. Sociodemographic data and subtype of disease were studied. The descriptive statistics such as percentage, proportion, mean, and standard deviation were calculated.

RESULTS

A total of 3000 students in the age group of 5–14 years were selected and studied clinically to assess the prevalence of skin disorders in this age group. In our study, there were 1800 male and 1200 female students [Table 1].

Infections and infestations combined constituted highest proportion 49% (1504), followed by eczematous dermatoses which constitute 18% (533) [Table 2].

Among the infectious and infestation disorders, most common was tinea corporis followed by pyoderma [Table 3].

Table 4: Prevalence of bacterial infections

Bacterial infection	Percentage
Impetigo and perioritis	50
Furunculosis	38
Ecthyma	1
Pitted keratolysis	2
Infectious eczematous dermatitis	9

Table 5: Prevalence of fungal infections

Fungal infection	Percentage
Tinea corporis	56
Tinea cruris	28
Tinea pedis	3
Tinea capitis	9
Tinea faciei	4

Table 6: Prevalence of viral infectious

Viral disease	Percentage
Warts	48
Molluscum contagiosum	23
Chicken pox	10
Herpes labialis	6
Hand, foot, and mouth disease	1
Pityriasis rosea	12

Table 7: prevalence of endogenous eczema

Disease	Number (%)
Juvenile plantar dermatosis	112 (30)
Pityriasis alba	146 (42)
Atopic dermatitis	60 (17)
Contact dermatitis	36 (10)

Among the bacterial infections, impetigo was the most common, amounting to 50% (8) of cases followed by furunculosis 38% [Table 4].

Dermatophytic infections constituted the maximum of the fungal infections involving the skin (48.5). Among dermatophytic infections, tinea corporis constituted the highest proportion, i.e., 56.12%, followed by tinea cruris 28% and tinea capitis 9% [Table 5].

Viral warts were the most common skin lesion caused by a viral infection in this study and constituted 48% (70) followed by molluscum contagiosum 23% (32) [Table 6].

Endogenous eczemas were more common than exogenous eczemas during the study period. Pityriasis alba was the most common endogenous eczemas, which constituted 42% (146) of cases of all eczemas followed by juvenile plantar dermatosis. Among the exogenous eczemas, allergic contact dermatitis (ACD) was the most common which constituted 9.8% (16) of cases. Irritant contact dermatitis was seen in 3% (5), photo ACD in 2.45% (4), and infectious eczematoid dermatitis in 1.2% (2) of the total eczema cases [Table 7].

2.6% of total pediatric dermatoses in this study were nutritional dermatoses, in which there were most cases of phrynoderma in 70%, zinc deficient acral erythema in 5%, angular cheilitis in 4%, and kwashiorkor in 3% of cases.

Congenital melanocytic nevus was the most common among all the nevoid and developmental disorders seen in this study, others which constituted were becker's nevus, nevus sebaceous, linear verrucous epidermal nevus, and achromic nevus seen in one patient each respectively.

The keratinization disorder constituted most of keratosis pilaris 32% (25). Plaque and guttate psoriasis constituted 30% (23.4) of papulosquamous disorders. Ichthyosis, palmoplantar keratoderma, and lichen spinulosus were seen in 12% (10).

Lichen planus was seen in 20% (16) and lichen nitidus in 2%, of all papulosquamous disorders. Pityriasis rubra pilaris was seen in four patients.

Among the disorders of sweat glands and sebaceous glands, acne was the most common to be seen. These cases constituted 68% (61). Miliaria cases constituted 26.2% (29) of sweat and sebaceous disorders, Fordyce spots were seen in 2.7% (1.8), and sebaceous cysts in 2.4% (2) of sweat and sebaceous disorders.

Among the vesiculobullous disorders, there were four cases of epidermolysis bullosa simplex and four cases of chronic

bullous disease of childhood. Only two cases were seen in the category of connective tissue disorders which included of systemic lupus erythematosus. Eight cases of morphea were present.

507 total cases of vitiligo were seen: Vitiligo vulgaris 53%, acrofacial vitiligo in 18%, segmental vitiligo in 12%, and mucosal vitiligo in 17% of cases.

Abnormal responses to light were seen in 48 cases during the period of the study. Polymorphic light eruption was the most common abnormality as seen in 85.7%. Hydroa vacciniforme was seen in one and juvenile spring eruptions in three cases.

The disorders of hair and nails were seen in 135 cases during the study period and most cases were of alopecia areata in 70% (94), uncombable hair disease in three, monilethrix and wooly hair nevus in on each, and short anagen syndrome in one case.

Paronychia was the most common nail disease seen, which constituted 20% (4). The other disorders belonging to this category included premature canities in 10% (14) and trichotillomania 5% (8).

34 cases were included in the miscellaneous disorder category. It comprised cases of insect bite reaction, urticaria, tuberous sclerosis, erythema multiforme, aphthous stomatitis, corns, pyogenic granuloma, Henoch–Schonlein purpura, acanthosis nigricans, granuloma annulare, parapsoriasis, angioedema, juvenile xanthogranuloma, and neurofibroma.

DISCUSSION

In the study from the Northern India by Dogra and Kumar,^[2] the age group was 6–14 years only, whereas in our study, the age group was 5–14 years. In the age group of 14–19 years, there is the excess of skin disorders in the form of acne.

A study conducted by Zamanian and Mahjub^[3] in Hamedan, Iran, showed eczematous disorders to be the most common of all disorders.

Among the eczematous disorders, pityriasis alba was the most common. Students in the age range of 9–14 years (64.7%) were most frequently affected. It was found more in males (62.6%) than in females (17.4%).

The prevalence of atopic dermatitis was 3% in our study. In England, the point prevalence in one study was 11.5–14% in 3–11-year-old children. This, therefore,

suggests that atopic dermatitis is more prevalent in western countries than in the developing countries like India, implicating thereby a strong environmental factor in causation of these disorders. We observed the prevalence of 3% for acne disorders, which include acne vulgaris, truncal acne, and post-acne scarring. Acne vulgaris, by far, was the most common (17.2%). Acne vulgaris was found more commonly in males (69.6%) than in females (30.4%).

CONCLUSION

This study was done to determine the characteristic clinical pattern and prevalence of pediatric dermatoses. The majority of the study population (48%) belonged to adolescent age group. Of them, males outnumbered females. Fungal infections were the most common infection noted in the study, followed by bacterial and viral infections. ACD was the most common exogenous eczema and Pityriasis alba was the most common endogenous eczema. Plaque psoriasis was the most common papulosquamous disorder, followed by lichen planus. Acne was the most common sweat and sebaceous gland disorder with female preponderance. Alopecia areata was the most common hair disorder. Paronychia was the most common nail disorder.

A detailed knowledge about the pattern of pediatric dermatoses in each geographic area will help us in implementing essential changes in health education, disease

control, preventive strategies in the area concerned and to compare data with other geographical areas in India and world.

REFERENCES

1. Grills N, Grills C, Spelman T, Stoope M, Hellard M, El-Hayek C, *et al.* Prevalence survey of dermatological conditions in mountainous North India. *Int J Dermatol* 2012;51:579-87.
2. Dogra S, Kumar B. Epidemiology of skin diseases in school children: A study from Northern India. *Pediatr Dermatol* 2003;20:470-3.
3. Zamanian A, Mahjub H. Prevalence of skin diseases in Hamedan, Iran in 2002. *Indian J Dermatol* 2005;50:208-11.
4. McNally N, Phillips D. Geographical studies of atopic dermatitis. In: Williams HC, editor. *Atopic Dermatitis: The Epidemiology, Causes and Prevention of Atopic Dermatitis*. Cambridge: Cambridge University Press; 2000. p. 71-84.
5. Stern RS. The prevalence of acne on the basis of physical examination. *J Am Acad Dermatol* 1992;26:931-5.
6. Grover S, Ranyal RK, Bedi MK. A cross section of skin diseases in rural Allahabad. *Indian J Dermatol* 2008;53:179-81.
7. Nevitt GJ, Hutchinson PE. Psoriasis in the community: Prevalence, severity and patients' beliefs and attitudes towards the disease. *Br J Dermatol* 1996;135:533-7.
8. Convit J. Investigation of the incidence of psoriasis among Latin American Indians. In: *Proceedings of the 12th Congress on Dermatology*. Amsterdam: Excerpta Medica; 1962. p. 196.
9. Sardana K, Mahajan S, Sarkar R, Mendiratta V, Bhushan P, Koranne RV, *et al.* The spectrum of skin disease among Indian children. *Pediatr Dermatol* 2009;26:6-13.
10. Last JM. *A Dictionary of Epidemiology, A Handbook Sponsored by IEA, Park's Textbook of Preventive and Social Medicine*. New York: Oxford University Press; 1983.
11. Shakkoury WA, Abu-Wandy E. Prevalence of skin disorders among male schoolchildren in Amman, Jordan. *East Mediterr Health J* 1999;5:955-9.

How to cite this article: Gupta AK, Mohammad A, Mohan L, Singh SK, Snehlata, Soni AK, Sushantika, Kumar N. Epidemiological Study of Childhood Dermatoses in Eastern Uttar Pradesh. *Int J Sci Stud* 2018;6(5):35-38

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

Breast Cancer Awareness in South India

Lalitha Subramanian¹, V U Salini², Heber Anandan³, U Insuvai²

¹Associate Professor, Department of Radiotherapy, Government Thoothukudi Medical College, Thoothukudi, Tamil Nadu, India, ²Senior Resident, Department of Radiotherapy, Government Thoothukudi Medical College, Thoothukudi, Tamil Nadu, India, ³Senior Clinical Scientist, Department of Clinical Research, Dr. Agarwal's Healthcare Limited, Tirunelveli, Tamil Nadu, India

Abstract

Background: Breast cancer is the most frequent cause of cancer death in women in both the developed and developing countries. Breast cancer accounts for 34% of all cancer cases among women in India. There is an increase in the incidence of breast cancer over the past decade. Early breast cancer in the developing countries constitutes only 30% compared to 60–70% in the developed countries.

Aim: The aim of this study is to assess the awareness about risk factors, screening, diagnosis, and treatment among the general public in South India.

Methods: We used a questionnaire from AJCC website translated to Tamil. It is a cross-sectional study covering 1000 people involving the general public and health workers.

Results: More than 90% of the population believe that breast cancer is hereditary and had little knowledge about other risk factors. Majority of the people are not aware that breast cancer can be cured if detected early. Although 80% of the population believe that self-breast examination helps in early detection, <50% of them are practicing it regularly. <2% of the population are aware of the mammogram and the treatment modalities.

Conclusion: Sociodemographic factors such as level of education, income, and marital status influence the percentage of people practicing self-breast examination. People with a family history of breast cancer and higher levels of education had better knowledge about the diagnostic methods and treatment modalities.

Key words: Breast cancer awareness, Breast cancer screening, Breast self-examination

INTRODUCTION

Breast cancer is the most prevalent condition of cancer death in both the developing and developed countries.^[1] Breast cancer contributes to 10.4% of the global burden. According to the National Cancer Registry, breast cancer is the most frequent cancer among women in Delhi, Mumbai, Kolkata, Ahmedabad, and Trivandrum.^[2,3] Moreover, data from National And Regional Cancer Registries from 1984 to 2002 show that breast cancer is significantly increasing and found to be gradually overtaking carcinoma of the uterine cervix. Early breast cancer constitutes only 30% of breast cancer cases in India, whereas it represents

60–70% of cases in the developed countries.^[4] Mortality due to breast cancer is found to be high in the developing countries because they seek medical attention at advanced stages due to the lack of awareness and low socioeconomic status.^[5] The American Cancer Society insists creating breast awareness and early detection, and effective treatment reduces the mortality. The Government of India initiated a national program for the prevention and control of cancers (breast and cervix), diabetes, cardiovascular diseases, and stroke (NPCDCS) during 2010–2011 after integrating the National Cancer Control Programme with national program for the prevention and control of diabetes, cardiovascular, and stroke. The primary focus of NPCDCS is on the promotion of healthy lifestyles, screening, early diagnosis, and treatment.

After the establishment of NCD clinic at primary health centers, district hospital, and tertiary hospitals, we have conducted this study to know the level of breast cancer awareness, breast changes, and knowledge about the treatment. As there is no uniform information education

Access this article online



www.ijss-sn.com

Month of Submission : 06-2018
Month of Peer Review : 07-2018
Month of Acceptance : 08-2018
Month of Publishing : 08-2018

Corresponding Author: Dr. Lalitha Subramanian, Department of Radiotherapy, Government Thoothukudi Medical College Hospital, Thoothukudi – 628 003, Tamil Nadu, India. Phone: +91-9894957990. E-mail: ramlalli90@yahoo.com

and communication policy for breast cancer prevention and there is no acceptable strategy for cancer prevention throughout the nation,^[6] we decided to know the level of awareness in our region through a questionnaire in the regional language.

Aim

The aim of this study is to assess the awareness levels regarding breast cancer risk factors, screening methods available, inheritance pattern, and treatment modalities and also to evaluate the level of awareness regarding breast self-examination (BSE) and its practice among women.

MATERIALS AND METHODS

The study population included a total of 730 people (both men and women) between the age group of 18 and 65 years. The study population consisted of persons who accompanied the patients attending our oncology outpatient department, students in educational institutions, women self-help groups, and the general public.

The data were collected using a structured questionnaire developed by the investigator in Tamil. The participants were requested to fill out the questionnaire face to face with the authors of the study after getting their willingness to participate through a written informed consent. The questionnaire sought sociodemographic information such as age, marital status, education, and family history. The survey aimed to measure the knowledge, risks, etiology, and symptoms. Furthermore, we asked the participants whether they knew about BSE and how frequently performed it. On completion of the questionnaire and interactive session, investigators of the study demonstrated the correct method of BSE performance. We computed knowledge score by totaling the number of correct responses.

RESULTS

We gave the questionnaire to 979 people including both males and females between the age group of 15 and 65 years. Of these, 33% included urban population, and 67% contained rural community. Among this, 32% of them were college students, 33% were the general public, 5% were office staffs, and 3% were women self-help groups. Totally, 66% of the study group were married, and 34% were unmarried. Nearly 8% of the study group had the family history of breast cancer. Only 30% of the study population know that cancer incidence is high above 50 years of age. More than 50% are doubtful about male breast cancer, and only about 15% were sure about its occurrence. About 43% are aware of risk factors such as smoking, alcohol, unhealthy

diet, and lack of exercise. The majority (64%) of our study group are not aware of the genetic association of breast cancer. The majority do not know the incidence about the maternal side inheritance. 92% of the study population know that all breast lumps are not malignant and knew the breast changes related to cancer.

When questioned about BSE, nearly 78% of the study group are aware that BSE helps in early detection. Only 36% have answered about mammogram as a screening method [Figure 1].

Married people, those with the family history of breast cancer and graduates, have better knowledge about BSE [Figure 2 and 3].

Although majority were aware of BSE, <40% were practicing it. Women residing in the urban area, married women, and those with family history performed BSE more regularly than others [Figure 4 and 5].

The NCD program aims to propagate the knowledge about breast cancer and attitude regarding its screening practice in different parts of India. Only 43% of the study group believe that breast cancer is curable. 85% of the study group is confident that early diagnosis increases longevity. Nearly half of the study group are aware of the treatment modalities such as surgery, radiotherapy, and chemotherapy [Figure 6].

DISCUSSION

In our study, the overall awareness about the risk factors was low. In July 2002 issue of the Saudi Medical Journal, Alam published a survey to assess the knowledge of breast cancer and its risk factors among women in Riyadh and concluded that knowledge about risk factors was moderate and varied according to the level of education and marital status.^[7] The results of the study are more similar to study regarding risk factors. In our study, 20% of women felt that smoking was a risk factor which means that they linked the carcinogenic effect of smoking to multiple types of cancer. It is important to teach women about the risk factors and emphasize the importance of healthy lifestyle. Knowledge about the genetic association of breast cancer will help to identify the high-risk group and initiate screening procedures earlier than the low-risk group.

BSE is one where women examine their breast once every month. A study by Hackshaw and Paul showed that BSE is not effective in reducing mortality.^[8] However, the current research has shown that the sensitivity and specificity of BSE have improved over a decade.^[9] Women should know how their breast usually feels and should be able to make out the difference associated with breast cancer to make BSE useful

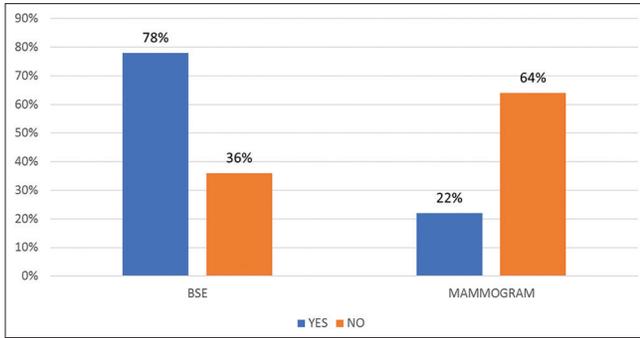


Figure 1: Awareness about screening methods

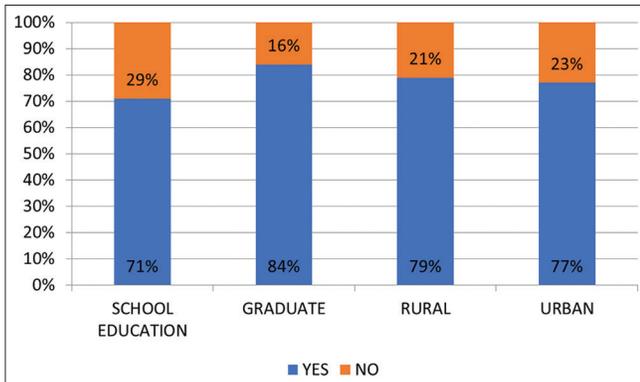


Figure 2: Relation between awareness about breast self-examination and sociodemographic factors

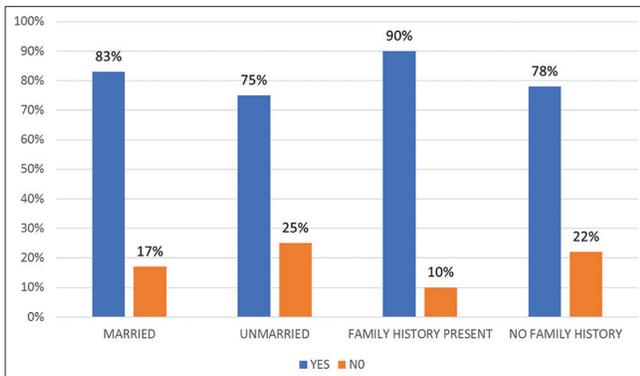


Figure 3: Relation of breast self-examination awareness to marital status and family history

(Zhao and Kanda, 2000). Friedman and Nelson *et al.*, in their paper in the American Journal of Preventive Medicine in 1994, noted that, whereas over 90% of women were of BSE practice, a mere 27% perform BSE monthly.^[10] Chaudhury *et al.* published a study on South Asian women aged above 40 years, residing in Toronto, Canada, in the Oncology Nursing Forum in November 1998. They found that only 12% of the participants practiced BSE monthly, and a majority (54%) said that they did not know much about breast cancer.^[11] Our study results were consistent with these studies. In another Jordanian cross-sectional study, women's age, level of education, and family history of breast cancer correlated with BSE performance.^[12]

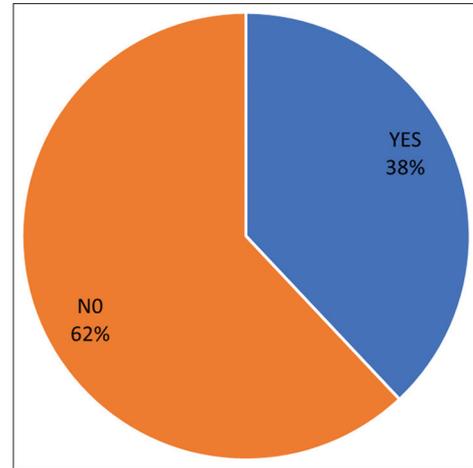


Figure 4: Percentage of people performing breast self-examination

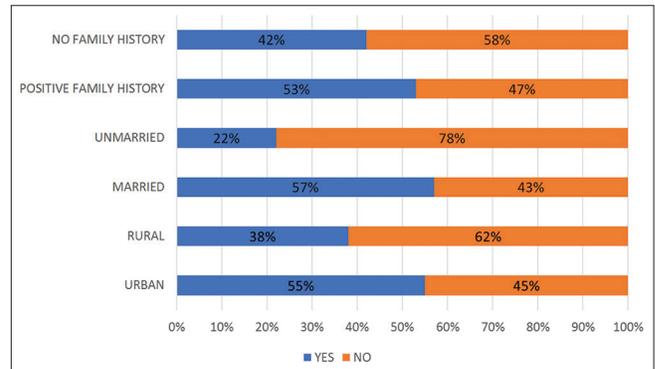


Figure 5: Relation of sociodemographic factors to performance

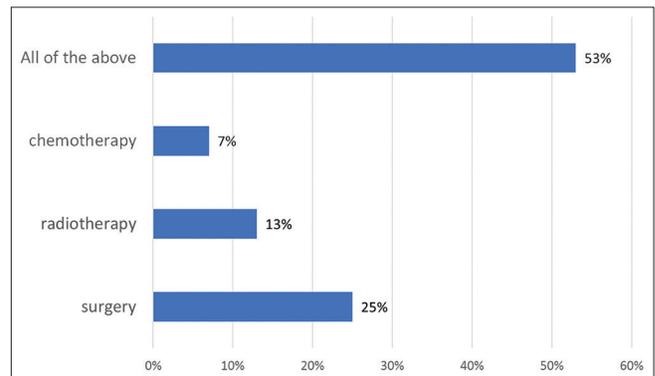


Figure 6: Awareness about treatment modalities

Our study outcome on BSE performance associated with this study. Among the screening procedures, mammography is the most efficient way since it helps in diagnosing cancer at the asymptomatic stage. A survey by Drukteinis *et al.* found that the mortality due to breast cancer decreased by 15% due to mammography screening.^[13] The mammogram has grown a step forward from plain-film to digital mammography which has improved sensitivity for dense breasts.^[14] Literature has shown that awareness about screening mammography is

higher in urban population compared to rural counterparts (Leung *et al.*, 2014). In our study, most people are unaware of the term mammogram but are familiar with ultrasonography of breast. Breast ultrasound computer-aided diagnosis system can be incorporated in community screening as a clinical diagnostic tool which will help the radiologist's accuracy.^[15] The sociodemographic factors did not have an impact on the awareness about the mammogram. Through NCD programs, most women have become aware of BSE. It is equally essential knowledge about the necessity for regular mammograms, especially for the high-risk groups.

There are many barriers to breast cancer screening, and they are related to knowledge, income, education, culture, psychosocial attributes, social factors, and language barriers.^[16] Knowledge regarding the breast cancer symptoms and screening procedures is an important element influencing mammography use and BSE.^[17] Higher levels of education, income, marital status, and employment are positive predictors of participation in screening programs.^[18] Fear of results, fear of treatment, and fear of test itself were other highlighted barriers.^[19] Influence of family, friends, or patients with breast cancer is significant for participation in screening.^[20]

A personal history of breast cancer was a factor studied by many researchers in various studies worldwide. Madanat and Merrill and Petro-Nustus *et al.* of Jordan, as well as Haji-Mahmoodi *et al.* of Tehran, Iran, all concluded that awareness about breast cancer and the practice of BSE significantly associated with a personal history and a family history of breast tumors.^[21,22] Our study also showed that persons with the family history had better knowledge about breast cancer regarding risk factors, screening procedures, and treatment modalities. Learning about the treatment modalities helps to alleviate the fear about breast lump and will increase the level of confidence. This will alter the health-seeking behavior of the population.

CONCLUSION

To deal with the arising epidemic of breast cancer, it is the responsibility of health professionals to make available information about breast cancer, risk factors, warning signs, and management. Breast cancer awareness was moderate in our study which substantiates the need to spread knowledge through mass media since it is available to a large number of people. The most frequently mentioned reason for not performing BSE was not knowing how to perform BSE. The NCD staffs must play an active role in demonstrating the

proper method of BSE. Improving social support networks will create the more positive attitude toward screening.

REFERENCES

1. Ferlay J, Bray F, Parkin DM, Pisani P, editors. Globocan 2000: Cancer Incidence and Mortality Worldwide (IARC Cancer Bases No. 5). Lyon: IARC Press; 2001. Available from: <http://www.who.int/2001>; <http://www.dep.iarc.fr/globocan/globocan.htm>. [Last cited on 2017 Sep 09].
2. Sreedevi A, Quereshi M, Kurian B, Kamalamma L. Screening for breast cancer in a low middle income country: Predictors in a rural area of Kerala, India. *Asian Pac J Cancer Prev* 2014;15:1919-24.
3. Chopra R. The Indian scene. *J Clin Oncol* 2001;19 18 Suppl:106S-11.
4. Kulkarni BB, Hiremath SV, Kulkarni SS, Hallikeri UR, Patil BR, Gai PB. Decade of breast cancer-trends in patients profiles attending tertiary care center in South India. *Asian J Epidemiol* 2012;5:103-13.
5. Rizwan MM, Saadullah M. Lack of awareness about breast cancer and its screening in developing countries. *Indian J Cancer* 2009;46:264-73.
6. National. Cancer. Control. Programmes. Policies and Managerial Guidelines. Available from: <http://www.who.int/2002>. <http://www.who.int/cancer/media/en/408.pdf>. [Last cited on 2017 Sep 09].
7. Alam AA. Knowledge of breast cancer and its risk and protective factors among women in Riyadh. *Ann Saudi Med* 2006;26:272-7.
8. Hackshaw AK, Paul EA. Breast self-examination and death from breast cancer: A meta-analysis. *Br J Cancer* 2003;88:1047-53.
9. Suh MA, Atashili J, Fuh EA, Eta VA. Breast self-examination and breast cancer awareness in women in developing countries: A survey of women in Buea, Cameroon. *BMC Res Notes* 2012;5:627.
10. Friedman LC, Nelson DV, Webb JA, Hoffman LP, Baer PE. Dispositional optimism, self-efficacy and health beliefs as predictors of breast self-examination. *Am J Prev Med* 1994;10:130-5.
11. Chaudhury UK, Srivastava R, Fitch MI. Breast cancer detection practices of South Asian women: Knowledge, attitudes, and beliefs. *Oncol Nurs Forum* 1998;25:1693-701.
12. Petro-Nustus W, Mikhail BI. Factors associated with breast self-examination among Jordanian women. *Public Health Nurs* 2002;19:263-712.
13. Drukteinis JS, Mooney BP, Flowers CI, Gatenby RA. Beyond mammography: New frontiers in breast cancer screening. *Am J Med* 2013;126:472-9.
14. Bluekens AM, Engen RE, Karssemeijer N, Schuur KH, Broeders MJ, den Heeten GJ. Consequences of digital mammography in population-based breast cancer screening: Initial changes and long-term impact on referral rates. *Eur Radiol* 2010;20:2067-73.
15. Grusauskas NP, Drukker K, Giger ML, Sennett CA, Pesce LL. Performance of breast ultrasound computer-aided diagnosis: Dependence on image selection. *Acad Radiol* 2008;15:1234-45.
16. Ahmadain M, Samah AA. A literature review of factors influencing breast cancer screening in Asian countries. *Life Sci J* 2012;9:585-98.
17. Jarvandi S, Montazeri A, Harirchi I, Kazemnejad A. Beliefs and behaviors of Iranian teachers towards early detection of breast cancer and breast self-examination. *Public Health* 2002;116:245-92.
18. Madan A, Barden C, Beech B. Socioeconomic factors, not ethnicity predict breast self-examination. *Breast J* 2000;6:263-6.
19. Bener A, Honein G, Carter AO, Da'ar Z, Miller C, Dunn EV, *et al.* The determinants of breast cancer screening behavior: A focus group study of women in the United Arab Emirates. *Oncol Nurs Forum* 2002;29:E91-8.
20. McCance KL, Mooney KH, Field R. The influence of other factors in motivating women to obtain breast cancer screening. *Cancer Pract* 1996;4:141-6.
21. Haji-Mahmoodi M, Montazeri A, Jarvandi S, Ebrahimi M, Haghight A, Harirchi I, *et al.* Breast self-examination: Knowledge, attitudes, and practices among female health care workers in tehran, iran. *Breast J* 2002;8:222-5.
22. Madanat H, Merrill RM. Breast cancer risk-factor and screening awareness among women nurses and teachers in Amman, Jordan. *Cancer Nurs* 2002;25:276-82.

How to cite this article: Subramanian L, Salini VU, Anandan H, Insuvai U. Breast Cancer Awareness in South India. *Int J Sci Stud* 2018;6(5):39-42.

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

Study on Clinical Profile of Dengue Fever in a Tertiary Care Centre of Bihar

Amit Kumar Mishra¹, Sudhir Kumar², Praveen Kumar¹, Arshad Ahmad², Shailesh Kumar²
Kalyan Kumar Saha³, Manoj Kumar Choudhary⁴, Naresh Kumar⁵

¹Associate Professor, Department of General Medicine, IGIMS, Sheikhpura, Patna, Bihar, India, ²Additional Professor, Department of General Medicine, IGIMS, Sheikhpura, Patna, Bihar, India, ³Senior Resident, Department of General Medicine, IGIMS, Sheikhpura, Patna Bihar, India, ⁴Assistant Professor, Department of General Medicine, IGIMS, Sheikhpura, Patna, Bihar, India, ⁵Professor and Head, Department of General Medicine, IGIMS, Sheikhpura, Patna, Bihar, India

Abstract

Introduction: Dengue is a common acute febrile illness caused by flavivirus and transmitted by the bite of female Aedes mosquito. The disease presents with myriad of clinical signs and symptoms. Symptoms of dengue range from mild fever to incapacitating high fever with severe headache, pain behind the eyes, muscle and joint pain, rash, nausea/vomiting, pain abdomen, bleeding, shock, breathlessness, cough, thrombocytopenia, leukopenia, liver dysfunction, and renal failure.

Purpose: This study was done to find out spectrum of clinical signs and symptoms of dengue fever.

Methods: The prospective observational study was undertaken among 96 confirmed dengue cases. The disease was analyzed for clinical profile.

Results: Among 96 dengue patients, majority were male (63.54%), fever (100%) was universal symptom, followed by headache (93.75%), myalgia (89.58%), and itching (83.33%). Less common symptoms were joint pain (32.29%), skin rash (29.16%), abdominal pain (14.58%), nausea/vomiting (14.58%), cough (8.33%), chest pain (5.3%), edema (5.2%), and breathlessness (3.12%). 14 (14.58%) patients developed warning signs, but only 3 (3.12%) patients developed severe dengue. Mortality was nil.

Conclusions: Dengue is a mild acute febrile illness; most of the patients do not develop complications and recover completely. Commonly patients present with fever, headache, and myalgia.

Key words: Clinical profile, Dengue, Fever, Rash, Severe Dengue, Thrombocytopenia.

INTRODUCTION

Dengue is an acute febrile illness caused by flavivirus and transmitted by the bite of female Aedes mosquito infected with one of the four dengue viruses. Symptoms of dengue range from mild fever to incapacitating high fever with severe headache, pain behind the eyes, muscle and joint pain, and rash. Severe dengue (also known as dengue hemorrhagic fever [DHF] or dengue shock syndrome) is characterized by abdominal pain, persistent vomiting, shock, bleeding, thrombocytopenia, and breathing difficulty.

Early diagnosis and careful management increase the survival of patients, so clinical suspicion of dengue is important which depends on the recognition of its signs and symptoms among patients of acute febrile illness. Recent studies indicated that the clinical presentation and epidemiology of dengue are changing.

Atypical manifestations of dengue fever (DF) are more common than that reported in the past, and neurological, cardiac, and other manifestations are being reported more frequent.^[1,2] It can have varied and multisystemic manifestations which can go unrecognized, so high index of suspicion required for atypical manifestations.^[3]

DF especially severe form typically acknowledged to be a disease of young adult and childhood. There is, however, evidence of increasing incidence of DHF among older age groups.^[5] Furthermore, a variation in disease severity from DF to DHF/dengue shock syndrome was noted over the years.^[6]

Access this article online



www.ijss-sn.com

Month of Submission : 06-2018
Month of Peer Review : 07-2018
Month of Acceptance : 08-2018
Month of Publishing : 08-2018

Corresponding Author: Dr. Sudhir Kumar, Department of General Medicine, IGIMS, Sheikhpura - 800 014, Patna, Bihar, India.
Phone: +91-8544413220. E-mail: sudh75@gmail.com

The first evidence of DF in the country was reported during 1956 from Vellore district in Tamil Nadu. Since 1956 recurrent outbreaks of dengue fever have been reported from different States of India

Currently, the disease is endemic in India and a cause of great concern to public health. Based on the data of National Vector Borne Disease Control Programme (NVBDCP), the number of cases reported in 2013 was about 74,454 for dengue with 167 deaths, and in 2007, it only about 6000 cases was reported.^[7] Hence, the number of dengue case has shown a steady rise in recent year.

Dengue encroached into the Bihar state of India in 2010, but there was no any study on clinical profile of the disease in this region. Therefore, this study was done to get accurate data regarding the clinical spectrum of disease.

Aim and Objective of the Study

This study was done to find out spectrum of clinical manifestation.

MATERIALS AND METHODS

After the Institutional Ethical Committee approval, this prospective observational study was carried out in IGIMS, Patna, Bihar, India, from January 1, 2017, to December 31, 2017. A total of 96 confirmed cases of DF were included in the study. Dengue cases were confirmed by NS1 antigen and IgM antibody.

Then following observation were done at presentation and during the course of illness. Age and sex of patients, clinical sign and symptoms, development of complications (shock, bleeding, adult respiratory distress syndrome, renal failure), total leucocyte count, differential leucocyte count, Haemoglobin, hematocrit, liver function test, blood urea nitrogen, serum creatinine, chest X-ray posteroanterior view, electrocardiography, Ultrasonography of whole abdomen.

After the first data collection, patients were monitored periodically (clinical as well as laboratory and radiological investigation) as and when required till recovery of patients.

RESULTS

Of total 96 patients selected for the study in 2017 from January to December, 61 (63.54%) were male and 35 (36.45%) were female. Maximum patients were in middle age group, of 96 patients, 59 (61.45%) were in the age group of 31–60 years, only 7 (7.29%) patients were <60 years of age [Table 1].

Fever was present in all 96 patients (100%), followed by headache (90%) and myalgia (86%), cough (8.33%), chest pain (5.2%), shortness of breath (3.12%), leg swelling (edema) (5.2%), and arthralgia (32.29%). Itching (83.33%) was common symptom during recovery phase of disease [Table 2].

Different warning signs and symptoms were present in 14 (14.58%) patients, and 3 (3.12%) of them developed severe dengue in the form of bleeding, shock, and renal failure. All 96 patients were recovered and death was nil. None of 96 patients develop any features of adult respiratory distress syndrome, neurological complications, or any features of myocarditis [Table 3].

A total of 90 patients had thrombocytopenia, but only 14 (14.58%) patients had severe thrombocytopenia (<20,000), leukopenia was found in 90 (93.75%) patients, liver enzyme was raised in 51 (53.12%) patients, and raised hematocrit level was noted in 20 (20.83%) patients [Table 4].

DISCUSSION

In our study, male patients were more common than female. Other similar studies by Deshwal *et al.*^[4] and Karoli *et al.*^[3] also support our finding.

About 61.45% of patients in our study were in the middle age group (31–60), elderly patients were only 7 (7.29%). Hence, our study result contradicts the earlier evidence of increasing incidence of dengue among older age groups.^[5]

The common symptom was fever, headache, and myalgia, other symptoms and signs were less common. Jassirali *et al.*^[8] reported the similar observations in their study. A study by Deshwal *et al.*^[4] also supports our finding.

Table 1: Age and sex characteristics

Age range (in years)	Number of cases (male)	Number of cases (female)	Number of cases (total%)
14–30	19	11	30 (31.25)
31–45	24	14	38 (39.58)
46–60	13	08	21 (21.87)
61–75	05	02	7 (7.29)
More than 75	00	00	0 (0)
Total cases	61 (63.54%)	35 (36.45%)	96

Table 2: Clinical features (signs and symptoms) of dengue fever at any point of time during the course of illness (total cases - 96)

Symptoms/signs	Number of cases (%)
Fever	96 (100)
Headache/retro-orbital pain	90 (93.75)
Myalgia	86 (89.58)
Joint pain	31 (32.29)
Abdominal pain	14 (14.58)
Nausea/vomiting	14 (14.58)
Skin rash	28 (29.16)
Edema	5 (5.2)
Shortness of breath	3 (3.12)
Cough	8 (8.33)
Chest pain	5 (5.2)
Seizure/delirium/other neurological symptoms	Nil
Itching	80 (83.33)
Hepatomegaly	10 (10.41)

Table 3: Complications developed during the course of illness (total patients - 96)

Complications	Number of patients (%)
Shock	3 (3.12)
Bleeding (nose/GI/hematuria/vaginal)	6 (6.25)
Renal failure	3 (3.12)
Pleural effusion	8 (8.33)
Ascites	8 (8.33)
ARDS	Nil
ECG changes for myocarditis	Nil
Any neurological complications	Nil
Death	Nil

ECG: Electrocardiography, ARDS: Adult respiratory distress syndrome, GI: Gastrointestinal

Table 4: Laboratory parameters

Parameters	Number of patients (%)
Thrombocytopenia <100,000/cumm	90 (93.75)
Thrombocytopenia <50,000/cumm	60 (62.5)
Thrombocytopenia <20,000/cumm	14 (14.58)
Leukopenia <4000/cumm	90 (93.75)
Raised AST/ALT (>45/50)	51 (53.12)
Raised hematocrit >45%	20 (20.83)
Raised BUN/serum creatinine	3 (3.12)

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, BUN: Blood urea nitrogen

However, Pawaria *et al.*^[1] have documented in their study that atypical manifestation of dengue was common, which is contrary to our finding, this could be due to pediatric patients selected by Pawaria in their study. Karoli *et al.*^[3] also showed high percentage (14%) of atypical manifestation in their study. Another similar study by Mandal SK *et al.* found high percentage of different atypical presentation of dengue fever.^[10]

Warning signs and symptoms were presents in 14 (14.58%) patients and only 3 (3.12%) patients developed severe dengue in the form of bleeding, shock, and renal failure, but all patients recovered; therefore, our study showed that most of the DF were mild and complication rate was very low. All who develop severe dengue were in the age range of 31–45 years. Guha *et al.* stated that there is increased incidence of DHF among older age groups, which is against our finding.^[5]

Neurological, cardiac, and pulmonary complications were not shown in any patients. Murthy stated that neurological manifestations are more frequent,^[2] which is against our observation.

Bleeding was shown in only 6 (6.25%) patients, but thrombocytopenia (<100,000/cumm) was shown in 90 patients (93.75%). Although thrombocytopenia was a common finding, there was poor correlation between thrombocytopenia and bleeding tendencies. A similar observation was found in a study by Maimoona *et al.*^[6]

Severe dengue was shown only in 3 (3.12%) patients. Mortality was nil in our study. In a similar study conducted by Barik *et al.* found nil mortality.^[12] Deshwal *et al.* have also documented low mortality in their patients.^[4] However, Karoli *et al.* in their study concluded that overall mortality was 6% (6.25%), and all fatal cases were due to multiorgan failure.^[3] In a similar study by Mohan *et al.* showed a high mortality and complication in their study.^[9] Severe dengue was shown in 75% of patients in the study conducted by Arti *et al.*^[1] In all these studies, only admitted patients were taken that could be the reason of high percentage of severe dengue and high mortality.

Higher mortality rate was observed by Kuo *et al.* in dengue patients who had develop renal failure.^[13] This finding is against our observation as all three cases who develop renal failure recovered completely.

Raised liver enzyme was shown in significant proportion of cases; this finding is supported by similar study conducted by Ooi *et al.*^[14] However Rachel D *et al.* in similar study found 83.9% of dengue had raised liver enzyme^[11].

CONCLUSIONS

Most cases of DF are mild and recover completely without any complications. Patients when present with fever, headache, myalgia, raised liver enzyme, thrombocytopenia, and leukopenia should prompt a clinician on the possibility of dengue infection. Early diagnosis and careful monitoring for the development of warning sign and complication are essential as proper management reduces the mortality.

REFERENCES

1. Pawaria A, Mishra D, Juneja M, Meena J. Atypical manifestations of dengue fever. *Indian Pediatr* 2014;51:495-6.
2. Murthy JM. Neurological complication of dengue infection. *Neurol India* 2010;58:581-4.
3. Karoli R, Fatima J, Siddiqi Z, Kazmi KI, Sultania AR. Clinical profile of dengue infection at a teaching hospital in north India. *J Infect Dev Ctries* 2012;6:551-4.
4. Deshwal R, Qureshi MI, Singh R. Clinical and laboratory profile of dengue fever. *J Assoc Physicians India* 2015;63:30-2.
5. Guha-Sapir D, Schimmer B. Dengue fever: New paradigms for a changing epidemiology. *Emerg Themes Epidemiol* 2005;2:1.
6. Ahmed MM. Clinical profile of dengue fever infection in king Abdul Aziz university hospital Saudi Arabia. *J Infect Dev Ctries* 2010;4:503-10.
7. Cecilia D. Current status of dengue and Chikungunya in India. *WHO South East Asia J Public Health* 2014;3:22-6.
8. Jassirali CA, Sathikali AS, Sirajuddin S. Clinical and haematological parameter in adult dengue patients. *MedPulse Int Med J* 2017;4:306-9.
9. Mohan DK, Dhananjaya MS. A study of clinical profile of dengue fever in a tertiary care teaching hospital. *Sch J App Med Sci* 2013;1:280-2.
10. Mandal SK, Ganguly J, Sil K, Chatterjee S, Chatterjee K, Sarkar P, *et al.* Clinical profiles of dengue fever in a teaching hospital of Eastern India. *Nat J Med Res* 2013;3:173-6.
11. Rachel D, Philip AZ. A study of clinical profile of dengue fever in Kollam, Kerala, India. *Dengue Bull* 2005;29:197-202.
12. Ahmed AB, Bhattacharyya DK, Baruah S, Brahma B, Bharadwaj R. A study on clinical and laboratory profile of dengue fever in a tertiary care hospital in Assam, India. *Int J Med Res Prof* 2017;3:113-6.
13. Kuo MC, Lu PL, Chang JM, Lin MY, Tsai JJ, Chen YH, *et al.* Impact of renal failure on the outcome of dengue viral infection. *Clin J Am Soc Nephrol* 2008;3:1350-6.
14. Ooi ET, Ganesanathan S, Anil R, Kwok FY, Sinniah M. Gastrointestinal manifestations of dengue infection in adults. *Med J Malaysia* 2008;63:401-5.

How to cite this article: Mishra AK, Kumar S, Kumar P, Ahmad A, Kumar S, Saha KK, Choudhary MK, Kumar N. Study on Clinical Profile of Dengue Fever in a Tertiary Care Centre of Bihar. *Int J Sci Stud* 2018;6(5):43-46.

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

Adult Attention Deficit Hyperactivity Disorder in Health Science Students of India

Bhushan Shashi¹, Piplani Shobhit¹, Tekkalaki Bheemsain²

¹Intern, Department of Psychiatry, Jawaharlal Nehru Medical College, KLE University, Belagavi, Karnataka, India, ²Assistant Professor, Department of Psychiatry, Jawaharlal Nehru Medical College, KLE University, Belagavi, Karnataka, India

Abstract

Introduction: Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder, diagnosed mostly in childhood. In adults, it is estimated at 2–7%, and 4% is generally accepted. Surprisingly very less research efforts are there to establish the prevalence of adult ADHD in India.

Purpose: The purpose of the present article was to assess the prevalence of ADHD among medical students and its impact on the self-esteem of these students.

Materials and Method : The study was conducted in a South East Asian Medical and Dental College. 900 students were randomly selected to fill up the questionnaire (620 from Medical College and 280 from Dental College). 618 students answered the questionnaire completely. Conner's Adult ADHD Rating Scales-Self Report: Screening Version was used to screen for ADHD. The Rosenberg self-esteem scale was used to measure the self-esteem. Students who were screened positive were subjected to clinical interview based on the diagnostic and statistical manual of the mental disorders fifth edition. IBM SPSS version 22 was used for statistical analysis.

Results : 45 students (7.3%) were diagnosed to be at risk with ADHD. It was also found that ADHD has no statistically significant association with age, sex, course of study, and self-esteem. The study concluded that there was a high prevalence of risk of ADHD among students of health sciences. It was found that students in dental college showed a higher prevalence of ADHD compared to students of medical college, but their self-esteem was comparable to their peers.

Conclusion: More frequent screening should be made available at the childhood for prompt detection of ADHD

Key words: Adult attention deficit hyperactivity disorder, Undergraduate students, Self-esteem, prevalence

INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder, diagnosed mostly in childhood. It is recognized by attention deficit, hyperactivity, and impulsiveness. This results in poor social makeup, unsatisfactory academic performance, and occupational failures in the future.^[1]

Etiology of ADHD as reported by Curatolo, D'Agati and Moavero in 2010 included environmental factors such as prenatal exposure to alcohol and cigarette smoke, exposure to high levels of lead during infancy and malnutrition along with genetic and hereditary factors (DRD4, DRD5, SLC6A3, SNAP-25, and HTR1B), and low levels of a chemical in brain called dopamine that helped in regulating mood, movement, and attention. These factors acted together to form an array of neurobiological burden.^[2] There was an increase in the prevalence of childhood ADHD from 7.8% in 2003 to 11% in 2011.^[3]

Although, initially regarded as a childhood condition, evidences states that ADHD, being a neurodevelopmental disorder, persists into adulthood although the symptoms may be somewhat modified with age.^[4,5] Studies have

Access this article online



www.ijss-sn.com

Month of Submission : 06-2018

Month of Peer Review : 07-2018

Month of Acceptance : 08-2018

Month of Publishing : 08-2018

Corresponding Author: Shashi Bhushan, H-601, Indian Oil Apartments, C-58/23, Sector-62, Noida, Uttar Pradesh, India. Phone:+91-9844420359. E-mail: teenshashi@gmail.com

reported that 30–70% of children suffering from ADHD would continue suffering from it during puberty.^[6]

For an adult to be diagnosed with ADHD, he should have a history of ADHD along with present symptoms.^[7] It was observed that adults with ADHD usually had job instability and interpersonal difficulties.^[8] In students, ADHD was associated with weaker academic performance, because of which many of them were unsuccessful in reaching the college level. Those who got into college probably showcased better cognitive skills and coping strategies of their latent disorder.^[9] Many researchers found similarity in social satisfaction and psychological welfare in college students with ADHD compared to control while other researchers found that ADHD in students was associated with poor quality of life and adjustment issues, below par academic performance, substance abuse, and depression.^[10] They had difficulties in organizing and doing their tasks on time and decision-making. They also had a problem in awareness and understanding of one's own thought processes.^[11]

The prevalence of ADHD in adults is estimated at 2–7%, and 4% is generally accepted.^[4,12] In a previous study done on college students in Chandigarh, India, showed the prevalence of adult ADHD to be 5.4%.^[13] Another cross-sectional study done in an outpatient setting in India, the prevalence of ADHD in adults was calculated to be 8.8%.^[14] Apart from few studies conducted in India surprisingly very less research efforts are there to establish the prevalence of ADHD. Therefore, the purpose of the present article is to assess the prevalence of ADHD among college students in India, particularly medical students and assess the impact of Adult ADHD on the self-esteem of these students.

MATERIALS AND METHODS

The study was conducted by the Department of Psychiatry, Jawaharlal Nehru Medical College (JNMC), KLE University, India, in a South East Asian Medical and Dental College.

A sample size of 456, using determinants of ADHD with 95% confidence interval (CI), and 20% tolerable error was estimated. Keeping in mind larger drop-out rate from the study, 900 (design effect =2) students were randomly selected (620 from Medical College and 280 from Dental College). Institutional Ethical Clearance was taken for the same (IEC Reference No. – MDC/DOME/181). Students having positive medical and family history were not selected for the study.

Of 900 students, 618 students answered the questionnaire completely. Two standardized questionnaires were used for assessment.

Conner's Adult ADHD rating self-report scale: Screening version^[15] was used to screen for students susceptible to ADHD. There was an inconsistency-adjusted sensitivity of 1.0, a specificity of 0.71, a positive predictive value of 0.52, and a negative predictive value of 1.0.^[16] The ASRS consists of 18 questions which are based on the diagnostic and statistical manual of mental disorders, fourth edition, text revision (DSM-IV-TR) criteria and are divided into two parts: Part A and B. Six of these questions were the most predictive of adult ADHD and are included in Part A. Part B consists of the remaining 12 questions which were used just as additional cues in making the diagnosis. Both the parts were used in this study.

The Rosenberg Self-esteem Scale (RSES)^[17] was used to measure the self-esteem. It was a scale of 0–30 where a score of <15 may indicate problematic low self-esteem. The RSES was designed similar to social survey questionnaires. It was a 10-item Likert-type scale with items answered on a four-point scale - from strongly agrees to strongly disagree. Five of the items had positively worded statements, and five had negatively worded ones. The scale measured state self-esteem by asking the respondents to reflect on their current feelings.

In addition, questions regarding sociodemographic, and academic performance of the 1st year, along with family/medical/drug history were asked.

Students who were screened positive under ASRS were further subjected to clinical interview based on the DSM of the mental disorders fifth edition (DSM-5)^[18] by a trained interviewer.

Descriptive analysis was carried out by the mean and standard deviation for quantitative variables, frequency, and proportion for categorical variables.

The association between categorical explanatory variables and quantitative outcome was assessed by comparing the mean values. The mean differences along with their 95% CI were presented. Independent sample *t*-test was used to assess statistical significance. Correlation between quantitative explanatory and outcome variables was assessed by calculating the Pearson correlation coefficient.

The association between explanatory variables and categorical outcomes was assessed by cross-tabulation and comparison of percentages. Chi-square test was done. $P < 0.05$ was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.^[19]

RESULTS

There were 618 participants comprising 461 students from medical college and 157 students from dental college

were evaluated. The mean ages of the participants were 20.03 ± 1.45 years. A total of 382 females and 236 males participated in the study.

The prevalence rate of self-reported ADHD symptoms using the ASRS screener was 20.2%. After using the DSM-5 criteria for diagnosing ADHD, the prevalence rate of ADHD in the study population was calculated to be 7.3% [Tables 1 and 2].

The adult ADHD was considered as a primary outcome variable. Course, age group, and gender were considered as an explanatory variable.

On studying the association of ADHD with gender, it was found out that there was no significant difference between both the genders. There was also no significant association of ADHD with the age which can be inferred from the table.

Furthermore, it was found that students in the dental college showed a higher prevalence of risk for developing ADHD compared to students of the medical college, but it was not statistically significant.

On using RSES for measuring the self-esteem of the students, we found that there was also no significant difference in the ratio of participants who had low self-esteem in the ADHD group as compared to the students who did not have ADHD. Therefore, no significant association was found between ADHD and low self-esteem.

Therefore, it was found that ADHD is quite prevalent in health sciences, but it has no statistically significant association with age, sex, or course of study. Furthermore, there is no statistically significant association of ADHD with self-esteem [Tables 3].

DISCUSSION

There have been very less studies pertaining to adult ADHD in India. The study done on 224 college students in Chandigarh, showed the prevalence of adult ADHD to be 5.4%, but the study population recruited by the author consisted of students from different streams and colleges and the diagnosis were made only on the basis of self-assessing questionnaires.^[13] Another cross-sectional study was done in an outpatient setting in India where 283 adults were screened and interviewed for ADHD. The prevalence of ADHD in adults was calculated to be 8.8%. The limitation of this study was that the investigators conducted it in an outpatient setting. Thus, the results could not be generalized for the adult population.^[14]

In our study, 7.2% of the respondents had ADHD symptoms. Although the average prevalence of ADHD in adults is taken as 4%, it has been reported to be 2–7% in previous studies.^[4,12] A study conducted on medical students to determine the prevalence rate of ADHD in Kenya was found out to be 8.7%^[20] while in a study conducted in Iran; it was found to be 15.4%.^[21] Thus, our findings have been consistent with many of the studies done previously in this field.

In this study, we found that the ADHD was higher in males as compared to females by a very little margin. This is, however, not concordant with the earlier research which states that males have almost double the chances of presenting ADHD in both childhood (2:1) and adulthood (3:2).^[14] It might be possible that this ratio tends to decrease as the students enroll in colleges where ADHD can be found commonly in both males and females.^[22]

We also found that the percentage of college students with ADHD did not vary from students without ADHD in terms of self-esteem. Several researches have shown that low self-esteem is associated comorbidity of ADHD.^[23,24]

Table 1: Classification of ADHD according to dominant presentation

Baseline characteristic (n)	Inattention (%)	Hyperactivity/impulsivity (%)	Combined symptoms (%)	Total (%)
Age group*				
17–18 (88)	3 (3.4)	1 (1.1)	3 (3.4)	7 (7.9)
19–20 (302)	9 (2.9)	8 (2.6)	6 (2)	23 (7.6)
21–22 (197)	6 (3)	5 (2.5)	4 (2)	15 (7.6)
23–24 (31)	0 (0)	0 (0)	0 (0)	0 (0)
Total (n=618)	18 (2.9)	14 (2.3)	13 (2.1)	45 (7.3)
Sex†				
Male (236)	5 (2.1)	8 (3.4)	5 (2.1)	18 (7.6)
Female (382)	13 (3.4)	6 (1.6)	8 (2.1)	27 (7.1)
Total (n=618)	18 (2.9)	14 (2.3)	13 (2.1)	45 (7.3)
Course of study‡				
MBBS (461)	13 (2.9)	10 (2.2)	10 (2.2)	33 (7.1)
BDS (157)	5 (3.1)	4 (2.6)	3 (1.9)	12 (7.6)
Total (n=618)	18 (2.9)	14 (2.3)	13 (2.1)	45 (7.3)

*Chi-square: 0.003, $P=0.953$, †Chi-square: 6.187, $P=0.103$, ‡Chi-square: 0.311, $P=0.577$, ADHD: Attention deficit hyperactivity disorder

Table 2: Classification of ADHD according to the severity

Baseline characteristic (n)	Mild (%)	Moderate (%)	Severe (%)	Total (%)
Age group				
17–18 (88)	6 (6.8)	1 (1.1)	0 (0)	7 (7.9)
19–20 (302)	18 (6.0)	4 (1.3)	1 (0.3)	23 (7.6)
21–22 (197)	11 (5.6)	3 (1.5)	1 (0.5)	15 (7.6)
23–24 (31)	0 (0)	0 (0)	0 (0)	0 (0)
Total (n=618)	35 (5.7)	8 (1.3)	2 (0.3)	45 (7.3)
Sex				
Male (236)	14 (5.9)	3 (1.3)	1 (0.4)	18 (7.6)
Female (382)	21 (5.5)	5 (1.3)	1 (0.3)	27 (7.1)
Total (n=618)	35 (5.7)	8 (1.3)	2 (0.3)	45 (7.3)
Course of study				
MBBS (461)	26 (5.6)	6 (1.3)	1 (0.2)	33 (7.1)
BDS (157)	9 (5.7)	2 (1.3)	1 (0.6)	12 (7.6)
Total (n=618)	35 (5.7)	8 (1.3)	2 (0.3)	45 (7.3)

ADHD: Attention deficit hyperactivity disorder

Table 3: Relation between ADHD and self-esteem

Self-esteem ^s	ADHD positive (%)	ADHD negative (%)
High (499)	34 (6.8)	465 (93.2)
Low (119)	11 (9.2)	108 (90.8)
Total (n=618)	45 (7.3)	573 (92.7)

^sChi-square: 0.840, P=0.359. ADHD: Attention deficit hyperactivity disorder

However, our results are not in line with their findings. This states that although people with ADHD might be perceived as emotionally unstable, they had no problem in adjusting in the colleges. They already were academically qualified and at par with their peers thus showing better coping abilities.

The limitation of our study is that first, only 618 from the selected 900 students participated for the research. From the remaining 282 students, 131 people did not fill the form completely, 98 students were excluded on the basis of the positive family, medical, and drug history, and 53 students were absent on the day when the study was carried out. Second, the present percentage was calculated from a sample of college students, and external validity is affected by this. The generalization of the result should be limited only to the college student population. Furthermore, for a more elaborative investigation about the symptoms, parents, and teachers are also need to be interviewed to confirm the diagnosis of ADHD. Further studies are needed in India with a larger population size in general setting, and special importance should be given assessing the comorbidities associated with ADHD.

CONCLUSION

Although medicine is considered one of the most competitive branches for the intelligent students, ADHD

is still significantly prevalent in this stream. Citing the importance of early diagnosis, more frequent screening should be made available at the childhood. There is a need of prompt detection and management of ADHD in college students so that they might be able to cope up with the social and psychological problems in their occupational, educational, and familial lives they are at risk with.

ACKNOWLEDGMENT

The authors would like to thank Dr. Naresh Kumar Tyagi, Professor and Head, KLE University, Department of Epidemiology and Biostatistics, Belagavi, Karnataka, India.

REFERENCES

- Kalbag AS, Levin FR. Adult ADHD and substance abuse: Diagnostic and treatment issues. *Subst Use Misuse* 2005;40:1955-81, 2043-8.
- Curatolo P, D'Agati E, Moavero R. The neurobiological basis of ADHD. *Ital J Pediatr* 2010;36:79.
- Visser SN, Danielson ML, Bitsko RH, Holbrook JR, Kogan MD, Ghandour RM, et al. Trends in the parent-report of health care provider-diagnosed and medicated attention-deficit/hyperactivity disorder: United states, 2003-2011. *J Am Acad Child Adolesc Psychiatry* 2014;53:34-4600.
- Kessler RC, Adler L, Barkley R, Biederman J, Conners CK, Demler O, et al. The prevalence and correlates of adult ADHD in the United States: Results from the national comorbidity survey replication. *Am J Psychiatry* 2006;163:716-23.
- Polanczyk G, Jensen P. Epidemiologic considerations in attention deficit hyperactivity disorder: A review and update. *Child Adolesc Psychiatr Clin N Am* 2008;17:245-60, vii.
- Resnick RJ. Attention deficit hyperactivity disorder in teens and adults: They don't all outgrow it. *J Clin Psychol* 2005;61:529-33.
- Murphy KR, Adler LA. Assessing attention-deficit/hyperactivity disorder in adults: Focus on rating scales. *J Clin Psychiatry* 2004;65 Suppl 3:12-7.
- Smith T. *Children and Adults with Learning Disabilities*. Boston: Allyn and Bacon; 1997.
- Frazier TW, Youngstrom EA, Glutting JJ, Watkins MW. ADHD and achievement: Meta-analysis of the child, adolescent, and adult literatures and a concomitant study with college students. *J Learn Disabil* 2007;40:49-65.
- DuPaul GJ, Weyandt LL, O'Dell SM, Varejao M. College students with ADHD: Current status and future directions. *J Atten Disord* 2009;13:234-50.
- Alvarado JM, Puente A, Jiménez V, Arrebillaga L. Evaluating reading and metacognitive deficits in children and adolescents with attention deficit hyperactivity disorder. *Span J Psychol* 2011;14:62-73.
- Biederman J, Faraone S, Milberger S, Guite J, Mick E, Chen L, et al. A prospective 4-year follow-up study of attention-deficit hyperactivity and related disorders. *Arch Gen Psychiatry* 1996;53:437-46.
- Jhambh I, Arun P, Garg J. Cross-sectional study of self-reported ADHD symptoms and psychological comorbidity among college students in Chandigarh, India. *Ind Psychiatry J* 2014;23:111-6.
- Sitholey P, Agarwal V, Sharma S. An exploratory clinical study of adult attention deficit/hyperactivity disorder from India. *Indian J Med Res* 2009;129:83-8.
- Kessler RC, Adler L, Ames M, Demler O, Faraone S, Hiripi E, et al. The world health organization adult ADHD self-report scale (ASRS): A short screening scale for use in the general population. *Psychol Med* 2005;35:245-56.
- Hines JL, King TS, Curry WJ. The adult ADHD self-report scale for screening for adult attention deficit-hyperactivity disorder (ADHD). *J Am Board Fam Med* 2012;25:847-53.
- Rosenberg M. *Society and the Adolescent Self-Image*. Princeton, NJ: Princeton University Press; 1965.
- American Psychiatric Association. *Diagnostic and Statistical Manual*

- of Mental Disorders: DSM-5. Washington, D.C: American Psychiatric Association; 2013.
19. Machines IB. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp; 2013.
 20. Atwoli L, Owiti P, Manguro G, Ndambuki D. Attention deficit hyperactivity disorder symptom self-report among medical students in Eldoret, Kenya. *Afr J Psychiatry (Johannesbg)* 2011;14:286-9.
 21. Mosalanejad M, Mosalanejad L, Lashkarpour K. Prevalence of ADHD among students of Zahedan university of medical science in Iran. *Iran J Psychiatry Behav Sci* 2013;7:83-90.
 22. Swanson JM, Sergeant JA, Taylor E, Sonuga-Barke EJ, Jensen PS, Cantwell DP, *et al.* Attention-deficit hyperactivity disorder and hyperkinetic disorder. *Lancet* 1998;351:429-33.
 23. Kirino E, Imagawa H, Goto T, Montgomery W. Sociodemographics, comorbidities, healthcare utilization and work productivity in Japanese patients with adult ADHD. *PLoS One* 2015;10:e0132233.
 24. Dan O, Raz S. The relationships among ADHD, self-esteem, and test anxiety in young adults. *J Atten Disord* 2015;19:231-9.

How to cite this article: Shashi B, Shobhit P, Bheemsain T. Adult ADHD in Health Science Students of India. *Int J Sci Stud* 2018;6(5):47-51.

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

Knowledge of Cervical Cancer and Uptake of Pap Smear Test and Human Papillomavirus Vaccination among Gynecologic Clinic Attendees in Sokoto, Nigeria

Kehinde J Awosan¹, Mairo Hassan², Buhari M Ibrahim³

¹Senior Lecturer, Department of Community Health, Usmanu Danfodiyo University, Sokoto, Nigeria, ²Senior Lecturer, Department of Obstetrics and Gynecology, Usmanu Danfodiyo University, Sokoto, Nigeria, ³House Officer, Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria

Abstract

Introduction: The burden of cervical cancer is disproportionately high in the less developed regions where it is the second most common cancer in women. The progressive decrease in the burden of cervical cancer in the developed regions has been attributed to interventions targeting the risk factors of the disease.

Objectives: This study aimed to assess the knowledge of cervical cancer and uptake of Pap smear test and human papillomavirus (HPV) vaccination among gynecologic clinic attendees in Sokoto, Nigeria.

Materials and Methods: This was a cross-sectional study among 270 women (selected by multistage sampling technique) attending the gynecologic clinic of Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria. A structured interviewer-administered questionnaire was used to collect data on the research variables. Data were analyzed using IBM SPSS version 20 statistical computer software package.

Results: The mean age of the respondents was 32.8 ± 9.3 years. Majority of respondents were Muslims (74.8%) and married (74.4%). Less than a fifth of respondents had good knowledge of the risk factors (9.3%), symptoms and signs (14.8%), and prevention (16.7%) of cervical cancer. Uptake of Pap smear test was low (13.7%), while uptake of HPV vaccination was zero, and these were mainly attributed to lack of awareness.

Conclusion: The poor knowledge of cervical cancer and low uptake of Pap smear test and HPV vaccination among the respondents in this study underline the need for public health education through the mass media to create awareness about the disease. In addition, healthcare workers and other stakeholders should promote utilization of cervical cancer prevention services by women.

Key words: Cervical cancer, Human papillomavirus vaccination, Knowledge, Pap smear test, Uptake

INTRODUCTION

The burden of cervical cancer remains high worldwide with an estimated 528,000 cases and 266,000 deaths each year, and it is both the fourth most common cause

of cancer and the fourth most common cause of death from cancer in women.^[1,2] The most worrisome aspect is its disproportionately high burden in the less developed regions where it is the second most common cancer in women, with an estimated 445,000 new cases in 2012 (which accounts for 84% of the new cases worldwide), and with more than 85% of the estimated 270,000 deaths from the disease occurring in these countries.^[3,4]

Among the less developed regions of the world, sub-Saharan African countries have the largest burden of cervical cancer, particularly Nigeria (with an estimated 50.33 million women at risk, 14,089 new cases, and

Access this article online



www.ijss-sn.com

Month of Submission : 06-2018
Month of Peer Review : 07-2018
Month of Acceptance : 08-2018
Month of Publishing : 08-2018

Corresponding Author: Dr. Kehinde J Awosan, Department of Community Health, Usmanu Danfodiyo University, Sokoto, Nigeria.
E-mail: awosankj1@gmail.com

8240 deaths per year), South Africa (with an estimated 19.8 million women at risk, 7735 new cases, and 4248 deaths per year), Sudan (with an estimated 12.02 million women at risk, 833 new cases, and 534 deaths per year), and Zimbabwe (with an estimated 4.68 million women at risk, 2270 new cases, and 1451 deaths per year). In addition, while the disease ranks as the first most frequent cancer among women in Zimbabwe, it ranks as the second most frequent cancer among women in the other countries.^[5-8]

In Nigeria, the burden of cervical cancer is disproportionately high in the northern part of the country. A review of the gynecological malignancies seen at the Usmanu Danfodiyo University Teaching Hospital (UDUTH) Sokoto, Nigeria, between 2000 and 2009 showed that about two-thirds 274 (67.8%) of the 404 cases reported were cervical cancer.^[9] Cervical cancer was also the most common gynecological malignancy reported (65.7%) in a study conducted in the neighboring city of Zaria, North-Western Nigeria, with most of the patients (78%) having advanced disease at presentation.^[10]

The principal risk factors of cervical cancer include early marriage or early age at the first sexual intercourse, having sex with multiple male sexual partners, and with male sexual partners who themselves have had multiple sexual partners, and multiple pregnancies. These conditions increase exposure to persistent infection with high-risk human papillomavirus (HPV) types which are strongly associated with cervical cancer, with an estimated 75% of cases globally attributable to infection with HPV types 16 and 18.^[11-14] An estimated 62.2–78.9% of the invasive cervical cancers in Nigeria, South Africa, Sudan, and Zimbabwe, respectively (countries with very high burden of the disease in sub-Saharan Africa), are attributable to HPV types 16 or 18.^[5-8]

Prevention and control of cervical cancer is only feasible when those at risk of the disease know its risk factors, as this would enable them avoid behaviors that increase their exposure to them. Furthermore, knowing the symptoms and signs of the disease would enable those at risk seek medical care in the early stages of the disease, rather than the prevalent late presentation in the less developed countries when only palliative care is possible. In many countries worldwide, use of screening tests for cervical cancer and treatment for preinvasive disease of the cervix has been found to be highly successful in preventing progression to cervical cancer.^[15] The screening tests for cervical cancer include Papanicolaou (Pap) smear test, HPV DNA test, cytology, and visual inspection with acetic acid (particularly in low-resource settings); while preinvasive disease of the cervix is treated by ablative methods which include destruction of abnormal tissue by burning or

freezing (cryotherapy) and surgical removal of abnormal tissue.^[2] In the developed countries, the dramatic decrease in the rates of cervical cancer over the past decades has been attributed to the widespread use of cervical screening programs in these countries, thus facilitating early diagnosis and treatment at the preinvasive stage of the disease.^[15,16]

The high burden of cervical cancer in the sub-Saharan African countries is believed to be due to the poor knowledge of the disease (i.e., the risk factors, symptoms and signs, and prevention), the high prevalence of its risk factors, and the abysmally low uptake of cervical cancer screening services by women across the continent. A study among rural women in Zimbabwe reported poor knowledge of the causes, prevention, and treatment of cervical cancer, and most of the women interviewed (95.78%) have never done cervical cancer screening test.^[17] A similar study among Sudanese women reported poor knowledge of cervical cancer and its prevention, and only a few (15.8%) had undergone a Pap smear test, despite the fact that most of them (78.8%) were university degree holders, and almost all of them (97.2%) were resident in urban areas of Khartoum state, Sudan, where the services are available.^[18]

In the absence of any virus-specific treatment for HPV infection and the high prevalence of HPV-associated risk behaviors in sub-Saharan Africa, prevention and control of the prevalent HPV infection and the cancers caused by the high-risk HPV types (particularly 16 and 18) across the continent are contingent on high coverage (>70%) of full immunization against HPV infection among boys and girls aged 9–14 years as recommended by the World Health Organization.^[2]

Studies conducted across Nigeria generally showed poor knowledge of the risk factors, symptoms and signs, and prevention of cervical cancer, as well as abysmally low uptake of Pap smear test. A study among pregnant women in Enugu, South-Eastern Nigeria,^[19] reported that only 8.1% of respondents knew that cervical cancer is caused by HPV, and only 2.8% have had a Pap smear test done. A study among female secondary school teachers in Osogbo, Southwest Nigeria,^[20] also reported that less than half of respondents (44.5%) were aware of cervical cancer screening, and only 5.4% have had a Pap smear test done.

Despite the high burden of cervical cancer in North-Western Nigeria, and with most of the patients presenting with advanced disease, there is a dearth of literature on the knowledge and practices related to cervical cancer and its prevention among the women in the zone. A study among market women in Zaria, North-Western Nigeria,^[21] found that less than half of respondents (43.5%) had good

knowledge of cervical cancer and its screening, and less than a fifth of them (15.4%) have had a Pap smear test done. Another study among female healthcare workers in Sokoto, Nigeria,^[22] reported very low uptake (10.0%) of Pap smear test, even though almost all the respondents (98.0%) had good knowledge of cervical cancer. This study was conducted to assess the knowledge of cervical cancer and uptake of Pap smear test and HPV vaccination among gynecologic clinic attendees in Sokoto, Nigeria, with the view that the findings would provide evidence-based information that is useful for strategic interventions for reducing the high burden of cervical cancer among women in Nigeria.

MATERIALS AND METHODS

Study Design, Population, and Area

This cross-sectional study was carried out at UDUTH, Sokoto, Nigeria, in July and August 2014. The hospital serves the inhabitants of Sokoto state, neighboring Kebbi and Zamfara states, as well as people from the neighboring country (Niger Republic). The study population comprised women attending the gynecologic clinic of the hospital. Women presenting at the clinic and were not on treatment for cervical cancer were considered eligible and enrolled into the study.

Sample Size Estimation and Sampling Technique

The sample size was estimated at 263 using the formula for proportion,^[23] a 22.0% uptake of Pap smear test in a previous study,^[24] and a precision level of 5%. Two hundred and eighty eligible study participants were enrolled into the study in anticipation of a 95% response rate, and they were selected by systematic sampling technique. One of three patients presenting consecutively at the clinic was enrolled into the study over a 10 clinic day period until the required sample size was obtained.

Data Collection and Analysis

A structured interviewer-administered questionnaire was developed after a thorough review of relevant literature and used to obtain information on the sociodemographic characteristics of the study participants and their knowledge of the risk factors, symptoms and signs, and prevention of cervical cancer, as well as the uptake of Pap smear test and HPV vaccination by them. It was reviewed by researchers in the Department of Community Health, Usmanu Danfodiyo University, Sokoto, Nigeria. Corrections were made based on their inputs on content validity. The questionnaire was pretested on 20 women attending the Gynecologic Clinic of Specialist Hospital, Sokoto, Nigeria. The necessary modifications were made based on the observations made during the pretesting. Five

resident doctors assisted in questionnaire administration after pretraining on conduct of survey research, the objectives of the study, selection of study subjects, and questionnaire administration.

Data were analyzed using the IBM SPSS version 20 computer statistical software package. Respondents' knowledge of the risk factors of cervical cancer was scored and graded on a 9-point scale. One point was awarded for a correct response, while a wrong response or I do not know received no points. This gives a minimum score of "0" and a maximum score of "9" points. Those that scored ≥ 6 of 9 points were considered as having "good" knowledge, while those that scored < 6 of 9 points were graded as having "poor" knowledge. Respondents' knowledge of the symptoms and signs of cervical cancer was scored and graded on a 6-point scale. One point was awarded for a correct response, while a wrong response or I do not know received no points. This gives a minimum score of "0" and a maximum score of "6" points. Those that scored ≥ 4 of 6 points were considered as having "good" knowledge, while those that scored < 4 of 6 points were graded as having "poor" knowledge.

Respondents' knowledge of cervical cancer prevention was scored and graded on a 9-point scale. One point was awarded for a correct response, while a wrong response or I do not know received no points. This gives a minimum score of "0" and a maximum score of "9" points. Those that scored ≥ 6 of 9 points were considered as having "good" knowledge, while those that scored < 6 of 9 points were graded as having "poor" knowledge. Frequency distribution tables were constructed, and cross-tabulations were done to examine the relationship between categorical variables. The Chi-square test was used for bivariate analysis involving categorical variables, while multivariate logistic regression analysis was used to seek for the predictors of good knowledge of cervical cancer. All levels of statistical significance were set at $P < 0.05$.

Ethical Consideration

Institutional ethical clearance was obtained from the Ethical Committee of UDUTH, Sokoto, Nigeria. Permission to conduct the study was obtained from the management of the hospital and head of the Department of Obstetrics and Gynaecology; informed written consent was also obtained from the participants before data collection.

RESULTS

Sociodemographic Characteristics of Respondents

Of the 280 questionnaires administered, 270 were adequately completed and found suitable for analysis,

giving a response rate of 96.4%. The respondents ages ranged from 17 to 64 years (mean = 32.80 ± 9.30), and majority, 201 (74.5%) of the 270 respondents were aged 20–39 years. Most of them were married (74.4%) and practiced Islam as religion (74.8%). Majority of respondents (71.9%) had secondary and tertiary education [Table 1].

Awareness of Cervical Cancer by Respondents

Less than half, 118 (43.7%) of the 270 respondents had heard of cervical cancer. Majority, 63 (53.4%) of the 118 respondents that had heard of cervical cancer reported health workers as their source of information, while 30 (25.4%) and 22 (18.6%) reported friends/relatives and radio/television as their sources of information, respectively [Table 2].

Respondents’ Knowledge of Cervical Cancer

Very few, 25 (9.3%) of the 270 respondents had good knowledge of the risk factors, only 40 (14.8%) had good knowledge of the symptoms and signs, and less than a fifth, 45 (16.7%) had good knowledge of the prevention of cervical cancer [Figure 1].

There was no association between good knowledge of the risk factors of cervical cancer and any of the sociodemographic variables of respondents. Good knowledge of the symptoms and signs of cervical cancer was associated with the respondents’ level of education. The proportion of respondents with good knowledge of the symptoms and signs of cervical cancer was significantly ($P < 0.05$) higher among the respondents that had secondary or tertiary education (17.5%) as compared to those that had primary education and below (7.9%) as shown in Table 3. Multivariate logistic regression analysis did not show any predictor of good knowledge of the symptoms and signs of cervical cancer.

Good knowledge of cervical cancer prevention was associated with the respondents’ religion and level of education. The proportion of respondents with good knowledge of cervical cancer prevention was significantly ($P < 0.05$) higher among Christians and those that belong to other religion (26.5%) as compared to Muslims (13.4%), and those with secondary or tertiary education (19.6%) as compared to those with primary education and below (9.2%) as shown in Table 3. Multivariate logistic regression analysis did not show any predictor of good knowledge of cervical cancer prevention.

Uptake of Pap Smear Test by Respondents

Only a few, 37 (13.7%) of the 270 respondents have ever had a Pap smear test done. Most, 31 (83.8%) of the 37

Table 1: Sociodemographic characteristics of respondents

Variables	Frequency (%) n=270
Age group (years)	
<20	8 (3.0)
20–29	105 (39.3)
30–39	95 (35.2)
40–49	43 (15.9)
50–59	15 (5.6)
≥60	3 (1.1)
Marital status	
Single	46 (17.0)
Married	201 (74.4)
Separated	4 (1.5)
Divorced	11 (4.1)
Widowed	8 (3.0)
Religion	
Islam	202 (74.8)
Christianity	65 (24.1)
Others	3 (1.1)
Level of education	
Primary and below	76 (28.1)
Secondary and tertiary	194 (71.9)

Table 2: Awareness of cervical cancer by respondents

Variables	Frequency (%)
Ever heard of cervical cancer (n=270)	
Yes	118 (43.7)
No	152 (56.3)
Source of information (n=118)	
Radio/television	22 (18.6)
Newspaper/magazine	2 (1.7)
Friends/relatives	30 (25.4)
Health worker	63 (53.4)
Church/mosque	1 (0.8)

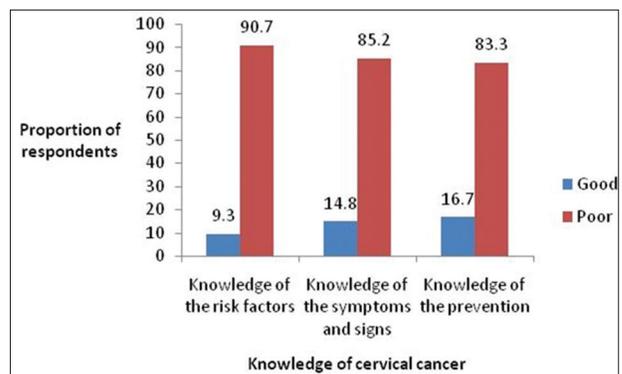


Figure 1: Respondents’ knowledge of cervical cancer

respondents that have ever done the test did it based on doctor’s request, while 6 (16.2%) did the test voluntarily. Lack of awareness of Pap smear test was cited as the main reason for non-uptake of the test by majority, 188 (80.7%) of the 233 respondents that have never done the test [Table 4].

Table 3: Distribution of respondents' knowledge of cervical cancer by their sociodemographic characteristics

Sociodemographic variables	Knowledge of cervical cancer					
	Knowledge of the risk factors, n=270		Knowledge of the symptoms and signs, n=270		Knowledge of the prevention, n=270	
	Good No (%)	Poor No (%)	Good No (%)	Poor No (%)	Good No (%)	Poor No (%)
Age (years)						
<40	21 (10.0)	188 (90.0)	31 (14.8)	178 (85.2)	37 (17.7)	172 (82.3)
40 and above	4 (6.6)	57 (93.4)	9 (14.8)	52 (85.2)	8 (13.1)	53 (86.9)
	$\chi^2=0.685, P=0.408$		$\chi^2=0.000, P=0.988$		$\chi^2=0.716, P=0.398$	
Marital status						
Single, separated, widowed	4 (5.8)	65 (94.2)	8 (11.6)	61 (88.4)	11 (15.9)	58 (84.1)
Married	21 (10.4)	180 (89.6)	32 (15.9)	169 (84.1)	34 (16.9)	167 (83.1)
	$\chi^2=1.322, P=0.250$		$\chi^2=0.762, P=0.383$		$\chi^2=0.035, P=0.852$	
Religion						
Islam	20 (9.9)	182 (90.1)	27 (13.4)	175 (86.6)	27 (13.4)	175 (86.6)
Christianity and others	5 (7.4)	63 (92.6)	13 (19.1)	55 (80.9)	18 (26.5)*	50 (73.5)
	$\chi^2=0.393, P=0.531$		$\chi^2=1.333, P=0.248$		$\chi^2=6.290, P=0.012$	
Education						
Primary and below	4 (5.3)	72 (94.7)	6 (7.9)	70 (92.1)	7 (9.2)	69 (90.8)
Secondary and tertiary	21 (10.8)	173 (89.2)	34 (17.5)*	160 (82.5)	38 (19.6)*	156 (80.4)
	$\chi^2=2.010, P=0.156$		$\chi^2=4.014, P=0.045$		$\chi^2=4.234, P=0.040$	

*Statistically significant

Table 4: Uptake of Pap smear test by respondents

Variables	Frequency (%)
Ever had a Pap smear test done (n=270)	
Yes	37 (13.7)
No	233 (86.3)
Indication for Pap smear test (n=37)	
Based on doctors' request	31 (83.8)
Did it voluntarily	6 (16.2)
Main reason for non-uptake of Pap smear test (n=233)	
Not aware of the test	188 (80.7)
No felt need for the test	18 (7.7)
Feels shy exposing the body	6 (2.6)
Fear of the outcome of the test	21 (9.0)

Uptake of HPV Vaccination by respondents

None (0%) of the respondents have ever had HPV vaccine administered to them. Lack of awareness of the vaccine was cited as the main reason for non-uptake of the vaccination by most 230 (85.2%) of the 270 respondents. Other reasons cited for non-uptake of the vaccination are as shown in Table 5.

Respondents' Attitude to Pap Smear Test and HPV Vaccination

Most of the respondents demonstrated positive attitude toward Pap smear test and HPV vaccination. Majority, 249 (92.2%) of the 270 respondents would voluntarily undergo Pap smear test periodically if it will protect them from developing cervical cancer. Similarly, majority, 255 (94.4%) of the 270 respondents would have HPV vaccine administered to them or their daughters if it will protect them from developing cervical cancer [Figure 2].

Table 5: Uptake of HPV vaccination by respondents

Variables	Frequency (%) (n=270)
Ever had HPV vaccine administered	
Yes	0 (0)
No	270 (100)
Main reason for non-uptake of HPV vaccination	
Not aware of the vaccine	230 (85.2)
I do not need it	20 (7.4)
Vaccine is not available	14 (5.2)
I am too old to take the vaccine	5 (1.8)
I do not believe in its efficacy	1 (0.4)

HPV: Human papillomavirus

DISCUSSION

This study assessed the knowledge of cervical cancer and uptake of Pap smear test and HPV vaccination among gynecologic clinic attendees in Sokoto, Nigeria. The low level of awareness of cervical cancer among the respondents in this study (43.7%), and the fact that only about a fifth of them (20.3%) obtained information about the disease through the mass media, indicates poor mass public enlightenment about the disease in Sokoto, Nigeria, and the need to scale-up education of the public about the disease through the mass media. This is supported by the finding in a study conducted among reproductive health clients at the University of Science and Technology Hospital, Sana'a Yemen, which reported a high level of awareness of cervical cancer (80.6%) with the mass media being the major source of information about the disease

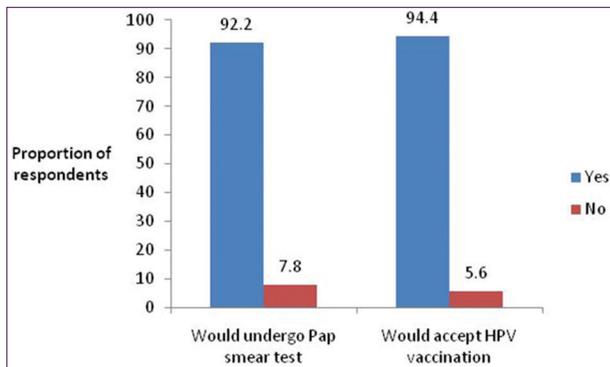


Figure 2: Respondents' attitude to Pap smear test and human papillomavirus vaccination

(54.3%).^[25] Another study among women in Uganda^[26] also reported a high level of awareness of cervical cancer (88.2%) with majority of respondents (70.2%) obtaining information about the disease through the radio.

The poor knowledge of cervical cancer among the respondents in this study with only 9.3, 14.8, and 16.7% of respondents having good knowledge of its risk factors, symptoms and signs, and prevention, respectively, correlates with the low level of awareness of the disease by them. This finding is in consonance with the finding in a study conducted in Elmina, Southern Ghana,^[27] which reported that 68.4% of respondents had never heard of cervical cancer, 93.6% had no knowledge of its risk factors, and 92.0% did not know about the treatment or prevention of the disease. The gap in the knowledge of cervical cancer among women in sub-Saharan Africa is further highlighted by the generally poor knowledge of the disease reported in studies conducted across Nigeria including Zaria,^[21] Nnewi,^[28] and Okada community^[29] and in other sub-Saharan African countries including Burkina Faso,^[30] Ethiopia,^[31] and Tanzania.^[32] These findings underscore the need for the governments of the respective countries across the continent to give education of the populace about the disease top priority in their national cancer control programs.

Noticeably, the poor utilization of cervical cancer prevention services among the respondents in this study with only 13.7% ever having a Pap smear test done, and with zero (0%) uptake of HPV vaccination, essentially mirror the poor knowledge of cervical cancer prevention by them.

Most, 31 (83.8%) of the 37 respondents that have ever had a Pap smear test done in this study did so based on physicians' request, and lack of awareness was the main reason cited by most 188 (80.7%) of the 233 respondents that have never done the test. This is of serious concern as it brings to the fore the insufficient attention given to

primary prevention of cervical cancer in Nigeria despite its high burden in the country. This is corroborated by the findings in a study conducted in Nnewi, Nigeria,^[28] which reported that only 12.6% of the respondents were aware of Pap smear test, and none of them (0%) was aware of HPV vaccination. In addition, most 15 (60.0%) of the 25 respondents that were aware of Pap smear test in the Nnewi study had it done, and all of them did the test based on physicians' request.^[28] It is, therefore, imperative that healthcare workers promote primary prevention of cervical cancer among all the "at risk" women accessing health-care services in their respective facilities, irrespective of the disease condition they presented with; as the women are more likely to utilize the cervical cancer prevention services if they are adequately counseled by their health-care providers.

The positive attitude shown by most of the respondents in this study to Pap smear test (92.2%) and HPV vaccination (94.4%) is not surprising, considering the fact that the low uptake of Pap smear test and the zero uptake of HPV vaccination by them were mainly due to lack of awareness. This is inspiring as it implies that periodic and sustained sensitization of women on cervical cancer and its prevention would improve the uptake of Pap smear test and HPV vaccination by them.

CONCLUSION

The poor knowledge of cervical cancer and low uptake of Pap smear test and HPV vaccination among the respondents in this study underline the need for public health education through the mass media to create awareness about the disease. In addition, healthcare workers and other stakeholders should promote utilization of cervical cancer prevention services by women.

ACKNOWLEDGMENTS

The authors appreciate the Management of UDUTH, Sokoto, Nigeria, the Head of Department of Obstetrics and Gynecology, and all the patients that participated in the study for their cooperation.

REFERENCES

1. World Health Organization (WHO). World Cancer Report 2014. Geneva, Switzerland: WHO; 2014. Available from: <http://www.who.int/mediacentre/factsheets/fs099/en/>. [Last accessed on 2015 Nov 06].
2. World Health Organization (WHO). Human papilloma virus vaccines, WHO position paper, May 2017. Weekly Epid Records 2017;92:241-68. Available from: <http://www.apps.who.int/iris/bitstream/handle/10665/255353/WER9219.pdf?sequence=1>. [Last accessed on 2018 July 11].
3. World Health Organization (WHO). Human Papilloma Virus (hpv) and

- Cervical Cancer. Key facts. Geneva, Switzerland: WHO; 2018. Available from [http://www.who.int/en/news-room/fact-sheets/detail/human-papillomavirus\(hpv\)-and-cervical-cancer](http://www.who.int/en/news-room/fact-sheets/detail/human-papillomavirus(hpv)-and-cervical-cancer). [Last accessed on 2018 July 14].
4. World Health Organization (WHO). WHO Guidelines for Screening and Treatment of Precancerous Lesions for Cervical Cancer Prevention. Geneva, Switzerland: WHO; 2013. Available from: <http://www.apps.who.int/iris/bitstream/10665/94830/1/97892415-48694>. [Last accessed on 2018 July 11].
 5. Bruni L, Barrionuevo-Rosas L, Alberto G, Serrano B, Mena M, Gomez D, *et al.* ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). Human Papillomavirus and Related disease in Nigeria, Summary Report 27th July 2017. Available from: <http://www.hpvcentre.net/statistics/reports/NGA.pdf> [Last accessed on 2018 July 11].
 6. Bruni L, Barrionuevo-Rosas L, Alberto G, Serrano B, Mena M, Gomez D, *et al.* ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). Human Papillomavirus and Related disease in South Africa, Summary Report 27th July 2017. Available from: <http://www.hpvcentre.net/statistics/reports/ZAF.pdf>. [Last accessed on 2018 July 11].
 7. Bruni L, Barrionuevo-Rosas L, Alberto G, Serrano B, Mena M, Gomez D, *et al.* ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). Human Papillomavirus and Related disease in Sudan, Summary Report 27th July 2017. Available from: <http://www.hpvcentre.net/statistics/reports/SDN.pdf>. [Last accessed on 2018 July 11].
 8. Bruni L, Barrionuevo-Rosas L, Alberto G, Serrano B, Mena M, Gomez D, *et al.* ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). Human Papillomavirus and Related Disease in Zimbabwe, Summary Report 27th July 2017. Available from: <http://www.hpvcentre.net/statistics/reports/ZWE.pdf>. [Last accessed on 2018 July 11].
 9. Nnadi DC, Singh S, Ahmed Y, Siddique S, Bilal S. Histopathological features of genital tract malignancies as seen a tertiary health centre in north-western Nigeria: A 10 year review. *Annals Med Health Sci Res* 2014;4 Suppl 3:S213-7.
 10. Oguntayo OA, Zayyan M, Kolawole AO, Adewuyi SA, Ismail H, Koledade K. Cancer of the cervix in Zaria, Northern Nigeria. *Ecancer Med Sci* 2011;5:219.
 11. Gadducci A, Barsotti C, Cosio S, Domenici L, Genazzani AR. Smoking habit, immune suppression, oral contraceptive use, and hormone replacement therapy use and cervical carcinogenesis: A review of the literature. *Gynecol Endocr* 2011;27:597-604.
 12. Agboola A. Textbook of Obstetrics and Gynaecology for Medical Students. Ibadan, Nigeria: Heinemann Education Books; 2006.
 13. Marrazzo JM, Koutsky LA, Kiviat NB, Kuypers JM, Stine K. Papanicolaou test screening and prevalence of genital human papillomavirus among women who have sex with women. *Am J Public Health* 2001;91:947-52.
 14. Renschmidt C, Kaufmann AM, Hagemann I, Vartazarova E, Wichmann O, Deléré Y. Risk factors for cervical human papillomavirus infection and high-grade intraepithelial lesion in women aged 20 to 31 years in Germany. *Int J Gynaec Cancers* 2013;23:519-26.
 15. World Health Organization (WHO). WHO Guidelines for Screening and Treatment of Precancerous Lesions for Cervical Cancer Prevention. Geneva, Switzerland: WHO; 2013. Available from: http://www.apps.who.int/iris/bitstream/handle/10665/94830/9789241548694_eng.pdf;jsessionid=3F96286FB96D8844D6CCCAA1B2FD0E9E?sequence=1. [Last accessed on 2018 July 14].
 16. Canavan TP, Doshi NR. Cervical cancer. *Am Fam Physician* 2000;61:1369-76.
 17. Mangona JF, Chirenje MZ, Chimbari MJ, Chandiwana SK. An assessment of rural women's knowledge, constraints and perceptions on cervical cancer screening: The case of two districts in Zimbabwe. *Afr J Reprod Health* 2006;10:91-103.
 18. Almobarak AO, Elbadawi AA, Elmadhoun WM, Elhoweris MH, Ahmed MH. Knowledge, attitude and practice of Sudanese women regarding the Pap smear test and cervical cancer. *Asian Pacific J Canc Prev* 2016;17:625-30.
 19. Ingwu JA. Knowledge and screening practices of cervical cancer among pregnant women attending antenatal clinic in tertiary hospitals in Enugu, south-Eastern Nigeria. *J Canc Tum Int* 2016;4:1-9.
 20. Adekanle DA, Adeyemi AS, Afolabi AF. Knowledge, attitude and cervical cancer screening among female secondary school teachers in Osogbo, Southwest Nigeria. *Academic J Canc Res* 2011;4:24-8.
 21. Ahmed SA, Sabitu K, Idris SH, Ahmed R. Knowledge, attitude and practice of cervical cancer screening among market women in Zaria, Nigeria. *Niger Med J* 2013;54:316-9.
 22. Oche MO, Kaoje AU, Gana G, Ango JT. Cancer of the cervix and cervical screening: Current knowledge, attitude and practices of female health workers in Sokoto, Nigeria. *Int J Med Med Sci* 2013;5:184-90.
 23. Taofeek I. Research Methodology and Dissertation Writing for Health and Allied Health Professionals. Abuja: Cress Global Link Limited.; 2009.
 24. Gichangi P, Estambale B, Bwayo J, Rogo K, Ojwang S, Opiyo A, *et al.* Knowledge and practice about cervical cancer and Pap smear testing among patients at Kenyatta national Hospital, Nairobi, Kenya. *Int J Gynecol Cancer* 2003;13:827-33.
 25. Abdul-Aziz M. Knowledge, attitude and practice towards cervical cancer among reproductive health clients at the University of Science and Technology Hospital, Sana'a in Yemen. *Yemeni J Med Sci* 2012;6:21-7.
 26. Mukama T, Ndeji R, Musabyimana A, Halage AA, Musoke D. Women's knowledge and attitude towards cervical cancer prevention; A cross-sectional study in Eastern Uganda. *BMC Womens Health* 2017;17:9.
 27. Ebu NI, Mupepi SC, Siakwa MP, Sampselle CM. Knowledge, practice and barriers towards cervical cancer screening in Elmina, Southern Ghana. *Int J Women's Health* 2015;7:31-9.
 28. Mbamara SU, Ikpere OC, Okonkwo JE, Onyiaorah IV, Ukah CO. Knowledge, attitude and practice of cervical cancer screening among women attending gynecologic clinics in a tertiary level medical care centre in Southeastern Nigeria. *J Reprod Med* 2011;56:491-6.
 29. Igwilo AI, Igwilo UU, Hassan F, Idanwekhai M, Igbinomwanhia O, Popoola AO. The knowledge, attitude and practice of the prevention of cancer of the cervix in Okada community, Nigeria. *Asian J Med Sci* 2010;4:95-8.
 30. Sawadogo B, Gitta SN, Rutemberwa E, Sawadogo M, Meda N. Knowledge and beliefs on cervical cancer and practices on cervical cancer screening among women aged 20 to 50 years in Quagadougou, Burkina Faso 2012: A cross-sectional study. *Pan Afr Med J* 2014;18:175.
 31. Getahun F, Mazengia F, Abuhay M, Birhanu Z. Comprehensive knowledge about cervical cancer is low among women in Northwest Ethiopia. *BMC Cancer* 2013;13:2.
 32. Urasa M, Darj E. Knowledge of cervical cancer and screening practices of nurses at a regional hospital in Tanzania. *Afr Health Sci* 2011;11:48-57.

How to cite this article: Awosan KJ, Hassan M, Ibrahim BM. Knowledge of Cervical Cancer and Uptake of Pap Smear Test and Human Papillomavirus Vaccination among Gynecologic Clinic Attendees in Sokoto, Nigeria. *Int J Sci Stud* 2018;6(5):52-58.

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

An Insight in Sexual Behavior of Married Women

Shashi Prateek¹, Himani Goyal², Yamini Verma³, Geetika Nain³

¹Professor and Head, Department of Obstetrics and Gynecology, Subharti Medical College Meerut, Uttar Pradesh, India, ²Senior Resident, Department of Obstetrics and Gynecology, Subharti Medical College Meerut, Uttar Pradesh, India, ³Resident, Department of Obstetrics and Gynecology, Subharti Medical College Meerut, Uttar Pradesh, India

Abstract

Background: Disharmony in sexual relationship affects life of a woman, which sometimes remains silent and causes distress to the woman and accepted as a normal. A woman sexual response involves not just body but mind also. Emotional factors play a role in sexual satisfaction.

Objectives: How sexual life of a married women is affected by demographic and relationship factors?

Study design: Cross sectional descriptive survey.

Settings: Gynaecological OPD of Subharti Medical College, Meerut from Jan 2018 to April 2018.

Results: Two hundred women were interviewed and questionnaire filled. Out of which 40 women reported problems with their sexual life. Loss of Libido was found in 29%, difficulty in arousal in 10% for one or other reasons and 27% were not satisfied after sexual act. The reasons mentioned were job responsibilities, children education and care, lack of contraceptive use, lack of foreplay, imposed sex, abusive behavior of partner and discomfort during the act.

Conclusion: Intimacy, emotional and sexual relations are necessary for a healthy life. Which can be improved by counselling in outdoor visits. So doctors should sensitively ask woman about their personal life problems to improve their quality of life.

Key words: Sexual health, Relationship satisfaction, Quality of life

INTRODUCTION

A woman's expression of her sexuality is unique and is likely to change over time. Pleasure or anhedonia from sex can also have a considerable impact on the overall quality of life.^[1] Although basic sexual drive is biological, its expression is determined by a variety of psychological, social, environmental, spiritual, and learned factors. Thus, sexual satisfaction, for women, is often less dependent on the physical components of sex than on the quality of the relationship and the context in which sexual behavior is undertaken.

Sexual problems can be present when there is a problem in either emotional or physical part of life.

Emotional Causes

The emotional causes are stress, relationship problems, depression or anxiety, a memory of sexual abuse, and unhappiness with your body.

Physical Causes

Physical causes include pain from an injury or other problems, certain hormonal disorders, diabetes or arthritis, and medications, for example, for depression, anxiety, and seizures, and aging, which can cause changes in the vagina as dryness.

One may notice a change in desire or sexual satisfaction. When this happens, it helps to look at what is and is not working in a woman's body and her life. It can be hard or embarrassing to talk to a doctor about this. Hence, we have prepared a questionnaire to ask the patient about her problems in a friendly environment.

MATERIALS AND METHODS

Aim

The aim is to study how sexual life of married women is affected by demographic and relationship factors?

Access this article online



www.ijss-sn.com

Month of Submission : 06-2018
Month of Peer Review : 07-2018
Month of Acceptance : 08-2018
Month of Publishing : 08-2018

Corresponding Author: Dr. Himani Goyal, Subharti Medical College, Meerut, Uttar Pradesh, India. Phone: +91-9458687874.
E-mail: hgoyal.dr@rediffmail.com

Study Design

The study design was a cross-sectional descriptive survey.

Settings

The study was conducted at Gynaecological OPD of Subharti Medical College, Meerut, from January 2018 to April 2018.

Participants

A total of 200 married women attending OPD for various reasons, sexually active and staying with husband. Women having chronic health problems, hysterectomized or with psychological illness were excluded.

Measures

A predesigned structured questionnaire having sociodemographic details, relationship status, and sexual life was prepared. The questionnaire included age, primary language, employment, education, income, whether children/other persons living in a same place, physical health, and menstrual cycle status. Sexual history variables included four questions about sexual problems.

- Having less desire for sex.
- Having trouble feeling aroused.
- Not being able to have an orgasm.
- Having pain during sex.

Data were compiled and statistical analysis was done [Figure 1].

RESULTS

A total of 200 women were interviewed and questionnaire filled. Of which 40 women reported problems with their sexual life. Loss of Libido was found in 29%, difficulty in arousal in 10% for one or other reasons and 27% were not satisfied after the sexual act. The reasons mentioned were job responsibilities, children education and care, lack of contraceptive use, lack of foreplay, imposed sex, abusive behavior of partner, and discomfort during the act [Table 1 and Figures 2 and 3].

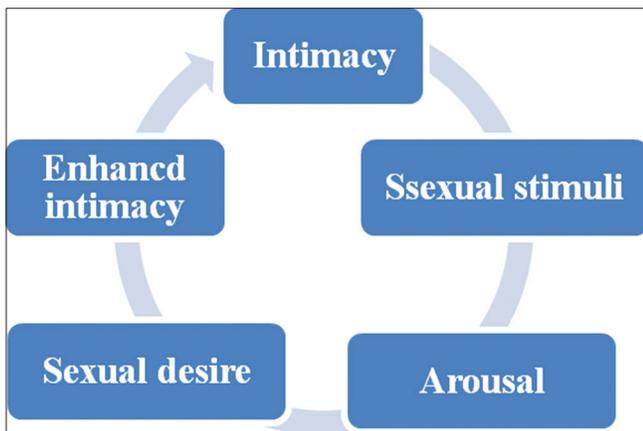


Figure 1: Biologic cycle Basson, 2000^[2]

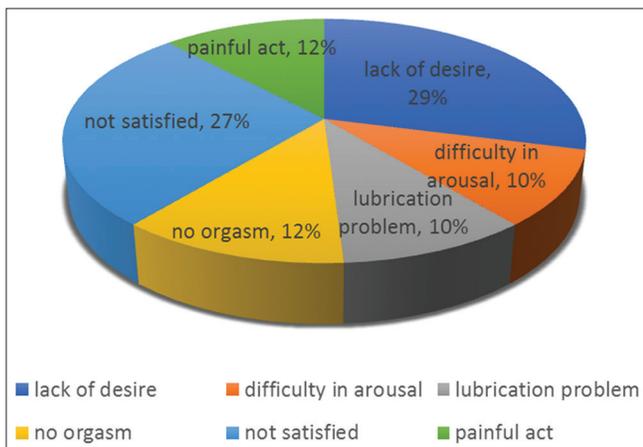


Figure 2: Causes of sexual dysfunction

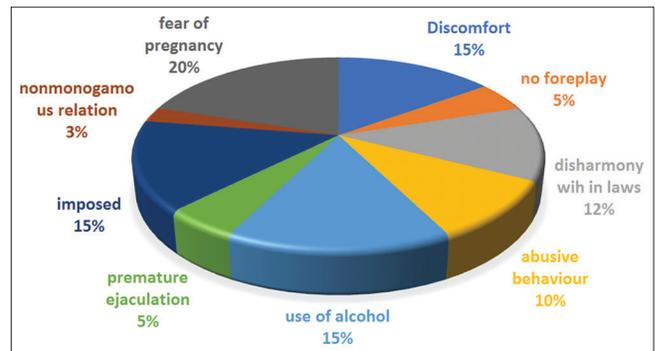


Figure 3: Factors affecting sexual life

Table 1: Sociodemographic factors

Sociodemographic Variables	Total	Sexual dysfunction
Age in years	No of women (%)	No of women (%)
19–25	62 (31)	12 (6)
26–35	80 (40)	15 (8)
36–45	58 (29)	13 (6.5)
Education		
Primary	34 (17)	5 (3)
Graduate	106 (53)	20 (10)
Above	60 (30)	15 (7.5)
Occupation		
Home maker	120 (60)	10 (5)
Part time worker	65 (32.5)	18 (9)
Full-time worker	15 (7.5)	12 (6)
Parity		
Nulliparous	60 (30)	5 (3)
Parous	140 (70)	35 (13)
Residence		
Rural	40 (20)	4 (2)
Semiurban	100 (50)	16 (8)
Urban	60 (30)	20 (10)

DISCUSSION

Causes for sexual problems may include:

Getting Older

A woman's sex drive often decreases with age. Age showed significant positive bivariate correlations with reports of current sexual problems and with lifetime experience of both arousal difficulties and low sexual interest.^[3]

Employment

Women working outside have less interest in sex. Women who currently worked fulltime had higher reports of both of these specific problems.

Parity

High parity more children more time demanding and tired females. In the study by Mercer *et al.* (2005), women with young children in the home were more likely to report sexual problems.^[4]

Education

Canadian survey, which found that highly educated women were more likely to report both low sexual desire and infrequent coital orgasm (Gruszecki *et al.*, 2005).^[5]

According to a Korean survey, risk factors were increasing age, a low frequency of sex, depression, a sexually abused history, and voiding dysfunction.^[6]

Sexuality is negatively affected by abusive behavior, alcoholism, and disharmony in relationships as studied by Santtila *et al.* Sexual satisfaction with vaginal intercourse as well as kissing and petting was positively associated with relationship satisfaction.^[7]

In study results reflect diversity in women's motivations for sex and there is evidence that responsive desire occurs in women with and without arousal difficulties. It was strongly recommended that relationship duration as well as the adequacy of partner sexual stimulation to give importance.^[8]

Sexual dysfunctions were detected as desire problems (39.3%), arousal problems (25.8%), lubrication problems (21.5%), orgasm problems (16.6%), satisfaction problems (21.5%), and pain problems (16.6%). Those who practiced contraception were less likely to have FSD found by Ishak *et al.*^[9]

CONCLUSION

Intimacy, emotional, and sexual relations are necessary for a healthy life which can be improved by counseling in outdoor visits. Hence, doctors should sensitively ask a woman about their personal life problems to improve their quality of life.

Limitations

- Limitation of the present study was that we asked rarely talked questions about the experience of sexual problems.
- Survey depends on the chosen sampling frame.
- Interviewer error or bias can be there.

ACKNOWLEDGMENT

I thank 200 women who shared this important information about their sexual lives despite many taboos attached to talking about it.

REFERENCES

1. Wylie K, Mimoun S. Sexual response models in women. *Maturitas* 2009;63:112-5.
2. Basson R. The female sexual response: A different model. *J Sex Marital Ther* 2000;26:51-65.
3. Sanders SA, Graham CA, Milhausen RR. Predicting sexual problems in women: The relevance of sexual excitation and sexual inhibition. *Arch Sex Behav* 2008;37:241-51.
4. Mercer CH, Fenton KA, Johnson AM, Copas AJ, Macdowall W, Erens B, *et al.* Who reports sexual function problems? Evidence from the 2000 national survey of sexual attitudes and lifestyles ('Natsal 2000'). *Sex Transm Infect* 2005;81:394-9.
5. Gruszecki L, Forchuk C, Fisher WA. Factors associated with common sexual concerns in women: New findings from the Canadian contraception study. *Can J Hum Sex* 2005;14:1-13.
6. Song SH, Jeon H, Kim SW, Paick JS, Son H. The prevalence and risk factors of female sexual dysfunction in young Korean women: An internet-based survey. *J Sex Med* 2008;5:1694-701.
7. Santtila P, Wager I, Witting K, Harlaar N, Jern P, Johansson A, *et al.* Discrepancies between sexual desire and sexual activity: Gender differences and associations with relationship satisfaction. *J Sex Marital Ther* 2008;34:31-44.
8. Carvalheira AA, Brotto LA, Leal I. Women's motivations for sex: Exploring the diagnostic and statistical manual, fourth edition, text revision criteria for hypoactive sexual desire and female sexual arousal disorders. *J Sex Med* 2010;7:1454-63.
9. Ishak IH, Low WY, Othman S. Prevalence, risk factors, and predictors of female sexual dysfunction in a primary care setting: A survey finding C. *J Sex Med* 2010;7:3080-7.

How to cite this article: Prateek S, Goyal H, Verma Y, Nain G. An Insight in Sexual Behavior of Married Women. *Int J Sci Stud* 2018;6(5):59-61.

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

Knowledge of Human Papillomavirus Infection and Vaccination, and Practices Regarding Human Papillomavirus Vaccination among Female Health-care Professionals in Sokoto, Nigeria

Mairo Hassan¹, Kehinde Joseph Awosan²

¹Senior Lecturer, Department of Obstetrics and Gynecology, Usmanu Danfodiyo University, Sokoto, Nigeria, ²Senior Lecturer, Department of Community Health, Usmanu Danfodiyo University, Sokoto, Nigeria

Abstract

Introduction: The high human papillomavirus (HPV) infection transmission rates in the less developed regions of the world are believed to be responsible for the concomitantly high burden of cervical cancer in these regions.

Objectives: This study aimed to assess the knowledge of HPV infection and vaccination, and practices regarding HPV vaccination among female health-care professionals in Sokoto, Nigeria.

Materials and Methods: This was a cross-sectional study among 256 female health-care professionals (selected by multistage sampling technique) practicing in the secondary and tertiary health-care facilities in Sokoto metropolis, Nigeria. A structured self-administered questionnaire was used to collect data on the research variables. Data were analyzed using IBM SPSS version 24 statistical computer software package.

Results: The mean age of the respondents was 36.74 ± 8.9 years. Most, 208 (81.3%) of the 256 respondents were married and majority of them (58.6%) were nurses. Less than half of the respondents (47.7%) had good knowledge of HPV infection and only a few of them (7.4%) had good knowledge of HPV vaccination. Uptake of HPV vaccination was low (2.3%) among the respondents, with the main reasons cited being non-availability of the vaccines (42.7%) and lack of awareness (24.8%).

Conclusion: This study showed suboptimal knowledge of HPV infection and low levels of knowledge and uptake of HPV vaccination among the respondents. Government and the Management of Health Institutions should organize periodic training of health-care professionals on the strategies for preventing the transmission of HPV infection and also make HPV vaccines consistently accessible to the target population.

Key words: Health-care professionals, Human papillomavirus infection and vaccination, Knowledge, Practices.

INTRODUCTION

The high human papillomavirus (HPV) infection transmission rates in the less developed regions of the world are believed to be responsible for the concomitantly high burden of cervical cancer in these regions. A meta-analysis

of the cervical HPV prevalence among 1 million women with normal cytological findings in 5 continents showed that sub-Saharan Africa had the highest prevalence (24.0%), followed by Latin America and the Caribbean (16.1%), and with the prevalence in sub-Saharan Africa being more than twice the global prevalence of 11.7%.^[1] Persistent infection with high-risk HPV types is strongly associated with cervical cancer, with an estimated 75% of cases globally attributable to infection with HPV types 16 and 18.^[2] In concomitance with the disproportionately high prevalence of HPV infection in the less developed regions, most (>85%) of the cervical cancer cases globally occur in these regions where it accounts for almost 12% of all

Access this article online



www.ijss-sn.com

Month of Submission : 06-2018

Month of Peer Review : 07-2018

Month of Acceptance : 08-2018

Month of Publishing : 08-2018

Corresponding Author: Dr. Mairo Hassan, Department of Obstetrics and Gynecology, Usmanu Danfodiyo University, Sokoto, Nigeria.
E-mail: mayroh123@gmail.com

cancers in women, as compared to the more developed regions where it accounts for less than 1% of all cancers in women.^[3]

In Nigeria, cancers attributable to HPV infections constitute a substantial cancer burden in women. Findings from two population-based cancer registries in the country showed that 488 (11.0%) of the 14336 new cancer cases seen from 2012 to 2014 were HPV associated, with cervical cancer being the most common HPV attributable cancer in women ($n = 392$, ASR = 28.3/100,000), and anal cancer being the most common in men ($n = 21$, ASR = 1.2/100,000). The authors submitted that a significant proportion of cancers in Nigerian women would be prevented if strategies such as HPV DNA-based screening and HPV vaccination are implemented.^[4]

Since there is no virus-specific treatment for HPV infection, and with the high prevalence of HPV associated risk behaviors in many sub-Saharan African countries, high coverage (>70%) of full immunization against HPV infection among girls and boys aged 9–14 years (as recommended by the World Health Organization) remains the only feasible option for halting and reversing the persistent rise in the burden of cervical cancer across the continent.^[3]

Although HPV vaccination is known to prevent up to 95% of cervical cancers,^[5] the major challenge remains unavailability of the vaccines in the less affluent countries, as the respective prophylactic HPV vaccines (bivalent, quadrivalent, and nonavalent vaccines) are intended to be administered before the onset of sexual activity (i.e., before first exposure to HPV infection) and according to specified dose schedules to be effective.^[3]

Studies conducted among health-care professionals in different populations worldwide showed wide variations in the knowledge of HPV infection and vaccination; as well as in the uptake of HPV vaccination, and promotion of HPV vaccination among their clients and patients. A study conducted among physicians in the Western Region of Saudi Arabia reported that less than half of them (48.5%) knew about the HPV vaccine and only 50% of them intended recommending it to their patients.^[6] Similarly, a study conducted among 590 health-care professionals in Delhi, India, reported that while most of the respondents (81.0%) were aware of HPV vaccine, less than half (47%) recommended HPV vaccination for young women.^[7] A study among 602 health-care professionals in 3 of the 6 geopolitical zones in Nigeria reported that while most of the respondents (91.0%) were aware of HPV infection, less than half of them (44.0%) were aware of HPV vaccine.

The most worrisome aspect is the poor knowledge of HPV infection and vaccination, and the abysmally low uptake of HPV vaccination in studies conducted among female health-care professionals across the globe. A study among female nurses in Iran reported that only about a third of respondents (36.7%) knew about HPV infection,^[8] while a recent study among female nurses in Turkey reported that only 2 (1.8%) of 110 participants had received HPV vaccine.^[9] A study among nurses in Nigeria reported that while most of them (85%) were aware of HPV infection, only a quarter of respondents (25.3%) were aware of HPV vaccines.^[10]

Health-care professionals have crucial roles to play in educating their clients, patients, and members of the public on the prevention of HPV infection through avoidance of high-risk behaviors and HPV vaccination. Importantly, female health-care professionals (being at risk of cervical cancer themselves) are expected to be role models in promoting the practices and interventions for the prevention and control of the disease among the patients and clients presenting at their respective health facilities. In addition, adolescent girls and women are more likely to discuss sensitive issues pertaining to their reproductive tract with the female health-care professionals in detail, as compared to the male health-care professionals.

It is therefore not surprising that studies conducted among adolescent girls and women in different populations across the globe (including the developed regions) showed wide variations in the knowledge of HPV infection and vaccination, as well as in the uptake of HPV vaccination, thus mirroring the variations observed among the health-care professionals. While a study among young Australian women reported high uptake (84%) of HPV vaccine,^[11] a study among female high school and university students in Krakow, Poland, reported that 30.1% of respondents did not know that HPV vaccination is a method of preventing cervical cancer, 47.9% did not know where to go and get vaccinated, and most of them (91.5%) had not been vaccinated against HPV.^[12] Similarly, a study conducted among women in Beijing reported that only 26.9% of respondents knew HPV as a risk factor for cervical cancer;^[13] and another study among women attending a tertiary care hospital in Puducherry, India, reported that most of the respondents (97.2%) were unaware of HPV vaccination as prevention for cervical cancer.^[14]

A cause for concern is the predominantly poor knowledge of HPV infection and vaccination, and the abysmally low uptake of HPV vaccination in studies conducted among adolescent girls and women in many countries in sub-

Saharan Africa (including Nigeria), thus reflecting the poor knowledge, acceptance, and promotion of HPV vaccination by the health-care professionals across the continent. A study among Sudanese women reported that less than half (46.6%) were aware of HPV infection, 39.2% were aware of HPV vaccination, and only 11.4% had received HPV vaccine.^[15] A recent community-based study across three states in Nigeria reported that only 31.97% of respondents were aware of HPV infection and less than a fifth of respondents (17.5%) were aware of HPV vaccine.^[16] The enormity of the poor awareness of HPV infection and vaccination being major obstacles to the uptake of HPV vaccination in Nigeria is highlighted in a study among mothers in Lagos, Nigeria, that reported low awareness of HPV infection (27.9%) and HPV vaccination (19.7%), but there was high willingness and intention to vaccinate their adolescent daughters (88.9%) and to recommend the vaccine to others (91.0%).^[17] A previous study among female health-care workers in Sokoto principally examined their knowledge, attitude, and practice regarding cervical cancer and cervical cancer screening,^[18] there is a dearth of literature on the knowledge of HPV infection and vaccination, as well as the uptake of HPV vaccination among women (particularly female health-care professionals) in Sokoto, Nigeria. This study was conducted to assess the knowledge of HPV infection and vaccination, and practices regarding HPV vaccination among female health-care professionals in Sokoto, Nigeria.

MATERIALS AND METHODS

Study Design and Population

This cross-sectional study was carried out among female health-care professionals practicing in the secondary and tertiary health-care facilities in Sokoto metropolis, Nigeria, in April and May 2018. All those that consented to participate in the study were considered eligible for enrolment into the study.

Sample Size Estimation and Sampling Technique

The sample size was estimated at 243 using the statistical formula for calculating sample size in cross-sectional studies,^[19] a 49.2% prevalence of immunization of adolescent daughters with HPV vaccine among female health-care workers from a previous study,^[20] a precision level of 5%, and an adjustment for a finite population of 658 female health-care professionals (obtained from institutional records). It was reviewed upward to 260 in anticipation of 95% participant response rate.

The eligible participants were selected by a multistage sampling technique. At the first stage, 1 of 2 tertiary health-care facilities (Usmanu Danfodiyo University Teaching Hospital [UDUTH], Sokoto), and 1 of

3 secondary health-care facilities (Maryam Abacha Women and Children Hospital, Sokoto) were selected by simple random sampling using the ballot option. At the second stage, whereas 6 of the 24 departments involved in clinical services at UDUTH, Sokoto, were selected by simple random sampling using the ballot option, selection of participants in the 3 units at the Maryam Abacha Women and Children Hospital, Sokoto, was done by systematic sampling technique using the staff list in the respective units to constitute the sampling frame. At the third stage, selection of participants in the selected departments at UDUTH was done by systematic sampling technique using the staff list in the respective departments to constitute the sampling frame. Proportionate allocation of the study participants was done based on the staff strength in the selected departments.

Data Collection and Analysis

A structured, self-administered questionnaire was developed after a thorough review of relevant literature and used to obtain information on the sociodemographic characteristics of the study participants, their knowledge of HPV infection and vaccination, and their practices regarding HPV vaccination. It was reviewed by researchers in the Department of Obstetrics and Gynecology, Usmanu Danfodiyo University, Sokoto, Nigeria. Corrections were made based on their inputs on content validity. The questionnaire was pretested on 15 female health-care professionals at Women and Children Welfare Clinic, Sokoto, Nigeria. The questions were well understood and no modification was necessary. Four resident doctors assisted in questionnaire administration after pre-training on conduct of survey research, the objectives of the study, selection of study subjects, and questionnaire administration.

Data were analyzed using the IBM SPSS version 24 computer statistical software package. Respondents' knowledge of HPV infection was scored and graded on a 19-point scale. One point was awarded for a correct response, while a wrong response or I don't know response received no points. This gives a minimum score of "0" and a maximum score of "19" points. Those that scored ≥ 12 of 19 points were considered as having "good" knowledge, while those that scored < 12 of 19 points were graded as having "poor" knowledge. Respondents' knowledge of HPV vaccination was scored and graded on an 11-point scale. One point was awarded for a correct response, while a wrong response or I don't know response received no points. This gives a minimum score of "0" and a maximum score of "11" points. Those that scored ≥ 7 of 11 points were considered as having "good" knowledge, while those that scored < 7 of 11 points were graded as having "poor" knowledge. Frequency distribution tables

were constructed and cross-tabulations were done to examine the relationship between categorical variables. The Chi-square test was used for bivariate analysis involving categorical variables, while multivariate logistic regression analysis was used to determine the predictors of good knowledge of HPV infection and vaccination. All levels of significance were set at $P < 0.05$.

Ethical Consideration

Institutional ethical clearance was obtained from the Ethical Committees of Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria, and Sokoto State Ministry of Health, Sokoto, Nigeria. Permission to conduct the study was obtained from the Management of the selected hospitals; informed written consent was also obtained from the participants before data collection.

RESULTS

Sociodemographic Characteristics of Respondents

Two hundred and fifty-six out of the 260 questionnaires administered were adequately completed and used for analysis, giving a response rate of 98.5%. The respondents ages ranged from 21 to 59 years (mean = 36.74 ± 8.90); and a larger proportion of them were in the 30–39 years age group (35.5%), followed by those in the 40–49 years age group (28.5%). Most of the respondents were married (81.3%) and majority of them were Muslims (69.9%). Majority of respondents had bachelor or post-graduate degree (62.2%) and were nurses (58.6%). A larger proportion of respondents (47.3%) have spent less than a decade in practice (47.3%) as shown in Table 1.

Awareness of HPV by Respondents

Mostly, 235 (91.8%) of the 256 respondents had heard of HPV. Furthermore, 188 (80.0%) of the 235 respondents that had heard of HPV obtained information about it through lectures, while about a tenth of them (26 [11.1%]) obtained information about it from their colleagues. Only a few respondents (19 [8.14%]) obtained information about HPV from the mass media [Table 2].

Respondents' Knowledge of HPV Infection

Less than half, 122 (47.7%) of the 256 respondents had good knowledge of HPV infection. Whereas, majority of respondents (55.1%) knew HPV as the most common viral infection of the female reproductive tract, only about a fifth of them (21.9%) knew HPV 16 and 18 as the most frequent HPV types worldwide. In addition, only about two-thirds and less (24.2–68.4%) knew its routes of transmission. Majority of respondents (72.3%) knew that HPV can cause cervical cancer, but less than half of respondents knew the other cancers caused by

Table 1: Sociodemographic characteristics of respondents

Variables	Frequency (%) <i>n</i> =256
Age group (years)	
20–29	64 (25.0)
30–39	91 (35.5)
40–49	73 (28.5)
50–59	28 (10.9)
Marital status	
Single	42 (16.4)
Married	208 (81.3)
Separated	1 (0.4)
Widowed	5 (2.0)
Religion	
Islam	179 (69.9)
Christianity	77 (30.1)
Level of education	
Diploma	76 (29.7)
Associate degree	21 (8.2)
Bachelor	101 (39.5)
Post-graduate	58 (22.7)
Cadre	
Doctor	49 (19.1)
Nurse	150 (58.6)
Laboratory scientist	39 (15.2)
Others (pharmacist, radiographer etc.)	18 (7.0)
Length of practice (years)	
<10	121 (47.3)
10–19	80 (31.3)
20–29	34 (13.3)
≥30	21 (8.2)

Table 2: Awareness of HPV by respondents

Variables	Frequency (%)
Ever heard of HPV (<i>n</i> =256)	
Yes	235 (91.8)
No	21 (8.2)
Source of information (<i>n</i> =235)	
Radio/Television	15 (6.4)
Newspaper/Magazine	4 (1.7)
Lecture	188 (80.0)
Friends	2 (0.9)
Colleagues	26 (11.1)

HPV: Human papillomavirus

it. Whereas, majority of respondents knew that HPV infection can be prevented by having sex with only one faithful partner (70.7%) and immunization with HPV vaccine (67.6%), less than half of them knew the other methods of preventing the transmission of the infection [Table 3].

Respondents' Knowledge of HPV Vaccination

Only a few 19 (7.4%) of the 256 respondents had good knowledge of HPV vaccination. Whereas, majority of respondent knew that HPV vaccination should be recommended for both males and females (51.2%), and it should be given before onset of sexual activity (61.7%), only about a third of them (31.6%) knew

that individuals aged 9 to 26 years are eligible for HPV vaccination. Less than a third of respondents (28.9%) knew that HPV vaccination offers herd immunity (i.e. protects those who have not been vaccinated, if a sufficient proportion of the population at risk has been vaccinated), and only a few respondents (16.0% and below) knew the recommended doses for the subgroups of those eligible for HPV vaccination. Furthermore, less than half of respondents (40.6%) knew that the vaccine cannot treat women who have developed HPV-related diseases [Table 4].

Factors Influencing Respondents' Knowledge of HPV Infection and Vaccination

Good knowledge of HPV infection was associated with the respondents' age, level of education, cadre, and length of practice. The proportion of respondents with good knowledge of HPV infection was significantly

higher ($P < 0.05$) among those that were aged 40 years and above (54.2%) as compared to those that were aged less than 40 years (37.6%), those with Bachelor or Post-graduate degree (54.1%) as compared to those with diploma or associate degree (37.1%), doctors (87.8%) as compared to nurses and those in the other cadres (38.2%), and those that have practiced for <10 years (54.5%) as compared to those that have practiced for 10 years and above (41.5%) as shown in Table 5. In multivariate logistic regression analysis, the only predictor of good knowledge of HPV infection among the respondents was their cadre. Being a doctor was associated with an 11.674 fold (adjusted odds ratio [aOR]: 11.674, 95% confidence interval (CI): 4.566–29.850, $P < 0.001$) greater likelihood of having good knowledge of HPV infection [Table 6].

Good knowledge of HPV vaccination was associated with the respondents' marital status, level of education, and cadre. The proportion of respondents with good knowledge of HPV vaccination was significantly higher ($P < 0.05$) among those that were married (9.1%) as compared to those that were single, separated, or widowed (0%), those with Bachelor or Post-graduate degree (11.9%)

Table 3: Respondents' knowledge of HPV infection

Variables	Frequency (%) (n=256)
Knowledge of transmission of HPV	
Knew HPV as the most common viral infection of the female reproductive tract	141 (55.1)
Knew HPV 16 and 18 as the most frequent HPV types worldwide	56 (21.9)
Knew that HPV can be transmitted through:	
Open-mouthed kissing	62 (24.2)
From an infected mother to her baby during delivery	97 (37.9)
Contact with infected genital skin, mucous membrane, and bodily fluid	153 (59.8)
Sexual intercourse	175 (68.4)
Oral sex	97 (37.9)
Knew that both males and females can become infected with HPV	161 (62.9)
Knowledge of diseases caused by HPV	
Knew that most people with genital HPV infection are asymptomatic	168 (65.6)
Knew that HPV can cause the following diseases:	
Oropharyngeal cancer	77 (30.1)
Cervical cancer	185 (72.3)
Genital warts	122 (47.7)
Anogenital cancer	88 (34.4)
Knew that cervical cancer is caused by HPV types 16 and 18	77 (30.1)
Knew that anogenital wart is caused by HPV types 6 and 11	64 (25.0)
Knowledge of HPV prevention	
Knew that HPV infection can be prevented by:	
Sexual abstinence	113 (44.1)
Having sex with only one faithful partner	181 (70.7)
Consistent use of condom	113 (44.1)
Immunization with HPV vaccine	173 (67.6)
Knowledge grading	
Good	122 (47.7)
Poor	134 (52.3)

HPV: Human papillomavirus

Table 4: Respondents' knowledge of HPV vaccination

Variables	Frequency (%) (n=256)
Knew that HPV vaccines offer herd immunity (i.e., protect those who have not been vaccinated if a sufficient proportion of the population at risk has been vaccinated)	74 (28.9)
Knew the following types of HPV vaccines:	
Bivalent	58 (22.7)
Quadrivalent	31 (12.1)
Nonavalent	23 (9.0)
Knew that both males and females should be vaccinated	131 (51.2)
Knew that individuals aged 9 to 26 years are eligible for HPV vaccination	81 (31.6)
Knew that HPV vaccination should be done before onset of sexual activity	158 (61.7)
Knew that 2 doses of vaccines are recommended for individuals aged 9 to 14 years	26 (10.2)
Knew that 3 doses of vaccines are recommended for individuals aged 15 years and above	41 (16.0)
Knew that 3 doses of vaccines are recommended for immune-compromised individuals	27 (10.5)
Knew that HPV vaccines cannot treat women who have developed HPV related disease	104 (40.6)
Knowledge grading	
Good	19 (7.4)
Poor	237 (92.6)

HPV: Human papillomavirus

Table 5: Distribution of respondents' knowledge of HPV infection and vaccination by their sociodemographic characteristics

Sociodemographic variables	Knowledge of HPV infection and vaccination			
	Knowledge of HPV infection n=256		Knowledge of HPV vaccination n=256	
	Good n (%)	Poor n (%)	Good n (%)	Poor n (%)
Age (years)				
<40	84 (54.2)*	71 (45.8)	15 (9.7)	140 (90.3)
40 and above	38 (37.6)	63 (62.4)	4 (4.0)	97 (96.0)
	$\chi^2=6.731, P=0.009$		$\chi^2=2.909, P=0.088$	
Marital status				
Single, separated, and widowed	26 (54.2)	22 (45.8)	0 (0)	48 (100.0)
Married	96 (46.2)	112 (53.8)	19 (9.1)*	189 (90.9)
	$\chi^2=1.004, P=0.316$		$\chi^2=4.736, P=0.030$	
Religion				
Islam	92 (51.4)	87 (48.6)	15 (8.4)	164 (91.6)
Christianity	30 (39.0)	47 (61.0)	4 (5.2)	73 (94.8)
	$\chi^2=3.338, P=0.068$		$\chi^2=0.795, P=0.373$	
Level of education				
Diploma and associate	36 (37.1)	61 (62.9)	0 (0)	97 (100.0)
Bachelor and post-graduate	86 (54.1)*	73 (45.9)	19 (11.9)*	140 (88.1)
	$\chi^2=6.959, P=0.008$		$\chi^2=12.520, P<0.001$	
Cadre				
Doctors	43 (87.8)*	6 (12.2)	18 (36.7)*	31 (63.3)
Nurses and others	79 (38.2)	128 (61.8)	1 (0.5)	206 (99.5)
	$\chi^2=39.061, P<0.001$		$\chi^2=0.75.781, P<0.001$	
Length of practice				
<10	66 (54.5)*	55 (45.5)	6 (5.0)	115 (95.0)
≥10	56 (41.5)	79 (58.5)	13 (9.6)	122 (90.4)
	$\chi^2=4.366, P=0.037$		$\chi^2=2.026, P=0.115$	

*Statistically significant. HPV: Human papillomavirus

Table 6: Predictors of good knowledge of HPV infection and vaccination among the respondents

Variables	Adjusted odds ratio	95% CI		P value
		Lower	Upper	
Knowledge of HPV infection				
Age (below 40 versus 40 years and above)	1.477	0.684	3.191	0.320
Education level (diploma and associate versus bachelor and post-graduate)	0.859	0.487	1.516	0.601
Cadre (doctors versus nurses and others)*	11.674*	4.566	29.850	<0.001
Length of practice (below 10 versus 10 years and above)	1.547	0.732	3.268	0.253
Knowledge of HPV vaccination				
Marital status (single, separated, and widowed versus married)	0.000	0.000		0.997
Education level (diploma and associate versus bachelor and post-graduate)	0.000	0.000		0.996
Cadre (doctors versus nurses and others)	72.857*	9.198	577.114	<0.001

*Statistically significant, CI: Confidence interval, HPV: Human papillomavirus

as compared to those with diploma or associate degree (0%), and doctors (36.7%) as compared to nurses and those in the other cadres (0.5%) as shown in Table 5. In multivariate logistic regression analysis, the only predictor of good knowledge of HPV vaccination among the respondents was their cadre. Being a doctor was associated with a 72.857 fold (aOR: 72.857, 95% CI: 9.198–577.144, $P < 0.001$) greater likelihood of having good knowledge of HPV vaccination [Table 6]

Respondents' Risk Perception of HPV Infection and Practices Regarding HPV Vaccination

Whereas majority, 141 (55.1%) of the 256 respondents perceived themselves to be at risk of HPV infection, only a few of them have ever had HPV vaccination (2.3%) or had the vaccine administered to their adolescent daughters (2.3%). The main reasons cited for not accepting HPV vaccination were non-availability of the vaccines (47.2%) and lack of awareness (24.8%). Other reasons cited for not accepting HPV vaccination are as shown in Table 7. Only 31 (12.1%) of the 256 respondents have ever recommended HPV vaccination to their clients or their friends/neighbors' adolescent daughters. There was no association between uptake

Table 7: Respondents' risk perception of HPV infection and practices regarding HPV vaccination

Variables	Frequency (%)
Perceived self at risk of HPV infection (n=256)	
Yes	141 (55.1)
No	115 (44.9)
Have ever had HPV vaccination (n=256)	
Yes	6 (2.3)
No	250 (97.7)
Have ever had HPV vaccine administered to adolescent daughters (n=256)	
Yes	6 (2.3)
No	250 (97.7)
Main reason for not accepting HPV vaccination (n=250)	
Not aware of the vaccine	62 (24.8)
Vaccine is not available	118 (47.2)
Fear of adverse reaction	15 (6.0)
I am too old to take the vaccine	37 (14.8)
Daughter is not of age	12 (4.8)
No felt need	6 (2.4)
Have ever recommended HPV vaccination to their clients or their friends/neighbors' adolescent daughters (n=256)	
Yes	31 (12.1)
No	225 (87.9)

HPV: Human papillomavirus

of HPV vaccination and any of the respondents' sociodemographic variables.

DISCUSSION

This study assessed the knowledge of HPV infection and vaccination, and practices regarding HPV vaccination among female health-care professionals in Sokoto, Nigeria. Although awareness of HPV infection was high among the respondents in this study (91.8%), similar to the finding in studies conducted among health-care professionals in other centers in Nigeria,^[10,21] less than half of them (47.7%) have good knowledge of it. This is of serious concern considering the high burden of cervical cancer in Nigeria, with an estimated 14,089 new cases and 8240 deaths from the disease each year; and the fact that health-care professionals cannot educate their patients and clients on HPV infection and its prevention if they lack adequate knowledge of its transmission.

Considering the high prevalence of HPV infection and cervical cancer in Nigeria, and the absence of any specific drug treatment for the virus, the documented high potency of HPV vaccination in preventing cervical cancer is reassuring, as it is known to prevent up to 95% of cervical cancers.^[5] The low level of good knowledge of HPV vaccination (7.4%) among the respondents in this study, in which only about a fifth and less of them (9.0-22.7%) knew the 3 prophylactic HPV vaccines (bivalent,

quadrivalent, and nanovalent), about half (51.2%) knew that it is recommended for both males and females, and less than a fifth (16.0%) knew the recommended doses for the subgroups of those eligible for HPV vaccination, therefore, constitutes a serious threat to the prevention and control of HPV infection and cervical cancer in the study area.

The worrisome aspect is the fact that reports from studies conducted among medical students in sub-Saharan Africa suggest that sufficient attention was not given to the prevention and control of HPV infection and cervical cancer in their training curriculum, despite the high burden of cervical cancer across the continent. A study conducted among female medical and dental students in a tertiary institution in Benin City, Nigeria, reported that only about a third of respondents (31.2%) had good knowledge of HPV infection and vaccination.^[22] Another study conducted at the Mulago Hospital, Uganda,^[23] reported that only 14% of final year medical students felt skilled enough to perform speculum examination of the vagina, and 87% of them had never performed a Pap smear (to screen for cervical cancer). These findings confirm the multidimensional challenges facing cervical cancer prevention across sub-Saharan Africa, as students graduate from the medical schools with poor knowledge of HPV infection and vaccination, insufficient skills on cervical cancer screening, and inadequate promotion of cervical cancer prevention practices among their clients and patients when they start practicing. It is therefore necessary for the training institutions to review their curricula to address these deficiencies, while the Management of the Healthcare Facilities should organize periodic continuing medical education programs for their staff to enable them effectively prevent and control the prevalent diseases in their respective communities. The need for these interventions is further supported by the finding in this study, in which being a doctor was the sole predictor of good knowledge of HPV infection and vaccination among the respondents, with doctors having an 11.674 fold, and a 72.857 fold greater likelihood of having good knowledge of HPV infection and vaccination, respectively, as compared to the other cadres of staff; and it could be related to the depth of the medical training curricula (both undergraduate and post-graduate), and their practice environment that involves continuous in-service training (at the ward rounds, seminars, mortality reviews, etc.).

The very low uptake of HPV vaccination (2.3%) among the respondents in this study, with the main reasons cited being non-availability of the vaccines (42.7%) and lack of awareness (24.8%), essentially reflects the situation across sub-Saharan Africa. A systematic review

of the knowledge and awareness of HPV vaccine and acceptability to vaccinate in sub-Saharan Africa revealed high levels of willingness and acceptability of HPV vaccine but low levels of knowledge and awareness of cervical cancer.^[24] An international comparison of HPV infection and vaccination showed higher levels of HPV awareness among men and women in the United States of America, than the United Kingdom and Australia. In addition, implementation of vaccination programs, availability of HPV vaccines, and their promotion by the pharmaceutical companies varied across the countries, and this was believed to be responsible for the higher levels of awareness of the vaccines in the United States as compared to the other countries.^[25]

The poor awareness and uptake of HPV vaccines by the respondents in this study could be responsible for the low proportion (12.1%) of those that had recommended it to their clients or friends/neighbors' adolescent daughters. Similar to the finding in this study, a nationwide survey among primary care pediatrician in Italy reported poor implementation of the WHO's guideline to recommend HPV vaccines to boys and girls aged 9–14 years; while most of the respondents (77.4%) always recommend the vaccine to 11–12 year old girls, only 18.4% of respondents always recommend it to 11–12 year old boys.^[26] The findings of this study underscore the need for Government and the Management of Health Institutions to organize periodic training of health-care professionals on the strategies for preventing the transmission of HPV infection and also make HPV vaccines consistently accessible to the target population.

CONCLUSION

This study showed suboptimal knowledge of HPV infection and low levels of knowledge and uptake of HPV vaccination among the respondents. Government and the Management of Health Institutions should organize periodic training of health-care professionals on the strategies for preventing the transmission of HPV infection and also make HPV vaccines consistently accessible to the target population.

ACKNOWLEDGMENTS

The authors appreciate the Management of the Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria, and Maryam Abacha Women and Children Hospital, Sokoto, Nigeria, and all the female health-care professionals that participated in the study for their cooperation.

REFERENCES

1. Bruni L, Diaz M, Castellsague X, Ferrer E, Bosch FX, de Sanjose S. Cervical human papillomavirus prevalence in 5 continents: Meta-analysis of 1 million women with normal cytological findings. *J Infect Dis* 2010;202:1789-99.
2. Bosch FX, Lorincz A, Munoz N, Meijer CJ, Shah KV. The causal relation between human papillomavirus and cervical cancer. *J Clin Pathol* 2002;55:244-65.
3. World Health Organization (WHO). Human papillomavirus vaccines WHO position paper May 2017. *Weekly Epid Records* 2017;92:241-68. Available from: <http://www.apps.who.int/iris/bitstream/handle/10665/255353/WER9219.pdf?sequence=1>. [Last accessed on 2018 Jul 11].
4. Jedy-agba EE, Dareng EO, Adebamowo SN, Odutola M, Oga EA, Igbinoaba F, *et al*. The burden of HPV associated cancers in two regions in Nigeria 2012-2014. *Cancer Epid* 2016;45:91-97.
5. Tran NP, Hung CF, Roden R, Wu TC. Control of HPV infection and related cancers through vaccination. *Recent Results Cancer Res* 2014;193:149-71.
6. Sait KH. Knowledge attitude and practice regarding cervical cancer screening among physicians in the western region of Saudi Arabia. *Saudi Med J* 2011;32:1155-60.
7. Chawla PC, Chawla A, Chaudhary S. Knowledge, attitude and practice on human papillomavirus vaccination: A cross-sectional study among healthcare providers. *Indian J Med Res* 2016;144:741-49.
8. Mojaheed S, Zarchi MK, Bokaie M, Salimi T. Attitude and knowledge of Iranian female nurses about human papillomavirus infection and cervical cancer: A cross-sectional survey. *J Prev Med Hyg* 2013;54:187-90.
9. Goi I, Erkin O. Knowledge and practices of nurses on cancer prevention, HPV and HPV vaccine in Cankiri State Hospital, Turkey. *J Pak Med Assoc* 2016;66:1621-6.
10. Shand L, Burney S, Fletcher J. Knowledge of cervical cancer, pap testing and the human papillomavirus among young Australian women. *Health Prom J Austr* 2010;21:202-7.
11. Kamzol W, Jaglarz K, Tomaszewski KA, Puskulluoglu M, Krzemieniecki K. Assessment of knowledge about cervical cancer and its prevention among female students aged 17-26 years. *Eur J Obs Gynecol Reprod Biol* 2013;166:196-203.
12. Xu C, Zhang W, Wu M, Zhang S. Knowledge of cervical cancer among 25-54 year old women in Beijing. *J Cancer Educ* 2011;26:555-9.
13. Siddhartar J, Rajkumar B, Deivasigamani K. Knowledge, awareness and prevention of cervical cancer among women attending a tertiary care hospital in Puducherry, India. *J Clin Diag Res* 2014;8:OC01-3.
14. Almobarak AO, Elbadawi AA, Elmadhoun WM, Elhoweris MH, Ahmed MH. Knowledge, attitude and practice of Sudanese women regarding the pap smear test and cervical cancer. *Asian Pac J Canc Prev* 2016;17:625-30.
15. Eni AO, Soluade MG, Efekemo OP, Igwe TT, Onile-ere OA. Poor knowledge of human papilloma virus and vaccination among respondents from three Nigerian State. *J Comm Health* 2018;1-7.
16. Ezenwa BN, Balogun MR, Okafor IP. Mothers' human papillomavirus knowledge and willingness to vaccinate their adolescent daughters in Lagos Nigeria. *Int J Women's Health* 2013;5:371-7.
17. Oche MO, Kaoje AU, Gana G, Ango JT. Cancer of the cervix and cervical screening: Current knowledge, attitude and practices of female health workers in Sokoto, Nigeria. *Int J Med Med Sci* 2013;5:184-90.
18. Araoye MO. *Research Methodology with Statistics for Health and Social Sciences*. 2nd ed. Ilorin, Nigeria: Nathadex Publishers; 2004.
19. Egwu EO, Obi SN, Ezechukwu PC, Okafor II, Ugwu AO. Acceptability of human papilloma virus vaccine and cervical cancer screening among female healthcare workers in Enugu Southeast Nigeria. *Nig J Clin Pract* 2013;16:249-52.
20. Audu B, Bukar M, Ibrahim A, Swende T. Awareness and perception of human papilloma virus vaccine among healthcare professionals in Nigeria. *J Obs Gynecol* 2014;34:714-7.
21. Makwe C, Anorlu R. Knowledge of and attitude towards human papillomavirus infection and vaccines among female nurses at a tertiary hospital in Nigeria. *Int J Women's Health* 2011;3:313-7.
22. Onowhakpor AO, Omuemu VO, Osagie OL, Odili CG. Human papilloma virus vaccination: Knowledge attitude and uptake among female medical

- and dental students in a tertiary institution in Benin-City Nigeria. *J Comm Med Prim Health Care* 2016;28:101-8.
23. Mutyaba T, Mmiro FA, Weiderpass E. Knowledge, attitude and practices on cervical cancer screening among the medical workers of Mulago Hospital Uganda. *BMC Med Educ* 2006;6:13.
 24. Perlman S, Wamai RG, Bain PA, Welty T, Welty E, Ogembo JG. Knowledge and awareness of HPV vaccine and acceptability to vaccinate in sub-Saharan Africa: A systematic review. *PLoS One* 2014;9.
 25. Marlow LA, Zimet GD, McCaffery KJ, Ostini R, Waller J. Knowledge of human papillomavirus (HPV) and HPV vaccination: An international comparison. *Vaccine* 2013;31:763-9.
 26. Napolitano F, Navaro M, Vezzosi L, Santagati G, Angelillo IF. Primary care pediatricians attitudes and practice towards HPV vaccination: A nationwide survey in Italy. *PLoS One* 2018;13.

How to cite this article: Hassan M, Awosan KJ. Knowledge of Human Papillomavirus Infection and Vaccination, and Practices Regarding Human Papillomavirus Vaccination among Female Health-care Professionals in Sokoto, Nigeria. *Int J Sci Stud* 2018;6(5):62-70.

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

Transvaginal Sonographic Measurement of Cervical Length during Midtrimester in Predicting Preterm Labor in Asymptomatic Singleton Pregnancies

Mahalakshmi Aravazhi¹, Madhumitha Chandrasekaran², Deepak Chandrasekaran³

¹Senior Assistant Professor, Department of Obstetrics and Gynaecology, Government Theni Medical College, Theni, Tamil Nadu, India, ²Junior Resident, Department of Obstetrics and Gynecology, Government Theni Medical College, Theni, Tamil Nadu, India, ³Department of Obstetrics and Gynaecology, Peregrine Cancer Cure Technologies, Bangalore, Karnataka, India

Abstract

Introduction: Preterm delivery is a significant obstetric problem worldwide due to various complications in the newborn in its neonatal period and throughout lifetime. Cervical length is considered as a definitive predictor of preterm labor. Transvaginal sonography (TVS) can detect cervical length shortening earlier and more accurately than digital assessment. Based on this idea, this study is being undertaken to assess the bearing of cervical length measured by TVS at 18–24 weeks gestation on the outcome of pregnancy.

Aims: The aims are as follows: (1) To establish the relationship between cervical length at mid-trimester in uncomplicated singleton pregnancies and time of delivery, (2) To assess the potential value of routine cervical length measurement in singleton pregnancy between 18 and 24 weeks in the prediction of risk for early spontaneous preterm delivery

Materials and Methods: Study design: This was a prospective case–control study, (1) Study period: The study period was from July 2016 to December 2017 (18 months), (2) Place of study: The study was conducted at the Department of Obstetrics and Gynecology, GTMCH, (3) Study population: All booked cases between 18 and 24 weeks of gestation attending GTMCH who are willing to participate in the study, (4) Sample size: The sample size was 200. Inclusion criteria: All singleton pregnancies who have correct dates (reliable LMP in the background of the regular menstrual cycle [or] ultrasonography dating in the 1st trimester), between 18 and 24 weeks of gestation. Exclusion criteria: Not willing to participate in the study, multiple gestation, polyhydramnios, iatrogenic termination of pregnancy, and patients who missed follow-up.

Results: Out of 200 antenatal women upon whom the study was conducted, majority were multigravida which accounts to 79.59%. Out of 200 patients studied, 41 cases had short cervix which constitutes 20.5% of the population and Out of 41 patients with cervical length less than 25mm, around 25 patients delivered preterm. There were 28 NICU admissions out of 43 preterm deliveries. There were 28 NICU admissions of 43 preterm deliveries.

Conclusion: Preterm delivery and its effect on perinatal and neonatal morbidity and mortality is a global issue which needs significant attention among health-care personnel. Transvaginal sonographic determination of cervical length in women with asymptomatic singleton pregnancy is both cost-effective and has good validity as an effective screening test.

Key words: Antenatal, Cervical Length, Preterm, Short Cervix

INTRODUCTION

Preterm birth is defined as birth between the age of viability and 37 completed weeks of gestation. Incidence of preterm birth ranges between 5% and 21% in India.

Preterm birth is the leading cause of perinatal mortality and morbidity worldwide. As compared to term babies, premature babies have increased morbidity due to organ system immaturity. Preterm birth contributes 75% of neonatal death based on observations worldwide, genital and urinary tract infections, and cervical insufficiency plays a major role in the occurrence of spontaneous preterm labor.

Numerous clinical and biochemical tests were studied for the prediction of preterm labor including patient demographics, cervical length measurement, fetal

Access this article online



www.ijss-sn.com

Month of Submission : 06-2018
Month of Peer Review : 07-2018
Month of Acceptance : 08-2018
Month of Publishing : 08-2018

Corresponding author: Madhumitha Chandrasekaran, Junior Resident, Department of Obstetrics and Gynecology, Government Theni Medical College, Theni, Tamil Nadu, India. E-mail: itzdrmadhu@gmail.com

fibronectin tests, and microbial screening. Transvaginal sonographic measurement of cervical length is the best available method in the prediction of spontaneous preterm birth.

Aim and Objectives

The objectives are as follows:

1. To determine cervical length by transvaginal sonography in asymptomatic singleton pregnancies between 18 and 26 weeks of gestation.
2. To establish the relationship between cervical length measured at mid-trimester and their time of delivery.
3. To assess the potential value of routine cervical length measurement in singleton pregnancy between 18 and 26 weeks in the prediction of risk for preterm delivery.

MATERIALS AND METHODS

- Study design: This was a prospective observational study
- Study place: The study was conducted at Government Theni Medical College and Hospital
- Sample size: The sample size was 200.

Inclusion Criteria

The following criteria were included in the study:

1. Asymptomatic antenatal women between 18 and 26 weeks gestation who have registered before 16 weeks of gestation with known LMP.
2. Antenatal women between 18 and 26 weeks gestation with one of the following high-risk factors:
 - History of threatened abortion in present pregnancy
 - Previous first-trimester abortions
 - Previous second-trimester abortion
 - History of preterm birth is included
 - Second gravida with an interpregnancy interval of <1 and hour years or more than 5 years
 - Evidence of infections like urinary tract infections/ bacterial vaginosis/periodontal disease

Exclusion Criteria

The following criteria were excluded from the study:

1. Multiple pregnancy
2. Congenital fetal anomaly
3. Polyhydramnios
4. Iatrogenic preterm birth due to severe preeclampsia, intrauterine fetal growth restriction, etc.
5. Patients who did not come for follow-up at GTMCH.

Methodology

The patients coming under inclusion criteria are explained about the study and consent for the same obtained. Using

transvaginal ultrasound, cervical length is measured, and they are asked to come for follow-up after 3–4 weeks. If cervical length is more than 25 mm, these patients are not subjected to further follow-up scan and their gestation age at delivery and mode of delivery are noted. If the length is <25 mm, follow-up scan up to 28 weeks is done, and the patients are followed up until delivery.

RESULTS

Among these 200 study population, 100 were without any high-risk factors for preterm delivery, and 100 were with high-risk factors for the same. Of 200 antenatal women, majority were multigravida which accounts to 79.59% and primigravida were accounting to 20.59% [Table 1].

Of 200 cases, 21.5% delivered before 37 weeks of gestation and 78.5% delivered at term [Table 2] of 41 primigravidas, 9 mothers delivered preterm babies whereas 32 mothers delivered term babies. Among 159 multigravidas, 34 delivered preterm and 125 delivered term [Table 3]. Of 200 study population, 96 were belonging to 21–24 years age group [Table 4] about 8 deliveries of 12 in teenage pregnancies resulted in preterm delivery (66.67%) followed by 23.95% and 23.07% in 21–24 and 25–29 age groups, respectively. Only 12.5% of the deliveries were preterm in women more than 35 years of age [Table 5].

Out of 200 patients studied, 41 cases had short cervix which constitutes 20.5% of the population, and 159 patients had cervical length more than 25 mm (79.5%) [Table 6].

Table 1: Distribution of study population based on parity (n=200)

Parity	n (%)
Primigravida	41 (20.5)
Multigravida	159 (79.5)

Table 2: Distribution of study population based on gestational age at delivery (n=200)

Gestational age	n (%)
Preterm	43 (21.5)
Term	157 (78.5)

Table 3: Relationship between parity and gestational age at delivery (n=100)

Parity	Preterm	Term
Primigravida	9	32
Multigravida	34	125
Total	43	157

Of 41 patients with cervical length <25 mm, around 25 patients delivered preterm and 14 patients out of 32 who had cervical length between 26 and 30 mm delivered preterm [Table 6].

In Table 7, the number of patients with a short cervix and their outcome versus number of patients with cervical length of more than 25 mm and their pregnancy outcome were given. The results showed that the sensitivity of this test is 58% and specificity is 89%. The efficiency of the test is 83%, and positive predictive value is 60%, negative predictive value is 89%, false positive rate is 10%, and false negative rate is 42%, Kappa agreement is moderate agreement. The mean cervical length is 32.35 mm, and standard deviation is 6.83. The mean gestational age at delivery is 38.28 weeks, and standard deviation is 2.03 (Tables 7a and 7b). P value of transvaginal ultrasound measurement of cervical length in the prediction of preterm labor in asymptomatic singleton pregnancy is 0.001 which is significant.

In Table 8, there were 28 NICU admissions of 43 preterm deliveries and 20 NICU admissions among 153 term babies [Table 8 and Charts 1-7].

Table 4: Age distribution of study population (n=200)

Age (years)	n (%)
<20	12 (6)
21-24	96 (48)
25-29	71 (35.5)
30-34	13 (6.5)
≥35	8 (4)

Table 5: Distribution of study population based in age and its relationship to preterm delivery (n=200)

Age (years)	n	Preterm	Percentage
≤20	12	8	66.67
21-24	96	23	23.95
25-29	71	8	11.26
30-34	13	3	23.07
≥35	8	1	12.5

Table 6: Distribution of study population based on cervical length (mm) and gestational age at delivery (n=200)

Cervix length (mm)	Number of cases	Preterm	Percentage
<25	41	25	60.97
26-30	32	14	43.75
31-35	43	2	4.65
36-40	70	2	2.85
>40	14	0	0

DISCUSSION

In our study including 200 antenatal women, about 12 patients were less than 20 years old and 8 out of 12 teenage pregnancies resulted in preterm deliveries which constitutes 66.67% This result showing teenage pregnancy as an independent risk factor for preterm delivery is comparable to the study result conducted by Athena JMG Crane1 al, Mukherji *et al.*^[5] which also establishes teenage as risk for preterm delivery.

In our study including 200 antenatal cases, 41 cases were identified to be having short cervix and 25 of them had preterm delivery which constitutes 60.97%. there is increased chance of preterm labour in patients having cervical length between 26 mm-30 mm which constitutes 43%. These results were comparable to the study conducted by Brien *et al.*^[2] which also gives a positive association between short cervix and occurrence of preterm delivery.

Table 7: Relationship between cervical length in mm and gestational age at delivery among study population (n=200)

Cervical length (mm)	Preterm	Term	Total
<25	25 (a)	16 (b)	41
>25	18 (c)	141 (d)	159

Table 7a: Statistical parameters

Parameters	Estimate (%)	95% CI
Sensitivity	58	42-73
Specificity	89	84-94
Efficiency	83	77-88
False positive rate	10	6-17
False negative rate	42	27-58
Positive predictive value	60	44-76
Negative predictive value	89	83-93
Kappa agreement	κ=0.49	Moderate agreement

Table 7b: Correlation of cervical length with gestational age at delivery

Variables	Cervical length (mm)	Gestational age (weeks)
Mean	32.35	38.28
SD	6.38	2.03
P value	r=0.10<0.001 significant	

Table 8: Gestational age versus NICU admission

GA	Total	NICU admission
Preterm	43	28
Term	153	20

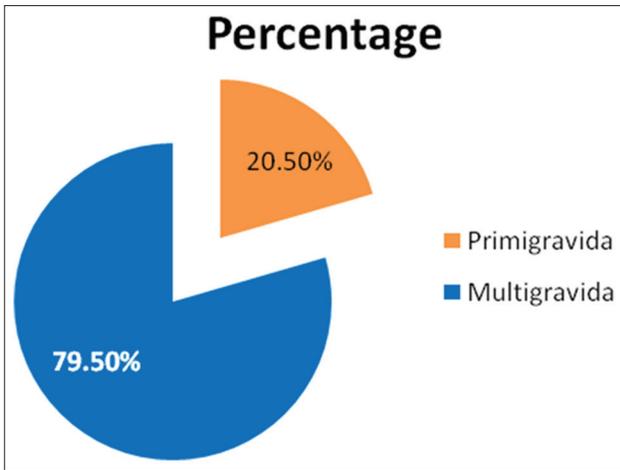


Chart 1: Distribution of study population based on parity

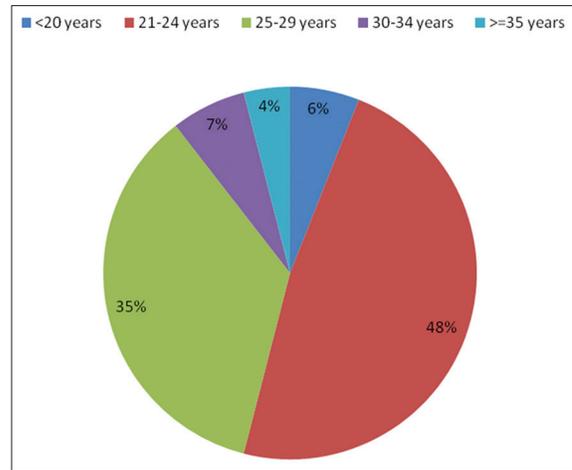


Chart 4: Age distribution of study population, n = 200

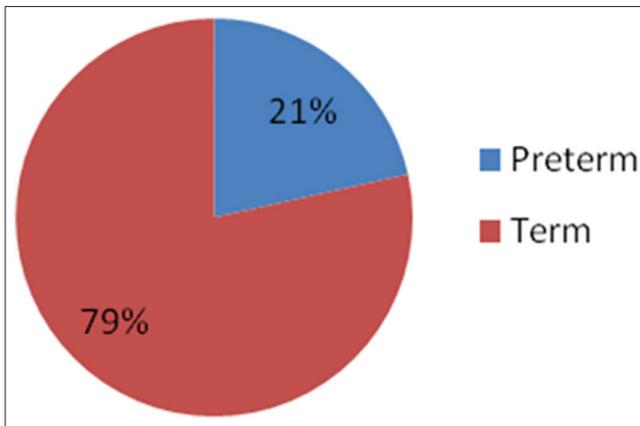


Chart 2: Distribution of study population based on gestational age at delivery. n=200

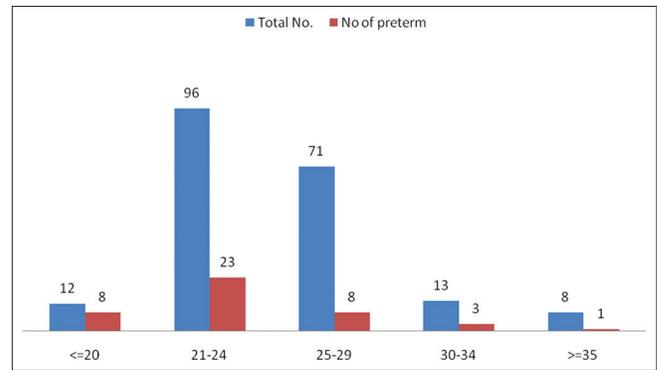


Chart 5: Distribution of study population based on age and relationship to preterm delivery

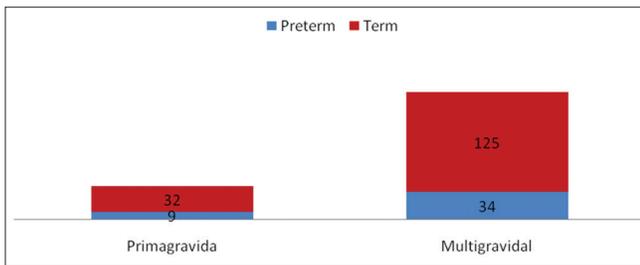


Chart 3: Relationship between parity and gestational age at delivery

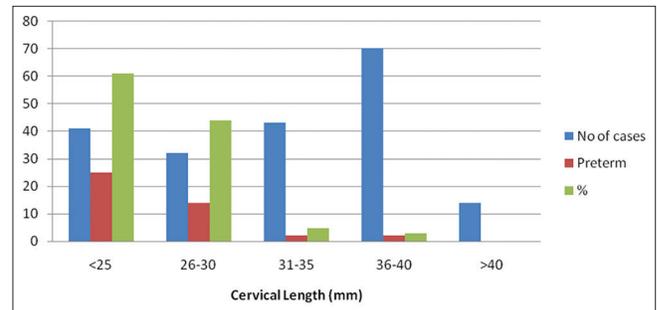


Chart 6: Cervical length (mm) versus gestational age at delivery

In asymptomatic women with singleton gestation, transvaginal measurement of cervical length with cut off of 25 mm has 58% sensitivity (present study) in predicting preterm labour (<37 weeks) which is comparable to study by Airoldi *et al.*^[3]

Specificity of TVS measurement of cervical length with 25mm cutoff in predicting preterm labour in present study was 89% which was comparable to other studies like J. Visintine *et al.*^[4]

Preterm delivery and its effect on perinatal and neonatal morbidity and mortality is a global issue which needs significant attention among health care personnel. prediction of preterm labour by suitable effective and reliable method is a boon to save innumerable young lives. By reducing preterm deliveries, we can manage huge economic ,medical and social burden on the country as well as the globe.

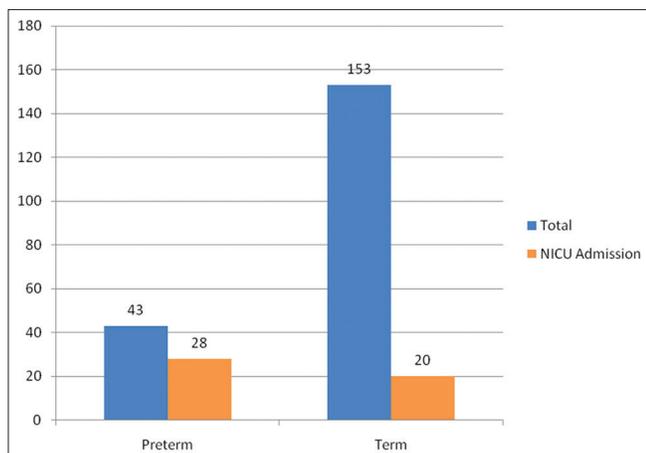


Chart 7: Relationship between gestational age at delivery and NICU admission

REFERENCES

1. Crane JM, Hutchens D. Use of transvaginal ultrasonography to predict preterm birth in women with a history of preterm birth. *Ultrasound Obstet Gynecol* 2008;32:640-5.
2. Conde-Agudelo A, Rosas-Bermúdez A, Kafury-Goeta AC. Birth spacing and risk of adverse perinatal outcomes: A meta-analysis. *JAMA* 2006;295:1809-23.
3. O'Brien JM, DeFranco EA, Adair CD, Lewis DF, Hall DR, How H, *et al.* Effect of progesterone on cervical shortening in women at risk for preterm birth: Secondary analysis from a multinational, randomized, double-blind, placebo-controlled trial. *Ultrasound Obstet Gynecol* 2009;34:653-9.
4. Airoidi J, Berghella V, Sehdev H, Ludmir J. Transvaginal ultrasonography of the cervix to predict preterm birth in women with uterine anomalies. *Obstet Gynecol* 2005;106:553-6.
5. Visintine J, Berghella V, Henning D, Baxter J. Cervical length for prediction of preterm birth in women with multiple prior induced abortions. *Ultrasound Obstet Gynecol* 2008;31:198-200.
6. Mukherji J, Anant M, Ghosh S, Bhattacharyya SK, Hazra A, Kamilya GS, *et al.* Normative data of cervical length in singleton pregnancy in women attending a tertiary care hospital in eastern India. *Indian J Med Res* 2011;133:492-6.

How to cite this article: Aravazhi M, Chandrasekaran M. Transvaginal Sonographic Measurement of Cervical Length during Midtrimester in Predicting Preterm Labor in Asymptomatic Singleton Pregnancies. *Int J Sci Stud* 2018;6(5):71-75.

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

Clinical Profile and Visual Outcome of Ocular Injuries Presenting to Tertiary Care Hospital Located on a State Highway

M Sunil Kumar¹, D Vishwas²

¹Senior Resident, Department of Ophthalmology, Raja Rajeswari Medical College, Bengaluru, Karnataka, India, ²Junior Resident, Department of Ophthalmology, Raja Rajeswari Medical College, Bengaluru, Karnataka, India

Abstract

Introduction: Ocular injury is a major cause of ocular morbidity and visual impairment worldwide.

Purpose: The purpose of this study is to identify the various types of ocular injury presented to our tertiary care center, to determine associated visual impairment, and to assess the visual outcome after treatment.

Materials and Methods: This was a hospital-based prospective study conducted over 1 year, and a total of 60 patients of ocular trauma were included in the study. All patients underwent eye examination including visual acuity, anterior segment examination, extraocular movements, intraocular pressure, and fundus examination.

Results: Ocular injuries were more commonly seen in middle-aged adults (43%). The most common mode of injury was road traffic accidents (RTA) (40%). 46.66% of the patients had visual acuity >6/60 at the time of presentation, while after complete treatment at the end of 6 weeks, 76.66% of patients had best-corrected visual acuity >6/60.

Conclusion: RTA is the most common cause of ocular injury presented to our institute as it is situated in a state highway that can be preventable, and the visual outcome depends on the site and size of the injury and the extent of the ocular damage.

Key words: Best-corrected visual acuity, Ocular injury, Road traffic accidents, State highway, Tertiary care center, Visual outcome

INTRODUCTION

Ocular trauma is one of the most common causes of ophthalmic morbidity and monocular blindness worldwide. They have a significant impact on an individual and society in terms of sufferings, medical cost, and loss of productivity.^[1] Of all types of ocular emergencies, ocular trauma is by far the most common constituting nearly 75%.^[2] It can be open globe or closed globe injuries.

In India, there are more than 50 million blind people and this number increases by about 3.8 million per year. Among

the total number of blind cases, 1.2% is contributed by injuries which are preventable.^[3] The WHO program for the prevention of blindness, indicated that there are approximately 55 million eye injuries per year that restrict activities for more than one day.^[4]

The aim of this study is to find the types of ocular injuries presented to our hospital nearby state highways frequently, the extent of visual impairment by these injuries, and the visual outcome after treatment.

MATERIALS AND METHODS

A Prospective cross-sectional study was conducted for 1 year (From December 2016-November 2017) including patients with ocular injuries reported to casualty and Ophthalmology OPD in Raja Rajeswari Medical College and Hospital, Bangalore.

Access this article online	
 www.ijss-sn.com	Month of Submission : 06-2018
	Month of Peer Review : 07-2018
	Month of Acceptance : 08-2018
	Month of Publishing : 08-2018

Corresponding Author: Dr. D Vishwas, Department of Ophthalmology, Raja Rajeswari Medical College and Hospital, Kambipura, Bengaluru, Karnataka, India. Phone: +91-9019923459. E-mail: vishwas00789@gmail.com

Inclusion Criteria

Patients with ocular injuries reported to our casualty and ophthalmology OPD were included in the study.

Exclusion Criteria

Patients with birth injuries, war injuries, ultrasonic injuries, and radiation injuries were not included in the study. A detailed workup of all patients including slit-lamp biomicroscope, direct and indirect ophthalmoscopy, intraocular pressure, color vision, and extraocular movements was done. B-scan ultrasonography was done where media prevent from fundus examination and to rule out retained intraocular foreign body. X-ray orbit and, in few cases, computed tomography (CT) orbit were also done.

The trauma cases were classified based on standardized Birmingham Eye Trauma Terminology, which was endorsed by the American Academy of Ophthalmology, International Society of Ocular Trauma, World Eye injury Registry, and the Vitreous and Retina societies.

The cases were managed on the basis of the guidelines given by the Eye Trauma Society. The visual outcome was recorded at the time of presentation, next day, after 1 week, and at the end of 6 weeks.

A record of pre- and post-treatment, clinical photographs of the patients is maintained. Frequency and percentage were calculated using bar diagram and pie chart for data presentation. The results so obtained are analyzed, discussed, and compared with the existing studies in the literature.

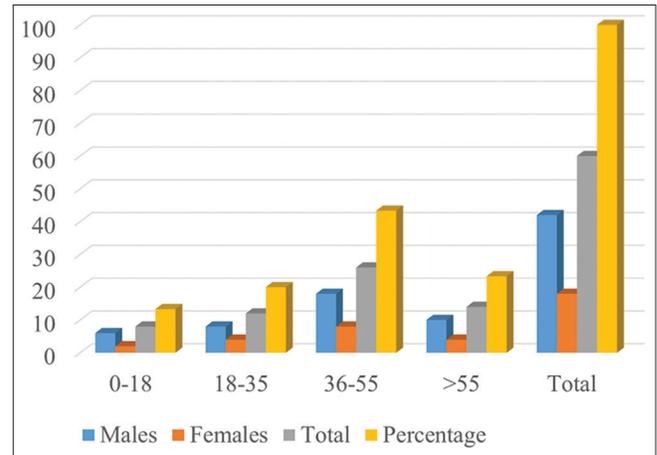
The injuries were classified into extraocular and intraocular. The intraocular injury was further classified into open and closed globe injury according to the Ocular Trauma Classification Scheme.

RESULTS

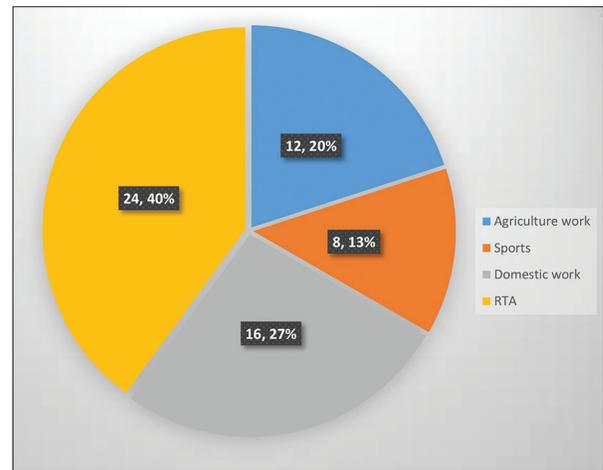
In our study, we found a higher incidence of ocular injuries in middle-aged males (36–55 years) (43.33%) [Table 1 and Graph 1]. Most common mode of injury was RTA (40%) followed by domestic work injury (26.66%) [Table 2 and Graph 2].

Closed globe injuries (80%) were more common than open globe injuries (20%) [Table 3 and Graph 3]. Conjunctiva was the commonly involved ocular structure (80%) followed by periorbital lesions (66.6%) [Table 4 and Graph 4]. Conjunctival chemosis was the most common conjunctival lesion (83.3%) followed by subconjunctival hemorrhage (79.16%) [Table 5 and Graph 5]. Periorbital

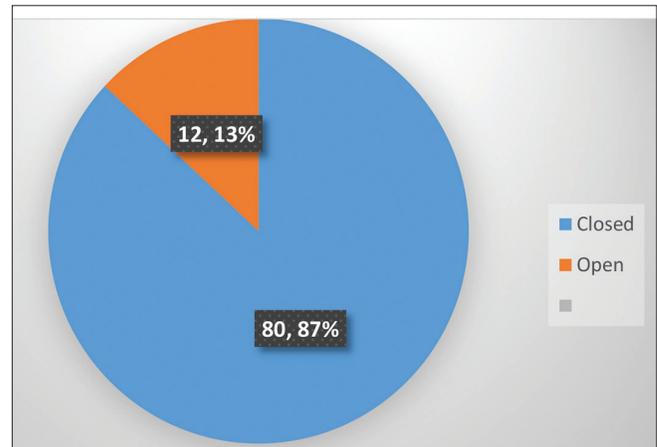
edema was the most common periorbital lesion (84.2%) [Table 6 and Graph 6].



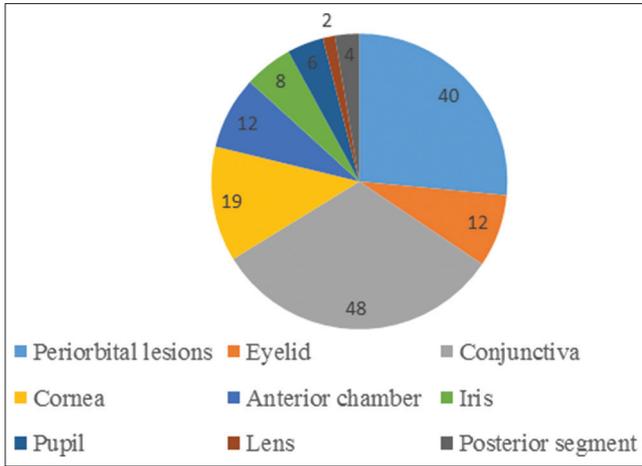
Graph 1: Our study showed that the highest incidence of ocular injuries was in the middle-aged adults (36–55 years). Furthermore, it is seen that ocular injuries are common in males compared to females



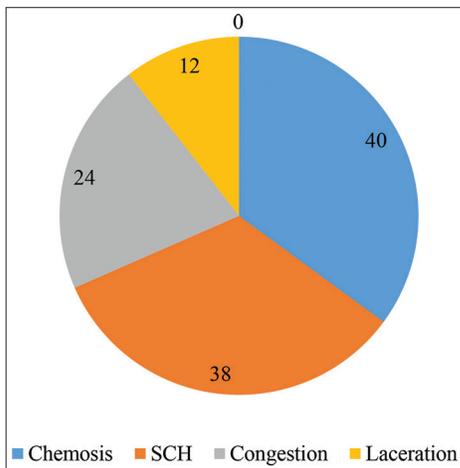
Graph 2: Our study showed that RTA-related ocular injuries was the most common mode of injury



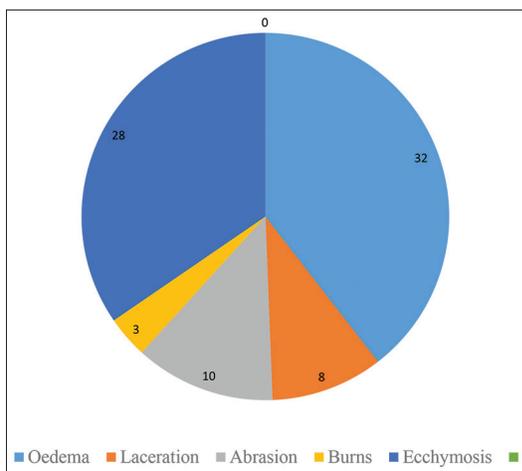
Graph 3: Our study showed that closed globe injuries were common than open globe injuries



Graph 4: Our study showed that conjunctiva was the commonly involved ocular structure



Graph 5: Our study showed that conjunctival chemosis was the most common conjunctival lesion



Graph 6: Our study showed that periorbital edema was the most common periorbital lesion

Our study showed that 46% had visual acuity better than 6/60 at presentation and 23% of patients presented with

Table 1: Our study showed that the highest incidence of ocular injuries was in the middle-aged adults (36–55 years). Furthermore, it is seen that ocular injuries are common in males compared to females

Age (years)	Males	Females	Total (%)
0–18	6	2	8 (13.33)
18–35	8	4	12 (20)
36–55	18	8	26 (43.33)
>55	10	4	14 (23.33)
Total	42	18	60 (100)

Table 2: Our study showed that RTA-related ocular injuries was the most common mode of injury

Mode of injury	Number of patients (%)
Agriculture work	12 (20)
Sports	8 (13.33)
Domestic work	16 (26.66)
RTA	24 (40)

RTA: Road traffic accident

Table 3: Our study showed that closed globe injuries were common than open globe injuries

Type of injury	Number of patients (%)
Closed	48 (80)
Open	12 (20)

Table 4: Our study showed that conjunctiva was the commonly involved ocular structure

Ocular structure	Number of patients (%)
Periorbital lesions	40 (66.6)
Eyelid	12 (20)
Conjunctiva	48 (80)
Cornea	19 (31.6)
Anterior chamber	12 (20)
Iris	8 (13.33)
Pupil	6 (10)
Lens	2 (3.33)
Posterior segment	4 (6.66)

visual acuity from 6/60 to 3/60. At 6 weeks' follow-up after treatment, 76% of patients had visual acuity better than 6/60. Four patients had just perception of light (PL) and 4 had no PL at the time of presentation. At the end of 6 weeks among 4 PL-positive patients, one of them improved to 2/60 of visual acuity.

DISCUSSION

Ocular trauma is an important cause of blindness and ocular morbidity. Most previous studies on the profile and prognostic factors in ocular trauma have been carried out

in more developed countries where modern facilities for managing ocular trauma are widely available.^[5]

There is a paucity of studies on the profile of ocular trauma from the less developed countries.^[6]

Hence, we conducted this study. The common injuries encountered in our study were as follows:

There was an increased incidence of ocular injuries in middle-aged adults (43%) with a male preponderance (70%). This study was in close relation with Ilisar *et al.*,^[7] Niiranen,^[8] and Jain *et al.*^[9] Male preponderance is seen because they are more frequently exposed to outdoor work compared to females. This was in correlation with Balaghafari *et al.*^[10] and Sharma *et al.*^[11] Ocular injury stands next to cataract and strabismus as a leading cause for hospitalization.^[12]

The most common cause of ocular injury was road traffic accident (RTA) (40%) presenting to our hospital as it is situated in a state highway. Enock *et al.*^[13] and Mowatt *et al.*^[14] found that motorcycle-related RTA was the most common cause of ocular injury.

Table 5: Our study showed that conjunctival chemosis was the most common conjunctival lesion

Conjunctiva lesions	Number of patients (%)
Chemosis	40 (83.3)
SCH	38 (79.16)
Congestion	24 (50)
Laceration	12 (25)

Table 6: Our study showed that periorbital edema was the most common periorbital lesion

Periorbital lesions	Number of patients (%)
Oedema	32 (84.2)
Laceration	8 (21.05)
Abrasion	10 (26.3)
Burns	3 (7.8)
Ecchymosis	28 (73.6)

Table 7: Visual acuity of patients at the time of presentation and at various follow-ups

Visual acuity	0 th day (%)	1 st day (%)	1 week (%)	6 weeks (%)
>6/60	28 (46.66)	32 (53.33)	40 (66.66)	46 (76.66)
6/60–3/60	14 (23.33)	11 (18.33)	7 (11.66)	4 (6.66)
3/60–1/60	10 (16.66)	9 (15)	5 (8.33)	2 (3.33)
PL present	4 (6.66)	4 (6.66)	4 (6.66)	3 (5)
No PL	4 (6.66)	4 (6.66)	4 (6.66)	4 (6.66)

In our study middle aged males were more frequently involved in driving vehicle owing to male preponderance. Ocular trauma due to road traffic accidents are preventable, this was in correlation with a study done in Northern Ireland in 1986 which found that there was 60% reduction in perforating eye injuries following seat belt legislation.^[14]

In our study we noted closed globe injuries (80%) were more common than open globe injuries (20%), which could be due to vehicular congestion causing slower moving traffic leading to lesser impact accidents. This was in correlation with the study done by Vasu *et al* who found that 38.10% were open globe injuries while 61.90% were closed globe injuries.^[15]

In our study, conjunctiva (80%) was the commonly involved ocular structure and this was in consistent with Pai *et al.*^[16] followed by periorbital lesions (66.6%). Conjunctival chemosis (83%) followed by subconjunctival hemorrhage (79%) [Figure 1] was frequent injuries in conjunctiva.

Periorbital edema [Figure 2] was the most common periorbital lesion seen in our study.

Patients with open globe injury were presented with a corneal tear with or without uveal tissue prolapse, traumatic cataract, corneoscleral tear, foreign body in anterior chamber, vitreous hemorrhage, retinal detachment [Figure 3], and intraocular foreign body.

Patients with closed globe injury were presented with full or partial thickness upper or lower lid tear, burns, conjunctival tear, subconjunctival hemorrhage, corneal lamellar laceration, corneal abrasions, hyphema, traumatic cataract, etc.

In our study, 48 (80%) patients were managed medically and the remaining 12 (20%) were managed surgically. Most of the patients showed improvement in vision after treatment. Four patients were severely injured came with no PL. Visual acuity at the time of presentation and on follow-up is shown in Table 7.

Factors associated with the final visual outcome were initial visual acuity, type, site, size of the injury, and extent of ocular damage.

In our study, we noticed that only few people use safety measures while driving. Panagiotidis *et al.* found that 5.2% of the car drivers were using seat belts and none of the two-wheeler accident victims had used helmets in their study.^[17] Schrader *et al.* in their study also observed that, despite compulsory seat belt legislation in Germany, majority of their study group had not worn their seat belts at the time



Figure 1: Sub conjunctival hemorrhage, ecchymosis



Figure 2: Periorbital edema

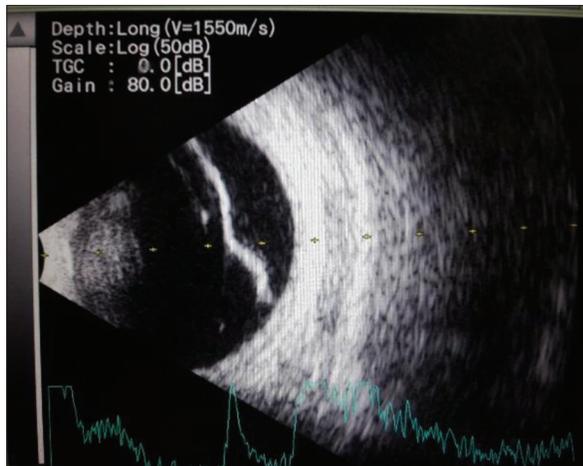


Figure 3: B-scan showing retinal detachment

of the accident.^[18] Schrader *et al.* also found that 50% of cases were inebriated at the time of accident. Probably a higher percentage of cases under the influence of alcohol would have been detected in our study if breath analysis

test or blood alcohol levels were done.

In our study most of the patients who were from poor economic background had less awareness regarding use of protective eye wear. This was comparable with the study done by Avinash Mishra *et al* (2014) who noted 5% wearing eye protection.^[18]

CONCLUSION

Ocular trauma is one of the most common causes of monocular blindness. Ocular injuries are more common in middle-aged adults seen more commonly in males. RTA is the most common cause of injury. Closed globe injuries are more common than open globe injuries. Conjunctiva is the most frequently injured structure.

Primary preventive approach such as promoting safe riding practices and strict implementation of traffic rules such as riding at safe speed, wearing seatbelts and helmet for head safety, and avoiding alcohol before driving is needed to prevent RTA and associated ocular morbidity.

Emphasizing the need to use eye protective measures among workers in industries and fireworks to prevent ocular injuries.

The impact of ocular trauma in terms of medical care, loss of income, and cost of rehabilitation services clearly highlight, the importance of preventive strategies.

REFERENCES

1. Sethi S, Khan MD. Childhood Ocular Trauma. J Postgrad Med Inst Peshawar 2011;15:51-5.
2. Park K. 17th.Ed. Park's Textbook of Preventive and Social Medicine. Jabalpur: Banarsidas Bhanot Publishers; 2002. p. 295-300.
3. Mowatt L, McDonald A, Ferron-Boothe D. Hospitalization trends in adult ocular trauma at the University Hospital of the West Indies. West Indian Med J 2012;61:605-9.
4. Esmaili B, Nanda SG, Schork A, Elner VM. Visual outcome and ocular survival after penetrating trauma. Ophthalmology 1995;102:393-400.
5. Saxena R, Sinha R, Purohit A, Dada T, Vajpayee RB, Azad RV. Pattern of pediatric ocular trauma in India. Indian J Pediatr 2002;69:863-67.
6. Ilsar M, Chirambo M, Belkin M. Ocular injuries in Malawi. Br J Ophthalmol 1982;66:145-8.
7. Niiranen M. Perforating eye injuries treated at Helsinki University Eye Hospital 1970-1977. Ann Ophthalmol 1981;13:957-61.
8. Jain BS, Soni SR. Ocular injuries: An analytical study in a teaching general hospital. Indian J Ophthalmol 1987;35:112-6.
9. Balaghafari A, Siamian H, Aligolbandi K. Ocular trauma: 2 years retrospective study in Sari, Iran. Mater Sociomed 2013;25:230-2.
10. Sharma AK, Aslami AN, Srivastava JP, Iqbal J. Visual outcome of traumatic cataract at a tertiary eye care centre in north India: A Prospective study. J Clin Diagn Res 2016;10:NC05-08.
11. Tielsch JM, Parver L, Shankar B. Time trends in the incidence of hospitalized ocular trauma. Arch Ophthalmol 1989;107:519-23.
12. Enock ME, Omoti AE, Alikah AA. Risk factors identification for ocular trauma in patients who presented in a suburban tertiary care hospital in

- Nigeria. Saudi Med J 2007;28:1385-8.
13. Johnston PB, Armstrong MF. Eye injuries in Northern Ireland two years after seat belt legislation. Br J Ophthalmol 1986;70:460-42.
 14. Schrader W, Gramer E, Gildmann F, Marcus U. Penetrating and perforating eye injuries in 343 patients due to auto accidents before and after compulsory seat belt legislation resulting in fines (1996-1998). Klin Monbl Augenheilkd 2000;217:23-9.
 15. Vasu U, Vasnaik A, Battu RR, Kurian M, George S. Occupational open globe injuries. Indian J Ophthalmol 2001;49:43-7.
 16. Pai SG, Kamath SJ, D'Souza S, Dudeja L. A Clinical study of blunt ocular trauma in a tertiary care centre. Online J Health Allied Sci 2013;12:10-3.
 17. Panagiotidis DN, Theodossiadis PG, Petsias CB, Kyriaki TE, Marakis TP, Friberg TR, *et al.* Ocular injuries secondary to motor vehicle accidents. Eur J Ophthalmol 2004;14:144-8.
 18. Mishra A, Parihar J, Verma A, Baranwal VK, Aggarwal S, Bhargava N. The pattern and visual outcomes of ocular trauma in a large zonal hospital in a non-operational role: A 36 months retrospective analysis. J Clin Ophthalmol Res 2014;2:141-4.

How to cite this article: : Kumar MS, Vishwas D. Clinical Profile and Visual Outcome of Ocular Injuries Presenting to Tertiary Care Hospital Located on a State Highway. Int J Sci Stud 2018;6(5):76-81.

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

Prevalence of Thrombophilia in Patients with Adverse Pregnancy Outcome

S Sooraj

Assistant Professor, Department of Obstetrics and Gynaecology, Government Medical College, Kozhikode, Kerala, India

Abstract

Background: Thrombophilia is hereditary and acquired conditions that predispose the patients to thrombosis. Pregnancy is hypercoagulable state. The tendency to thrombosis develops rapidly in adverse conditions in pregnancy and has been linked to many aspects of pregnancy. It is recently shown that severe pregnancy complications such as severe preeclampsia intrauterine growth retardation abruptio placentae and stillbirth have been shown to be associated with thrombophilia. Recurrent miscarriage has also been associated with thrombophilia. Finally, thromboembolism in pregnancy as in the non-pregnant state is linked to thrombophilia.

Aim of the Study: This study aims to study the prevalence of acquired and inherited thrombophilia in women with adverse pregnancy outcome (APO) and their diagnosis with the help of biological markers. The objective was also to study the incidence of each type of thrombophilia in patients with APO.

Materials and Methods: A total of 69 patients with a history of APO in previous pregnancies were included in this study to understand the prevalence of hemophilia in them. Various thrombophilic studies were undertaken using the blood samples of the patients. They included anticardiolipin antibodies test, lupus anticoagulant (LAC) test, protein C assay, protein S assay, activated protein C-resistant test, antithrombin assay, homocysteine estimation, prothrombin gene mutation test, anti- β -2 glycoprotein antibodies assay, Proglobal C assay, and factor V Leiden (FVL) mutation test. Based on the test results, the type of thrombophilia was diagnosed, analyzed, and compared with other studies.

Observations and Results: A total of 69 patients with a history of APO were screened for inherited and acquired thrombophilia. The patients were enrolled over a period of 2 years from July 2006 to June 2008 from the OPD at the Department of Obstetrics and Gynaecology, AIIMS, New Delhi. Recurrent abortion in 32 (58.18%) patients was the most common APO in women screened for thrombophilia. Other AOPs observed were intrauterine death of fetus (IUD) in 17 (24.63%), intrauterine growth retardation (IUGR) in 11 (15.94%), and severe preeclampsia in 9 (13.04%). The mean gravidity of the patients was 3.7 ± 1.25 . The mean gestation of the patients with recurrent abortion was 3.81 ± 0.86 , while that for patients with IUD was 3.41 ± 1.12 , with IUGR it was 4 ± 0.89 and preeclampsia it was 4.33 ± 0.87 . The thrombophilic tests were positive in 33/69 (47.82%) patients in the study, and among them, there were 8/69 (10.14%) patients with inherited thrombophilia in the present study. Protein C deficiency in 4 (5.79%) patients, hyperhomocysteinemia in 2 (2.89%), antithrombin III deficiency in 1 (1.44%), and FVL mutation in 1 (1.44%) patients each. 25 patients tested positive for Anti- β -2 glycoprotein antibodies, nine patients for ACL, and two for LAC.

Conclusions: Thrombophilia is common among patients with APO. Inherited thrombophilia is less common than the acquired ones. Biomarkers such as protein C deficiency, hyperhomocysteinemia, antithrombin III deficiency, and FVL mutation help to diagnose inherited type and treat these patients early. Among the acquired thrombophilia patients, anti- β -2 glycoprotein antibodies were positive as biomarker in majority of acquired type of thrombophilia. Other markers useful are anticardiolipin antibodies and deficient LAC.

Key words: Hypercoagulability, Inherited thrombophilia, Pregnancy, Thrombin assay, Thrombophilia

Access this article online



www.ijss-sn.com

Month of Submission : 06-2018
Month of Peer Review : 07-2018
Month of Acceptance : 08-2018
Month of Publishing : 08-2018

INTRODUCTION

The term thrombophilia was first introduced by Egerberg *et al.*, in 1965, when he reported a Norwegian family who had a remarkable tendency to venous thrombosis because of a deficiency in the natural anticoagulant antithrombin. At present, this term is generally used to describe a laboratory

Corresponding author: Dr. S Sooraj, Department of Obstetrics and Gynaecology, Government Medical College, Kozhikode, Kerala, India.
E-mail: drsoorajsaiims@gmail.com

abnormality (most often in the coagulation system) that increases the tendency to venous thromboembolism. Thrombophilic abnormalities can be acquired or inherited. Theoretically, the concept is that patients who have thrombophilia have an intrinsic prothrombotic state that in itself is insufficient to cause thrombosis, but may lead to an event when superimposed on (clinical) risk factors, including increasing age.^[1,2] There is a growing view that inherited and acquired thrombophilia may predispose to adverse pregnancy outcome (APO). As already known for the acquired antiphospholipid antibody syndrome, most inherited thrombophilic disorders are also associated with pregnancy-related disorders such as (recurrent) fetal loss, stillbirth, intrauterine growth restriction, preeclampsia, and the hemolysis-elevated liver enzyme-low platelets syndrome of pregnancy.^[3,4] Inherited thrombophilia types include antithrombin III deficiency, protein C deficiency, protein S deficiency, factor V Leiden (FVL) mutation, prothrombin 20210A mutation, and hyperhomocysteinemia. Antithrombin III, protein C, and protein S function as physiological inhibitors of coagulation cascade and are, therefore, referred to as natural anticoagulants. Deficiencies resulting in one of these proteins lead to an imbalance in basal coagulation activity toward a prothrombotic state. This has been confirmed in studies showing increased markers of thrombin generation in patients with one of these deficiencies.^[5,6] More recently, deficiency of protein Z has also been linked to pregnancy complications including preterm delivery. The FVL mutation is the most common inherited thrombophilic defect and is found in approximately 20% of patients who have venous thromboembolism (VTE) and in 5% of Caucasian population. It is a point mutation gene coding for clotting factor V (G1691 A), causing replacement of arginine by glutamine in the cleavage site for activated protein C (APC, Q), thereby making activated factor V more resistant to inactivation by this physiologic anticoagulant (APC resistance).^[7,8] The frequency of the FVL mutation varies among different ethnic groups. The mutation is present in 5.2% of Caucasians, 1.2% of African Americans,^[9] and 5–9% of Europeans, while it is rare in Asian and African populations.^[9,10] The FVL mutation is primarily inherited in an autosomal dominant fashion.^[8,10] Heterozygosity for the FVL mutation is present in 20–40% of non-pregnant patients with thromboembolic disease, while homozygosity, the rarer condition, is associated with a significantly higher (100-fold) risk of thromboembolism.^[10] The prothrombin 20210A mutation is a point mutation that leads to a normal protein, but higher average levels of inactive factor II (prothrombin) compared with wild-type genotype, which is the presumed mechanism of the prothrombotic phenotype.^[9] The most common acquired thrombophilia is due to antiphospholipid antibodies, which include lupus anticoagulant (LAC) and anticardiolipin antibodies and anti-B-2glycoprotein 1 antibodies.^[8] Thrombophilias derived

from a combination of hereditary and acquired components, such as the VIII C factor, hyperhomocysteinemia, and acquired APC resistance, are identified. In addition, pregnancy itself leads to a thrombophilic state as a result of hemostatic and fibrinolytic changes.^[7] During pregnancy, procoagulant factors (such as VIII, XII, VII, and V) and the von Willebrand factor and fibrinogen are increased, protein S and the APC are reduced, and fibrinolytic activity is diminished.^[9] All of these modifications, together with an enlarged plasmatic volume, prepare the mother to face the hemostatic state during delivery. Recently, anti-13-2glycoprotein 1 antibody is also considered as the marker for acquired thrombophilia.^[5] Although the relation of acquired thrombophilia to APO is well established, controversy still exists for inherited thrombophilia. Studies published in literature have shown varying results possibly because of ethnic differences.^[11] Deficiency of antithrombin was the first recognized inherited thrombophilia. Antithrombin deficiency is inherited in an autosomal dominant pattern, and the prevalence of the heterozygous state in the general population is estimated at 1:2000–1:5000.^[11,12] The prevalence of antithrombin deficiency in unselected patients with a history of VTE is approximately 1%^[13,14] and increasing up to 4.9% in recurrent VTE or VIE in individuals <45 years of age.^[15] The gene for antithrombin is at 1q 23–25 and a database of mutations associated with antithrombin deficiency has been compiled and recently updated.^[16] Protein C deficiency was the second inherited thrombophilia described. The prevalence of heterozygous protein C deficiency in the general population ranges from 0.15% to 0.8%.^[17,18] Protein S serves as a cofactor for protein C, thereby acting as a natural inhibitor of the coagulation cascade. Protein S circulates in plasma in two forms - about 40% in the free active form and 60% bound to C4b-binding protein, a regulator of the complement system. Levels of C4b-binding protein are increased in pregnancy, with the combined oral contraceptive pill and in inflammation. An increase in the level of C4b-binding protein leads to a reduction in the level of free active protein S, possibly contributing to a thrombophilic state.^[19] In 1996, Poort *et al.*^[20] first described a mutation in the 3'-untranslated region of the prothrombin gene that was more common in individuals with venous thrombosis. The mutation is a single base-pair substitution of guanine to adenine at position 20210 (G20210A)^[21] and is associated with increased levels of prothrombin. The prothrombin G20210A mutation is increased 2–5-fold in individuals with VTE (5.0–6.2%) compared with controls (1.2–2.6%).^[22,23] This study was carried out with an aim to study the prevalence of acquired and inherited thrombophilia in women with APO.

Aims and Objectives

This study aims to study the prevalence of acquired and inherited thrombophilia in women with APO and their

role on pregnancy complications. The objective was also to study the type of thrombophilia associated with each APO.

Type of Study

This is a prospective, cross-sectional, observational study.

Period of Study

The study duration was from July 2006 to June 2008.

Institute of Study

This study was conducted in the Department of Obstetrics and Gynaecology, AIIMS, New Delhi.

MATERIALS AND METHODS

A total of 69 patients with a history of APO in previous pregnancies were included in this study to understand the prevalence of hemophilia in them. Ethical committee clearance was obtained before the commencement of the study. An ethical committee approved pro forma and consent forms were used while conducting the study.

Inclusion Criteria

Patients with a history of APO in previous pregnancies such as:

1. Severe preeclampsia <36 weeks
 - a. Blood pressure more than 160/110
 - b. Proteinuria >5 g/day
 - c. Hemolysis
 - d. Elevated liver enzymes
 - e. Platelets <1 lakhs/mm³
 - f. Eclampsia.
2. Placental abruption.
3. Delivery of small for gestational age baby.
4. Unexplained intrauterine deaths.
5. Recurrent abortions (>3) were included in the study.

Exclusion Criteria

Patients with chronic hypertension, diabetes mellitus, cardiovascular disease, renal disease, multiple pregnancies, maternal drug or alcohol abuse, intrauterine infections, suspected chromosomal abnormalities, congenital malformations detected by ultrasound, and on anticoagulation therapy were excluded from the study.

Timing of Study

Patients with a history of APO fitting inclusion criteria were screened for thrombophilia in the preconception period or >6 weeks postpartum.

Method of Study

Detailed obstetric history was taken. Routine investigations such as hemogram and liver and renal function tests were done. Some special investigations such as TSH, glucose

tolerance tests with 75 g glucose, hysteroscopy, parental blood karyotyping, and TORCH screen if indicated were done to exclude other causes of APO. After proper counseling and informed consent, 20 mL of blood was drawn from the patient and sent to the department of hematology, to investigate for thrombophilia in the same hospital. Blood sample mixed with 3.2% trisodium citrate (1:9 ratios). Sample centrifuged at 3500–4000 rpm and stored at –70°C. This sample was used for various thrombophilic studies.

Test for Anticardiolipin Antibodies

Anticardiolipin antibodies were measured by ELISA method (AIDA cardiolipin - GM Germany). Both IgG and IgM types of ACL were assayed.

Principle of the Test

Diluted serum samples are incubated with cardiolipin immobilized on microliter wells. After washing away unbound serum components, rabbit antihuman IgG or IgM conjugated to horseradish peroxidase is added to the wells, and this binds to surface-bound antibodies in the second incubation. Unbound conjugate is removed by washing, and a solution containing 3, 3', 5, 5'-tetramethylbenzidine and enzyme substrate is added to trace specific antibody binding. Addition of stop solution terminates the reaction and provides the appropriate pH for color development. The optical densities of the standards, positive control, and samples are measured using a microplate reader at 450 nm. Optical density is directly proportional to antibody activity in the sample. For the assessment of patient's sera diagnosis, the following ranges are recommended [Table 1].

LAC Test

This was performed using Kaolin clotting time (Sigma Diagnostics, USA).

Principle

LAC act against the prothrombinase, thereby prolonging all phospholipids dependent tests such as APTT, PT, and RVVT. When the APTT is modified by omitting platelet substituting reagent, it becomes particularly sensitive to the LAC. If the test is performed on a range of mixtures of normal and patient's plasma, different patterns of response are obtained, indicating the presence of LAC, deficiency of one or more of the coagulation factors, or the lupus cofactor effect.

Table 1: The reference range for quantitative results of ACL

Range	Cardiolipin IgG (GPLU/mL)	Cardiolipin IgM (MPLU/mL)
Normal	<11	<10
Positive	>11	>10
Moderate	20–40	20–40
High	>40	>40

Requirements

1. Kaolin (10 mg/mL in Tris buffer) pH 7.4 2.
2. Normal platelet poor plasma.
3. Patient's plasma.
4. Calcium chloride (0.025 moL/L).

Procedure

1. The following dilutions were made [Table 2].
 1. Take 0.2 mL of above dilution +0.1 mL Kaolin (10 mg/mL).
 2. Incubate for 2 min with constant shaking.
 3. Add 0.2 mL of calcium chloride and observe for clot formation.
 4. Note down the clotting. Repeat the test with all other four dilutions.

Normal values: The reference range is taken between 60 and 120 s. Interpretation: If the kaolin clotting time of PP is >120 s, then the following calculations are performed: $Reference\% = (NP+PP)-(NP)/(PP) \times 100$. Normal sample shows a reference range <15%. Anything above 15% is abnormal. Proglobal C assay: It is a clotting-based technique (Dade Behring, Germany). It is a screening test for thrombophilia. For this assay, two test tubes marked blank (B) and test (T), respectively. 100 µL of citrated plasma is taken each tube. 100 µL of buffer is added to blank tube and 100 µL of Proglobal C activator is added to test tube. Then, 100 µL of APTT reagent added to both tubes and incubated for 3–4 min. 100 µL of calcium chloride added to both tubes. Then, clotting time assessed in both tubes. Then, ratio (T/B) assessed. Ratio multiplied with coefficient factor which is specific for the sample kit. Normal value is >0.8. Low Proglobal C <0.8 warrants further tests for protein C, protein S, and APCR. Protein C assay: It is a sandwich ELISA. "READS protein C antigen 96-microwell Test Kit" manufactured by Corgenix, Inc., USA was used. A capture antibody specific for human protein C was coated to 96-microwell polystyrene plates. Diluted plasma was incubated in the wells allowing any available protein C to bind to the antihuman protein C antibody on the microwell surface. The plates were washed to remove unbound proteins and other plasma molecules. Bound protein C was quantified using horseradish peroxidase (HRP) conjugated antihuman protein C detection antibody. Following incubation, unbound conjugate was removed by washing. A chromogenic substrate of tetramethylbenzidine (TMB) hydrogen peroxide is added to develop a colored reaction. The intensity of the color is measured in optical density

(O.D) units with spectrophotometer at 450 nm. Protein C antigen relative percent concentrations in PP are determined against curve prepared from the reference plasma provided with the kit. Reagents: Each READS protein C antigen 96-microwell test kit contains the following reagents.

1. 12 × 8 antihuman protein C antibody-coated microwells.
2. 60 mL sample diluents' (blue-green) solution contains sodium azide.
3. 3 vials ×0.5 mL lyophilized reference plasma, with assay sheet.
4. 12 mL antihuman protein C HRP conjugate (blue solution).
5. 13 mL substrate (TMB and H₂O₂) 15 mL stopping solution (0.36 N sulfuric acid).
6. 30 mL wash concentrate (×33 phosphate-buffered saline with 0.01% Tween 20).

Procedure

1. Reference plasma is prepared by adding 0.5 mL reagent grade water. Gently mix and allows standing for 10 min.
2. Predilute all plasmas (1:2 dilutions in sample diluent) as follows: Reference plasma: Add 100 µL reference plasma to 100 µL sample diluent.
3. Control and patient samples: Add 20 µL plasma to 20 µL sample diluents and mix well. These predilutions are utilized in preparing the working solutions in steps 4 and 5.
4. Using the 1:2 reference plasma dilutions from step 3, prepare six working reference dilutions.
5. Prepare working dilutions of control and patient samples by adding 20 uL of prediluted plasma (1:2 dilutions from step 3) to 500 pL sample diluent.
6. Mix thoroughly and add 10 µL of the working solutions (reference plasmas, controls, and patient samples) to the appropriate microwells.
7. Add 100 µL of sample diluent to the reagent blank well to leave the water blank well empty.
8. Incubate 40 min at room temperature. Then, invert the microwells and dump the sample fluid.
9. Wash 4 times with working solution.
10. Add 100 µL conjugate to each well.
11. Incubate for 10 min at room temperature. Then, invert the microwells and dump the conjugate solution.
12. Wash 4 times with wash solution.
13. Add 10 µL substrate to each well (except for the water blank well) and incubate for 10 min at room temperature. Blue color will develop in samples in wells with positive samples.

Table 2: The dilutions made

Normal platelet poor plasma (NP)	Normal platelet poor plasma+patient plasma (NP+PP)	PP
0.2 mL	0.1 mL+0.1 mL	0.2 mL

PP: Patient plasma

14. Add 100 μ L stopping solution to each well except for the water blank well to stop the enzyme reaction. Blue substrates will turn yellow and colorless substrate will remain colorless. Do not add stopping solution to the water blank well. Read the O.D at each well at 450 nm against 650 nm reference filter.

RESULTS

1. Calculate the mean O.D. for the duplicates of the reference plasma dilutions, controls selected for use, and patient samples.
2. Plot the mean O.D. obtained for each dilution of the reference plasma (x-axis), against the corresponding value of the reference level (y-axis). A log-log or point-to-point graph is recommended, although a semi-log may also be used.
3. Using the mean O.D., determine the control and patient relative value from the graph, or alternatively use linear regression to calculate from the reference curve.
4. To calculate protein C antigen level in percentage of normal, multiply the control and patient relative values obtained from the reference curve by the assigned value for the REIDS reference plasma (see vial label).

For example:

- Patient relative value (from the reference curve): 40
- Reference plasma assigned value (from vial label): 105% of normal
- Actual patient protein C antigen value (as percentage of normal): $40 \times 1.05 = 42\%$
- Normal range of protein C is 72–160%.

Protein S Assay

It is also a sandwich ELISA kit manufactured by the same company. Procedure and principle the same as previous test except for the antihuman protein S HRP conjugate. Normal level of protein S is 50–130%. APC resistance: It is a clot-based technique; kit is manufactured by “Stago Diagnostics, France.” Reagent includes factor V deficient plasma, venom as the cofactor, and calcium chloride (0.025M). Procedure: Patients plasma is diluted with buffer in 1:10 ratio. Control was also prepared. 100 μ L each of patient’s plasma, factor V deficient plasma, and venom was mixed with each other and incubated for 4 min. Then, additional 100 μ L of calcium chloride was kept in fully automated coagulometer and the clotting time noted. Normal value: For APCR, it was >120 s. If low, APCR was observed, then FVL mutation study was done. Antithrombin III assay: It is a chromogenic method. Kit is manufactured by Stago Diagnostics, France. Patient’s plasma is diluted with 1:10 ratio with buffer. Reagents included substrate and thrombin. Procedure: Patients plasma, substrate, and thrombin 100 μ L each added and mixed and incubated for 3–4 min. O.D. measured at 450 nm taken and

graph plotted. Normal value was taken as 70–130%. Anti- β -2 glycoprotein antibodies: It was measured by ELISA method. The kit was manufactured by AIDA, Germany. Normal range: 5–15 IU/mL. Homocysteine: ELISA method. Normal range: It was 5–15 IU/mL. Prothrombin gene mutation: Prothrombin gene mutation was not prevalent in Indian population as evidenced by the previous reports. Hence, it was not done in our laboratory. FVL mutation: Whole blood collected in EDTA vial and genomic DNA was extracted from whole blood as per standard protocols. The polymerase chain reaction (PCR) using known primers was used to amplify exon 10 of the factor V gene which contains the G \rightarrow A mutation at nucleotide position (1691). Following amplification, a 200 aliquot of the product was digested overnight with 5 IU of the enzyme Mnl1 (New England Biolabs, Hitchin, UK) at 37°C. Samples of the digested and undigested PCR product were separated electrophoretically in a 3% agarose gel and the bands visualized using ethidium bromide. The undigested PCR product measures 223 base pairs (bp) in size. Following cleavage with *Mnl1*, a normal allele produces bands of 37, 82, and 104 bp. A mutant allele produces bands of 82 and 141 by due to loss of one *Mnl1* cleavage site. Controls on each gel included a known heterozygote, a normal control known not to possess the FVL mutation and a water blank containing no input DNA.

Statistical Analysis

The prevalence of thrombophilia in each APO was calculated. Demographic data and clinical data are presented as patient group means with SE. SPSS software version 11.0 was used for analysis.

OBSERVATIONS AND RESULTS

A total of 69 patients with a history of APO were screened for inherited and acquired thrombophilia. The patients were enrolled over a period of 2 years from July 2006 to June 2008 from the OPD at the Department of Obstetrics and Gynaecology, AIIMS, New Delhi. Recurrent abortion in 32 (46.37%) patients was the most common APO in women screened for thrombophilia in the study. Other APOs were unexplained IUD in 17 (24.63%), IUGR in 11 (15.94%), and severe preeclampsia in 9 (13.04%) [Table 3 and Figure 1].

Age Distribution

The mean age of the patients in this study was 27.34 ± 3.28 with a range of 20–36 years. The mean age of patients with recurrent abortion was 27.38 ± 2.25 with a range of 22–32 years while that for the patients with intrauterine deaths it was 27.70 ± 1.99 with a range of 24–31 years, with intrauterine growth restriction it was 27.81 ± 2.92 with a range of 24–34 years and preeclampsia it was 28.66 ± 3.35 with a range of 25–36 years [Table 4].

Distribution of Gravidity

The mean gravidity of the patients in the present study was 3.7 ± 1.25 . The mean gestation of the patients with recurrent abortion was 3.81 ± 0.86 , while that for patients with IUD was 3.41 ± 1.12 , with IUGR it was 4 ± 0.89 and preeclampsia it was 4.33 ± 0.87 [Table 5].

The thrombophilic tests were positive in 33/69 (47.82%) patients in the study, and among them, there were 8/69 (10.14%) patients with inherited thrombophilia in the present study. Protein C deficiency was noted in 4 (5.79%) patients, hyperhomocysteinemia in 2 (2.89%),

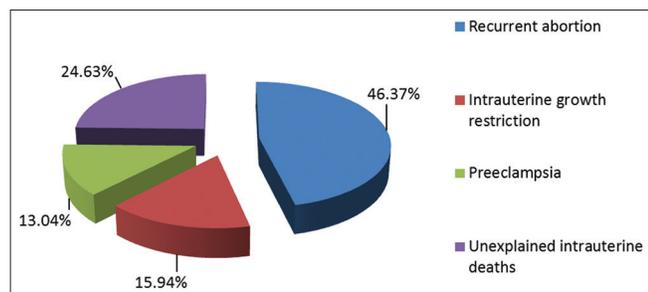


Figure 1: The incidence of adverse pregnancy outcome in the study (n = 69)

Table 3: The incidence of APO conditions in the study (n=69)

Type of APO	Number of patients 69 (%)
Recurrent abortion	32 (46.37)
Unexplained intrauterine deaths	17 (24.63)
IUGR	11 (15.94)
Preeclampsia	9 (13.04)

IUGR: Intrauterine growth retardation, APO: Adverse pregnancy outcome

Table 4: The age distribution of patients with different APO

APO	Age mean±SD (range in years)
All patients	27.34±3.28 (20–36)
Recurrent abortion	27.38±2.25 (22–32)
Unexplained intrauterine deaths	27.70±1.99 (24–31)
Intrauterine growth restriction	27.81±2.92 (24–34)
Preeclampsia	28.66±3.35 (25–36)

APO: Adverse pregnancy outcome

Table 5: The distribution of gravidity in the study group

APO	Mean gravidity±SD (range)
All patients	3.7±1.25 (1–8)
Recurrent abortion	3.81±0.86 (3–6)
Unexplained intrauterine deaths	3.41±1.12 (1–5)
Intrauterine growth restriction	4±0.89 (3–6)
Preeclampsia	4.33±0.87 (3–6)

SD: Standard deviation

antithrombin III deficiency in 1 (1.44%), and FVL mutation was noted in 1 (1.44%) patient each [Table 6].

Prevalence of Acquired Thrombophilia

25/69 (36.23%) patients tested positive for acquired thrombophilia. 25 patients tested positive for anti-β-2 glycoprotein antibodies, nine patients for ACL, and two for LAC [Table 7].

The prevalence of thrombophilia was observed in patients with in recurrent abortion and found that 18/32 (56.25%) tested positive for thrombophilia. 16 of 32 (50%) patients with recurrent abortions were detected to have acquired thrombophilia. 2/32 (6.25%) patients were observed to have inherited thrombophilia. Anti-β-2 glycoprotein antibody was positive in 10/32 (31.25%) patients. ACL IgG was positive in 3/32 and ACL IgM was positive in 3/32 of the patients (6/32–18.75%) [Table 8].

Table 6: The prevalence of inherited thrombophilia in the study group

Type of thrombophilia	Number of patients n=08/69 (%)
Protein C deficiency	4 (5.79)
Protein S deficiency	1 (1.44)
Antithrombin III deficiency	1 (1.44)
FVL mutation	1 (1.44)
Hyperhomocysteinemia	2 (2.89)
Total	8 (10.14)

FVL: Factor V Leiden

Table 7: The prevalence of acquired thrombophilia in the study group (n=69)

Laboratory test	Number of patients - 25
LAC	2
ACL IGG	6
ACL IGM	3
Anti-β-2 glycoprotein antibody	25
Total positive tests	36

LAC: Lupus anticoagulant

Table 8: The prevalence of thrombophilia among the patients with recurrent abortion (n=32)

Laboratory test	Number of patients (n=32) (%)
Protein C deficiency	0
Protein S deficiency	0
Antithrombin III deficiency	1 (3.12)
FVL mutation	0
Hyperhomocysteinemia	1 (3.12)
LAC	0
ACL IgG	3 (9.37)
ACL IgM	3 (9.37)
Anti-β-2 glycoprotein antibody	10 (31.25)
Inherited thrombophilia	2
Acquired thrombophilia	16
Total	18/32 (56.25)

LAC: Lupus anticoagulant

Prevalence of Thrombophilia in Unexplained IUD

There were 17/69 (24.63%) patients with preterm in intrauterine deaths. Among them, 2/17 (11.76%) were found to have inherited thrombophilia. Protein C deficiency was observed in 1/17 (5.88%) patients. 1 patient (5.88%) had FVL mutation. Acquired thrombophilia was seen in 10/17 (58.82%) patients. 7/17 patients (41.17%) had anti- β -2 glycoprotein antibody positive result [Table 9].

Prevalence of Thrombophilias in IUGR

In the present study, 11/69 (15.94%) patients had intrauterine growth restriction (birth weight below the 10th percentile). Seven of 11 patients screened positive for thrombophilia (63.63%). Inherited thrombophilia was present in 2/11 patients (18.18%). Protein C deficiency and hyperhomocysteinemia were present in 1 patient (9.09%) each with inherited thrombophilia in this group. Five of 11 patients (45.45%) screened positive for acquired thrombophilia. Anti- β -2 glycoprotein was present in 4/11 patients (36.36%) and ACL IgG was observed positive in 1/11 (9.09%) of the patients [Table 10].

Prevalence of Thrombophilia in Severe Preeclampsia

In this study, nine patients with severe preeclampsia were included in the study. 7/9 patients screened positive for thrombophilia (77.77%). Inherited thrombophilia was present in 2 (18.18%) of 11 patients and both showed positive for Protein C. One patient each was positive for protein S deficiency and 4 (44.44%) for anti- β -2 glycoprotein antibody test showing acquired thrombophilia in 5/9 patients (55.55%) [Table 11].

DISCUSSION

There are various causes for APO. Patients with a history of APO such as recurrent miscarriages, unexplained intrauterine deaths, severe preeclampsia, and intrauterine growth restriction need to be evaluated in the preconception period or 6-week postpartum. The common causes for these pregnancy complications such as thyroid disorder, diabetes mellitus, hypertension, and chronic systemic illnesses should be ruled out with proper history, physical examination, and relevant laboratory investigations. Special investigations such as parental karyotyping and diagnostic hysteroscopy are needed in recurrent spontaneous abortions. In the absence of these common causes of pregnancy complications, the patients have to be investigated for thrombophilia. Definite relationship of acquired thrombophilia with different APO has been reported in previous studies. Studies are available evaluating inherited thrombophilia and pregnancy complications but with conflicting reports. This could be due to the difference in the prevalence of inherited thrombophilia in ethnic groups or difference in the methodology of the studies

Table 9: The prevalence of thrombophilia in unexplained intrauterine deaths (n=17)

Laboratory test	Number of patients (n=17) (%)
Protein C deficiency	1 (5.88)
Protein S deficiency	0
Antithrombin III deficiency	0
FVL mutation	1 (5.88)
Hyperhomocysteinemia	0
LAC	1 (5.88)
ACL IgG	1 (5.88)
ACL IgM	0
Anti- β -2 glycoprotein antibody	7 (41.17)
Acquired thrombophilia	10 (58.82)
Inherited thrombophilia	2 (11.76)
Total	12 (70.58)

LAC: Lupus anticoagulant

Table 10: The prevalence of thrombophilia in intrauterine growth retardation group (n=11)

Laboratory test	Number of patients (%) (n=11)
Protein C deficiency	1 (18.18)
Protein S deficiency	0
Antithrombin III deficiency	0
FVL mutation	0
Hyperhomocysteinemia	1 (9.09)
LAC	0
ACL IgG	1 (9.09)
ACL IgM	0
Anti- β -2 glycoprotein antibody	4 (36.36)
Acquired thrombophilia	5 (45.45)
Inherited thrombophilia	2 (18.18)
Total	10 (90.90)

LAC: Lupus anticoagulant

Table 11: Prevalence of thrombophilia in severe preeclampsia patients (n=9)

Type of thrombophilia	Number of patients (n=9) (%)
Protein C deficiency	2 (18.18)
Protein S deficiency	1
Antithrombin III deficiency	0
FVL mutation	0
Hyperhomocysteinemia	0
LAC	0
ACL IgG	1 (11.11)
ACL IgM	0
Anti- β -2 glycoprotein antibody	4 (44.44)
Acquired thrombophilia	5 (55.55)
Inherited thrombophilia	2 (18.18)
Total	7 (77.77)

LAC: Lupus anticoagulant

reported. This study was an observational study in which 69 patients with APO were included from the OPD of Obstetrics and Gynecology Department of AIIMS and investigated for acquired inherited thrombophilia. The prevalence of thrombophilias in APO: In the present study, 33/69 women with thrombophilia happening in APOs were observed (47.82%). In a comparative study shown in Table 12, the incidence was ranging from 32% to 66%.

The number of patients screened in the present study is comparable to Kupfermenc *et al.*^[24] and Ariel *et al.*^[25] studies.

Prevalence of Inherited Thrombophilias in Recurrent Abortion

2/32 (6.25%) of the patients with recurrent abortion had inherited thrombophilia. Acquired thrombophilia was present in 16/32 (50%) of patients with recurrent abortion. Among these, majority (10/32 [31.25%]) were positive for anti- β -2 glycoprotein antibodies. 6/32 patients were positive for anticardiolipin antibodies (18.75%); 3/32 (9.37%) patients had each positive for IgG and IgM anticardiolipin antibodies. None had LAC positive. A comparative study [Table 13] was made and found that the incidence of inherited thrombophilia in women with recurrent abortion in the present study was low compared to the other studies. This may be due to the low prevalence of thrombophilic mutations in Indian population or could be because of small sample size. The prevalence was comparable to Rai *et al.*'s study, but he only screened for FVL mutation.

The prevalence of acquired thrombophilia in women with recurrent abortion in the present study was high

(50%) comparable to some large studies by Kumar *et al.*,^[35] Velayuthaprabhu *et al.*,^[36] etc. Anti- β -2 glycoprotein antibodies 10/32 (31.25%) were the most commonly detected in our study which is comparable to that in Kumar *et al.*'s^[35] studies? There were some studies screened for more classes of antibodies against antiphospholipid which were not included in this study such as Yamada *et al.*^[37] and Velayuthaprabhu *et al.*^[36] [Table 14].

Prevalence of Thrombophilias in Unexplained IUD

Of 17 patients with intrauterine deaths screened for thrombophilia, 2/17 (11.76%) patients had inherited thrombophilia. Protein C deficiency was present in 1/17 (5.88%) patient and one patient had FVL mutation (5.88%). Antithrombin III deficiencies, hyperhomocysteinemia, and protein C deficiency were not detected in this group. Acquired thrombophilia was present in 10/17 (58.82%) of patients. Most prevalent positive test for thrombophilia was anti- β -2 glycoprotein antibodies in 7/17 (41.17%). 1 patient (5.88%) had ACL IgG positive. The prevalence of inherited thrombophilia in this study was lower, whereas it was higher in Kupfermenc *et al.*^[24] and Alfirevic *et al.*^[27] studies. Similarly, the incidences of

Table 12: A comparative study of incidence of thrombophilia in APO

Study	Total number of patients screened	Prevalence of thrombophilia (%)
Kupfermenc <i>et al.</i> ^[24]	110	65
Ariel <i>et al.</i> ^[25]	40	42
Sarig <i>et al.</i> ^[26]	145	66
Alfirevic <i>et al.</i> ^[27]	102	53
Ogunyemi <i>et al.</i> ^[28]	75	32
Zahed <i>et al.</i> ^[29]	91	55
Hvas <i>et al.</i> ^[30]	414	42
Present study (2008)	69	47.82

APO: Adverse pregnancy outcome

Table 13: Comparative study of prevalence of inherited thrombophilia in recurrent abortion patients

Study	Number of patients screened	Prevalence of inherited thrombophilia (%)
Foka <i>et al.</i> ^[31]	80	36
Rai <i>et al.</i> ^[32]	1111	8
Couto <i>et al.</i> ^[33]	88	76
Xu <i>et al.</i> ^[34]	112	38.4
Present study (2008)	32	6.25

Table 14: The prevalence of acquired thrombophilia in recurrent abortion

Study	Number of patients	Prevalence of acquired thrombophilias (%)	LAC N/N (%)	ACL N/N (%)	Anti- β -2 glycoprotein antibodies (%)
Parazzini <i>et al.</i> ^[38]	220	15	16/220 (7)	19/99 (19)	-
Kumar <i>et al.</i> ^[35]	107	46%	11/107 (10.28)	-	33/82 (40.24)
Yamada <i>et al.</i> ^[37]	114	26.3*	2/114 (1.8)	9.7	5.3
Patarassi <i>et al.</i> ^[39]	64	48.4	-	31/64 (48.4)	-
Velayuthaprabhu <i>et al.</i> ^[36]	155	51.6**	-	62/155 (40)	-
Couto <i>et al.</i> ^[33]	88	13.6	1/88 (1.1)	11/88 (12.5)	-
Present study	32	31.25	0	6/32 (18.75)	10/32 (31.25)

*Included antiphosphatidyl ethanolamine antibody accounting 20%. **Included antiphosphatidyl serine antibody accounting 19%

acquired thrombophilia were lower in this study and higher in all other studies [Table 15].

Prevalence of Thrombophilias in IUGR

Of 11 patients with IUGR, two patients had inherited thrombophilia (18.18%). Inherited thrombophilia was proved by protein C deficiency in 1 patient (9.09%) and FVL mutation 1 patient (9.09%). Antithrombin III deficiencies, hyperhomocysteinemia, and protein S deficiency were not detected in this group. 4 patients (36.36%) showed anti-β-2 glycoprotein antibodies. One patient had anticardiolipin IgG antibodies (9.09%). Anticardiolipin IgM antibodies and LAC were not detected in patients with intrauterine growth restriction. The prevalence of inherited thrombophilia in IUGR in our study is comparable to the three previous studies^[24,27,40] may be due to the similar and small sample sizes. The prevalence differs from Van Pampus MG *et al.*'s^[43] studies because he included only FVL mutation. High prevalence of acquired thrombophilia in the present

study compared to the previous studies may be due to the high prevalence of anti-β-2 glycoprotein antibodies in our study population, which marker was not screened in these previous studies [Table 16].

Prevalence of Thrombophilias in Severe Preeclampsia

Nine patients with severe preeclampsia were screened for thrombophilia. Seven patients screened positive for thrombophilias (77.77%). Inherited thrombophilia was present in 2 of 9 patients (22.2%). Both were positive for protein C deficiency. Acquired thrombophilia was present in 5 (55.5%) patients. Four patients had anti-β-2 glycoprotein antibody accounting (44.44%) [Table 17]. Regarding inherited thrombophilias, the prevalence in the present study was comparable to the study of Van Pampus *et al.*,^[43] but the present study differs from having high prevalence of acquired thrombophilia. It may be due to the difference in the sample size. Dekker *et al.*'s^[44] and Kupfermirc *et al.*^[24] studies differ from the present study

Table 15: The comparative study of prevalence of thrombophilia in women with IUD

Study	Total number of patients with IUD	Prevalence of inherited thrombophilia (%)	Prevalence of acquired thrombophilia (%)
De Vries <i>et al.</i> ^[40]	18	22.2	22.2
Gris <i>et al.</i> ^[41]	232	81	14.22
Kupfermirc <i>et al.</i> ^[24]	12	50	-
Ariel <i>et al.</i> ^[25]	40	42.5	0
Alfirevic <i>et al.</i> ^[27]	18	55.5	5.5
Present study (2008)	17	11.76	58.82

Table 16: Studies comparing prevalence of thrombophilia in IUGR (n=11)

Study	Total number of patients with IUGR	Prevalence of inherited thrombophilia (%)	Prevalence of acquired thrombophilia (%)
Kupfermirc <i>et al.</i> ^[24]	44	50	4.5
De Vries <i>et al.</i> ^[40]	13	46.1	7.6
Alfirevic <i>et al.</i> ^[27]	25	40	24
Verspyck <i>et al.</i> ^[42]	203	8	-
Present study (2008)	11	18.18	45.45

IUGR: Intrauterine growth retardation

Table 17: The comparison between studies with data of prevalence of thrombophilia in patients with severe preeclampsia

Study	Number of patients with severe preeclampsia	Prevalence of inherited thrombophilia (%)	Prevalence of acquired thrombophilia (%)
Dekker <i>et al.</i> ^[44]	101	60	28.4
Kraus <i>et al.</i> ^[45]	21	41	-
Mello <i>et al.</i> ^[46]	46	32.6	3
Kupfermirc <i>et al.</i> ^[24]	97	60	2
Lin <i>et al.</i> ^[47]	50	22	-
Horstkamp <i>et al.</i> ^[48]	70	7.1	-
Degroot <i>et al.</i> ^[49]	163	12.9	-
Ozcan <i>et al.</i> ^[50]	44	42.3	-
Van Pampus <i>et al.</i> ^[43]	345	17.7	20.9
Ganzevoort <i>et al.</i> ^[51]	206	26	10
Mello <i>et al.</i> ^[46]	406	37.9	12.8
Present study (200)	9	22.2	55.5

in having high prevalence of inherited thrombophilias and comparatively low prevalence of acquired thrombophilias. It may be due to the highly prevalent thrombophilic mutations in those ethnic groups.

The present study has limitations. The major limitation is being the small sample size. The present study was done in a tertiary hospital so some degree of referral and selection bias cannot be excluded in the study. The study design is observational study.

CONCLUSIONS

Thrombophilia is common among patients with APO. Inherited thrombophilia is less common than the acquired ones. Biomarkers such as protein C deficiency, hyperhomocysteinemia, antithrombin III deficiency, and FVL mutation help to diagnose inherited type and treat these patients early. Among the acquired thrombophilia patients, anti- β -2 glycoprotein antibodies were positive as biomarker in majority of acquired type of thrombophilia. Other markers useful are anticardiolipin antibodies and LAC test.

REFERENCES

- Egeberg O. Inherited antithrombin deficiency causing thrombophilia. *Thromb Diath Haemorrh* 1965;13:516-30.
- Rosendaal FR. Venous thrombosis: A multicausal disease. *Lancet* 1999;353:1167-73.
- Lin J, Sun Y, Zhao S, Xu J, Zhao C. Safety and efficacy of thrombolysis in cervical artery dissection-related ischemic stroke: A meta-analysis of observational studies. *Cerebrovasc Dis* 2016;42:272-9.
- Rey E, Kahn SR, David M, Shrier I. Thrombophilic disorders and fetal loss: A meta-analysis. *Lancet* 2003;361:901-8.
- Bauer KA, Rosenberg RD. The pathophysiology of the prothrombotic state in humans: Insights gained from studies using markers of hemostatic system activation. *Blood* 1987;70:343-50.
- Boisclair MD, Ireland H, Lane DA. Assessment of hypercoagulable states by measurement of activation fragments and peptides. *Blood Rev* 1990;4:25-40.
- Bertina RM, Koeleman BP, Koster T, Rosendaal FR, Dirven RJ, de Ronde H, *et al*. Mutation in blood coagulation factor V associated with resistance to activated protein C. *Nature* 1994;369:64-7.
- Voorberg J, Roelse J, Koopman R, Büller H, Berends F, ten Cate JW, *et al*. Association of idiopathic venous thromboembolism with single point-mutation at arg506 of factor V. *Lancet* 1994;343:1535-6.
- Ridker PM, Miletich JP, Hennekens CH, Buring JE. Ethnic distribution of factor V Leiden in 4047 men and women. Implications for venous thromboembolism screening. *JAMA* 1997;277:1305-7.
- Lockwood CJ, Krikun G, Schatz F. Inherited thrombophilias in pregnant patients. *Prenat Neonat Med* 2001;6:3-14.
- Tait RC, Walker ID, Perry DJ, Islam SI, Daly ME, McCall F, *et al*. Prevalence of antithrombin deficiency in the healthy population. *Br J Haematol* 1994;87:106-12.
- Rosenberg RD. Actions and interactions of antithrombin and heparin. *N Engl J Med* 1975;292:146-51.
- Koster T, Rosendaal FR, Briët E, van der Meer FJ, Colly LP, Trienekens PH, *et al*. Protein C deficiency in a controlled series of unselected outpatients: An infrequent but clear risk factor for venous thrombosis (Leiden thrombophilia study) *Blood* 1995;85:2756-61.
- Heijboer H, Brandjes DP, Büller HR, Sturk A, ten Cate JW. Deficiencies of coagulation-inhibiting and fibrinolytic proteins in outpatients with deep-vein thrombosis. *N Engl J Med* 1990;323:1512-6.
- Pabinger I, Schneider B. Thrombotic risk in hereditary antithrombin III, protein C, or protein S deficiency. A cooperative, retrospective study. Gesellschaft für thrombose- und hamostaseforschung (GTH) study group on natural inhibitors. *Arterioscler Thromb Vasc Biol* 1996;16:742-8.
- Lane DA, Bayston T, Olds RJ, Fitches AC, Cooper DN, Millar DS, *et al*. Antithrombin mutation database: 2nd (1997) update. For the plasma coagulation inhibitors subcommittee of the scientific and standardization committee of the international society on thrombosis and haemostasis. *Thromb Haemost* 1997;77:197-211.
- Tait RC, Walker ID, Reitsma PH, Islam SI, McCall F, Poort SR, *et al*. Prevalence of protein C deficiency in the healthy population. *Thromb Haemost* 1995;73:87-93.
- Clark P, Brennand J, Conkie JA, McCall F, Greer IA, Walker ID, *et al*. Activated protein C sensitivity, protein C, protein S and coagulation in normal pregnancy. *Thromb Haemost* 1998;79:1166-70.
- Leeda M, Riyazi N, de Vries JI, Jakobs C, van Geijn HP, Dekker GA, *et al*. Effects of folic acid and vitamin B6 supplementation on women with hyperhomocysteinemia and a history of preeclampsia or fetal growth restriction. *Am J Obstet Gynecol* 1998;179:135-9.
- Poort SR, Rosendaal FR, Reitsma PH, Bertina RM. A common genetic variation in the 3'-untranslated region of the prothrombin gene is associated with elevated plasma prothrombin levels and an increase in venous thrombosis. *Blood* 1996;88:3698-703.
- Cumming AM, Keeney S, Salden A, Bhavnani M, Shwe KH, Hay CR, *et al*. The prothrombin gene G20210A variant: Prevalence in a U.K. Anticoagulant clinic population. *Br J Haematol* 1997;98:353-5.
- Brown K, Lnddington R, Williamson D. Risk of venous thromboembolism associated with a G to A transition at position 20210 in the 3'-untranslated region of the prothrombin gene. *Br J Haematol* 1997;98:907-09.
- Bremme KA. Hemostatic changes in pregnancy. *Ballieres Best Pract Res Clin Haematol* 2003;16:153-68.
- Kupferminc MJ, Eldor A, Steinman N, Many A, Bar-Am A, Jaffa A, *et al*. Increased frequency of genetic thrombophilia in women with complications of pregnancy. *N Engl J Med* 1999;340:9-13.
- Many A, Elad R, Yaron Y, Eldor A, Lessing JB, Kupferminc MJ, *et al*. Third-trimester unexplained intrauterine fetal death is associated with inherited thrombophilia. *Obstet Gynecol* 2002;99:684-7.
- Sarig G, Younis JS, Hoffman R, Lanir N, Blumenfeld Z, Brenner B, *et al*. Thrombophilia is common in women with idiopathic pregnancy loss and is associated with late pregnancy wastage. *Fertil Steril* 2002;77:342-7.
- Alfirevic Z, Mousa HA, Martlew V, Briscoe L, Perez-Casal M, Toh CH, *et al*. Postnatal screening for thrombophilia in women with severe pregnancy complications. *Obstet Gynecol* 2001;97:753-9.
- Ogunyemi D, Ku W, Arkel Y. The association between inherited thrombophilia, antiphospholipid antibodies and lipoprotein A levels with obstetrical complications in pregnancy. *J Thromb Thrombolysis* 2002;14:157-62.
- Zahed LF, Rayes RF, Mahfouz RA, Taher AT, Maarouf HH, Nassar AH, *et al*. Prevalence of factor V Leiden, prothrombin and methylene tetrahydrofolate reductase mutations in women with adverse pregnancy outcomes in Lebanon. *Am J Obstet Gynecol* 2006;195:1114-8.
- Hvas AM, Ingerslev J, Salvig JD. Thrombophilia risk factors are associated with intrauterine foetal death and pregnancy-related venous thromboembolism. *Scand J Clin Lab Invest* 2009;69:288-94.
- Foka ZJ, Lambropoulos AF, Saravelos H, Karas GB, Karavida A, Agorastos T, *et al*. Factor V Leiden and prothrombin G20210A mutations, but not methylenetetrahydrofolate reductase C677T, are associated with recurrent miscarriages. *Hum Reprod* 2000;15:458-62.
- Rai R, Shlebak A, Cohen H, Backos M, Holmes Z, Marriott K, *et al*. Factor V Leiden and acquired activated protein C resistance among 1000 women with recurrent miscarriage. *Hum Reprod* 2001;16:961-5.
- Couto E. Association between anticardiolipin antibodies and MTHFR mutation in recurrent miscarriage. *Sao Paulo Med J* 2005;8:110-5.
- Xu L, Liu XM, Zhang HY, Zhao J, Ri QW, Chang YF, *et al*. Relationship between three thrombophilic gene mutations and unexplained recurrent early spontaneous abortion. *Zhonghua Fu Chan Ke Za Zhi* 2007;42:180-3.
- Kumar KS, Jyothis A, Prakash MS, Rani HS, Reddy PP. Beta2-glycoprotein

- I dependent anticardiolipin antibodies and lupus anticoagulant in patients with recurrent pregnancy loss. *J Postgrad Med* 2002;48:5-10.
36. Velayuthaprabhu S, Archunan G. Evaluation of anticardiolipin antibodies and antiphosphatidylserine antibodies in women with recurrent abortion. *Indian J Med Sci* 2005;59:347-52.
 37. Yamada H, Atsumi T, Kato EH, Shimada S, Kishi T, Morikawa M, *et al.* Prevalence of diverse antiphospholipid antibodies in women with recurrent spontaneous abortion. *Fert Steril* 2003;80:1276-78.
 38. Parazzini F, Acaia B, Faden D, Lovotti M, Marelli G, Cortelazzo S, *et al.* Antiphospholipid antibodies and recurrent abortion. *Obstet Gynecol* 1991;77:854-8.
 39. Patarassi GM, Sartori MT, Saggiorato G, Girolami A. Familial thrombophilia associated with high levels of plasminogen activator inhibitor. *Fibrinolysis* 1992;6:99-103.
 40. de Vries JI, Dekker GA, Huijgens PC, Jakobs C, Blomberg BM, van Geijn HP, *et al.* Hyperhomocysteinaemia and protein S deficiency in complicated pregnancies. *Br J Obstet Gynaecol* 1997;104:1248-54.
 41. Gris JC, Quéré I, Monpeyroux F, Mercier E, Ripart-Neveu S, Tailland ML, *et al.* Case-control study of the frequency of thrombophilic disorders in couples with late foetal loss and no thrombotic antecedent – The nîmes obstetricians and haematologists study5 (NOHA5). *Thromb Haemost* 1999;81:891-9.
 42. Verspyck E, Hulsey TC, Marpeau L, Barau G, Roman H, Robillard PY. Obstetric and neonatal outcomes in grand multiparity. *Obstet Gynecol* 2004;103:1294-9.
 43. Van Pampus MG, Dekker G, Wolf H, Huijgens PC, Koopman MM, van Blomberg BM, *et al.* High prevalence of hemostatic abnormalities in women with a history of severe preeclampsia. *Am J Obstet Gynecol* 1999;180:1146-50.
 44. Dekker GA, de Vries JI, Doelitzsch PM, Huijgens PC, von Blomberg BM, Jakobs C, *et al.* Underlying disorders associated with severe early-onset preeclampsia. *Am J Obstet Gynecol* 1995;173:1042-8.
 45. Kraus FT, Arias F, Romero R, Joist H. Thrombophilia: A mechanism of disease in women with adverse pregnancy outcome and thrombotic lesions in the placenta. *J Matern Fetal Med* 1998;7:277-86.
 46. Mello G, Parretti E, Marozio L, Pizzi C, Lojaco A, Frusca T, *et al.* Thrombophilia is significantly associated with severe preeclampsia: Results of a large-scale, case-controlled study. *Hypertension* 2005;46:1270-4.
 47. Lin J, August P. Genetic thrombophilias and preeclampsia: A meta-analysis. *Obstet Gynecol* 2005;105:182-92.
 48. Horstkamp B, Lubke M, Kantenich H, Riess H, Buscher U, Lichtenegger W. Internal jugular vein thrombosis caused by resistance to activated protein C as a complication of ovarian hyperstimulation after *in-vitro* fertilization. *Hum Reprod* 1996;11:280-2.
 49. De Groot CJ, Bloemenkamp KW, Duvekot EJ, Helmerhorst FM, Bertina RM, Van Der Meer F, *et al.* Preeclampsia and genetic risk factors for thrombosis: A case-control study. *Am J Obstet Gynecol* 1999;181:975-80.
 50. Ozcan T, Rinder HM, Murphy J, Kohn C, Copel J, Magriples U. Genetic thrombophilia and thromboembolic complications. *Genetic thrombophilia and thromboembolic complications.* *Am J Obstet Gynecol* 2001;184:S189.
 51. Ganzevoort W, Rep A, De Vries JI, Bonsel GJ, Wolf H, PETRA-Investigators, *et al.* Relationship between thrombophilic disorders and type of severe early-onset hypertensive disorder of pregnancy. *Hypertens Pregnancy* 2007;26:433-45.

How to cite this article: Sooraj S. Prevalence of Thrombophilia in Patients with Adverse Pregnancy Outcome. *Int J Sci Stud* 2018;6(5):82-92.

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

Predictors of Visual Acuity in Traumatic Cataract

Shilpi Aggarwal, Sapan Phalod

Post Graduate Student, Department of Ophthalmology, Sri Aurobindo Medical College and Post Graduate Institute, Indore, Madhya Pradesh, India

Abstract

Aim: Traumatic cataract has many challenges. Strategic management to achieve the expected visual outcome is necessary. This study evaluates visual outcome and probable predictors of visual prognosis in traumatic cataract.

Materials and Methods: A retrospective study of 43 traumatic cataracts underwent meticulous evaluation for etiology, type of trauma, associated ocular comorbidities, surgical intervention, and final visual outcome. Cases were grouped as per Birmingham Eye Trauma Terminology System (BETTS) classification and managed accordingly with follow-up of 6 months. Secondary procedures were carried out when required. Probable predictors for visual prognosis were assessed and compared with final visual outcome.

Result: In traumatic cataract cases, open globe injury was observed more than closed globe. In mode of injury, iron rod and wooden chip were most common. Corneal tear was most common associated comorbidity and played an essential role in final visual outcome. BETTS classification was helpful to assess predictors for visual prognosis preoperatively.

Conclusion: Categorizing cases as per associated comorbidity and managing them according to BETTS played a key role in knowing probable predictors pre-operatively, which helped in assessing visual gain and explain realistic expectation to the patient.

Key words: Birmingham Eye Trauma Terminology System, Predictors, Traumatic cataract, Visual outcome

INTRODUCTION

Predictors of Visual Acuity [VA] in Traumatic Cataract

Ocular injuries result in approximately 19 million people blind unilaterally and 2.3 million people bilaterally^[1] with a prevalence of 2.4% in India.^[2]

Presentation of ocular trauma may vary as open or closed globe injury with one of the causes for diminished vision is traumatic cataract.^[3] Traumatic cataract can be isolated or associated with ocular comorbidities. They can be lens dislocation, subluxation, corneal tear, hyphema, uveal prolapse, angle recession, retinal detachment, choroidal rupture, retrobulbar hemorrhage, and globe rupture. This association of comorbidities is directly related to severity, type, and mode of injury.^[4]

Thus, associated comorbidities make the management different and challenging in every case.^[5] Primary procedures may not be sufficient to manage all comorbidities and required secondary procedures, and the time delay in such procedures affects visual improvement.^[6] Early careful assessment and categorizing each case using Birmingham Eye Trauma Terminology System (BETTS)^[7] simplify these difficult cases and help in understanding predictors for poor visual outcome, management, and prognosis preoperatively.^[8]

This study was undertaken to determine the factors affecting visual outcome in relation to associated ocular comorbidity and time interval between trauma to presentation, type, and mode of injury using BETTS classification.

MATERIALS AND METHODS

This is a mono-institutional retrospective study where 43 cases of traumatic cataract included with different modes of injury coming to ophthalmology department during June 2015–June 2017. The work has been approved by the ethical committee of our institute. Informed consents were taken. Collected data were recorded on a

Access this article online



www.ijss-sn.com

Month of Submission : 06-2018
Month of Peer Review : 07-2018
Month of Acceptance : 08-2018
Month of Publishing : 08-2018

Corresponding Author: Dr. Shilpi Aggarwal, 1936, Wright Town, Jabalpur, Madhya Pradesh, India. Phone: +91-9111727607.
E-mail: shilpiaggarg@gmail.com

standardized form and transferred to a structured database program for analysis (Excel Software, Microsoft Corp.).

All patients were evaluated and examined with detailed history including demographic information (patient age, sex, residence, and socioeconomic status), injury information (mechanism of injury, activity at the time of injury, object of injury, eye involved, VA, open-globe or closed-globe injury, and associated ocular injuries), and time interval between injury and presentation.

These collected data were grouped according to BETTS classification in open and closed globe injury.

Patients underwent detailed examination using a standard protocol. VA recorded using Snellen chart, and anterior segment evaluation was carried out using slit lamp. Photographic records were maintained for future assessment of ocular status. Posterior segment was assessed by an indirect ophthalmoscope, and in hazy optical media excluding severe ocular tissue damage cases, B-scan ultrasonography was performed.

Management strategies were followed according to the type of injury, mode of injury, time interval between injury and presentation of patient, presence of infection, inflammation, and associated ocular comorbidities.

Initial management was started according to the severity of ocular tissue damage, degree of inflammation, and infection. Topical and systemic antibiotics were started in infective cases with cycloplegics and intraocular pressure lowering drugs. In the absence of infection, systemic and topical corticosteroid was added. In cases requiring surgical management, surgery was scheduled after the control of inflammation and intraocular pressure.

In children <2 years, intraocular lens implantation as a part of the primary procedure was avoided.

Postoperatively, topical steroid, antibiotic, and cycloplegics were prescribed. Follow-up was done on 15th day, 30th day, 2nd month, 4th month, and 6th month for VA and anterior and posterior segment examination, and the details were recorded.

RESULTS

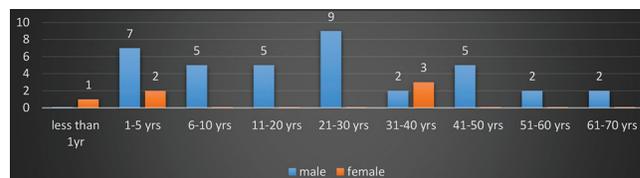
In 43 patients of traumatic cataract [Graph 1], gender distribution was 38 (88.37%) males and 5 (11.62%) females with mean age of 24 years, of which, the youngest patient was of 8 months and eldest was of 68 years. Majority patients were in the age group of 21–30 years, and all were male (9 [20.930%]).

In Table 1, the number of patients presented to our institute after trauma at different intervals is shown. Maximum 27 (62.79%) were reported in first 5 days followed by 14 (32.55%) cases in Group 2. No patient came in Groups 3 and 5. Only 1 (2.32%) case reported, respectively, in Groups 4 and 6. A higher number of cases reported in Groups 1 and 2 due to pain and diminution of vision. Average time interval between trauma and first consultation in the institute was 6 days.

In Graph 2, ocular trauma cases with traumatic cataract were divided according to BETTS classification. A total number of cases in this study were 43 (100%). They were divided into open globe injury (29 [67.44%]) and closed globe injury (14 [32.55%]). Open globe cases were again subdivided into laceration injury (28 [65.11%]) and rupture injury (1 [2.32%]). Patients having laceration were further divided into perforation injury (1 [2.32%]), penetrating injury (25 [58.13%]), and intraocular foreign body (2 [4.65%]). Closed globe injury cases were subdivided into lamellar laceration (1 [2.32%]) and contusion injury (13 [30.23%]).

Table 2 enumerates the etiology of trauma. A detailed history of injury was recorded to note down the etiology and to correlate it with different grades of injury. It was found that iron rod and wooden chip injury was the most common contributing 16.27% followed by road traffic accident (11.62%), firecracker (9.3%), scissor injury (6.9%), and iron wire (6.9%). Other less frequent causes were pencil tip (4.6%), iron nail (2.3%), and thorn injury (2.3%).

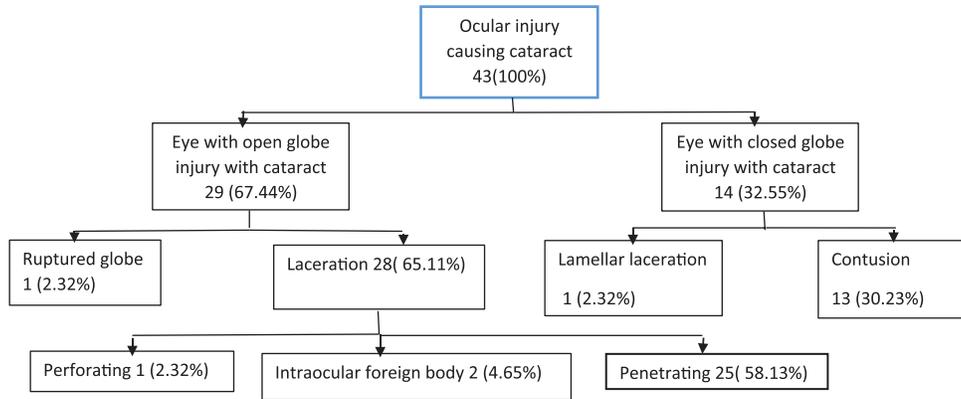
Table 3 shows the activity of patients which caused ocular injury. History helped to understand relationship of the severity of injury to activity while injury, and it was observed that most common activity was occupational work (25.58%)



Graph 1: Distribution of age and sex

Table 1: Time interval between injury and presentation

Groups	Number of days	Number of cases
Group 1	1–5 days	27 (62.79)
Group 2	6–10 days	14 (32.55)
Group 3	11–15 days	0 (0)
Group 4	16–20 days	1 (2.32)
Group 5	21–25 days	0 (0)
Group 6	26–30 days	1 (2.32)



Graph 2: Type of ocular trauma according to Birmingham Eye Trauma Terminology System classification

Table 2: Causes of trauma

Mode of injury	n (%)
Iron rod	7 (16.27)
Wooden chip	7 (16.27)
Scissors	3 (6.9)
Iron nail	1 (2.3)
Fire cracker	4 (9.3)
Thorn	1 (2.3)
Pencil tip	2 (4.6)
Iron wire	3 (6.9)
Cow horn	1 (2.3)
Stone	2 (4.6)
RTA	5 (11.62)
Wooden stick	4 (9.3)
Battery blast	1 (2.3)
Toy	2 (4.6)

Table 3: Activity during injury

Activity	n (%)
Fall	4 (9.3)
Fighting	2 (4.6)
Firework	3 (6.9)
Housework	5 (11.62)
Job work	11 (25.58)
Playing	11 (25.58)
RTA	5 (11.62)
Others	2 (4.6)

and ground activity such as playing (25.58%), followed by household job (11.62%), road traffic accident (11.62%), fall (9.3%), firework (6.9%), and fights (4.6%).

Table 4 enumerates the association of ocular comorbidities along with traumatic cataract. Corneal tear (60.46%) was the most common followed by anterior chamber shallowing (27.90%), uveal tissue prolapse (23.25%), and hyphema (20.93%).

In Table 5, surgical management in traumatic cataract was divided into primary and secondary procedures. It was different in each case which was according to associated

Table 4: Comorbidities with traumatic cataract at presentation

Comorbidity	Percentage
Corneal tear	60.46
AC shallow	27.90
Lens matter in anterior chamber	6.9
Hypopyon	2.3
Iridodialysis	6.9
Intraocular foreign body	4.6
Traumatic mydriasis	9.3
Retinal detachment	9.3
Corneal hazy	9.3
Hyphema	20.93
Vitreous matter in the anterior chamber	4.6
Uveal tissue prolapse	23.25
Posterior synechiae	9.3
Cystoid macular edema	2.3
Vitreous hemorrhage	6.9
Zonular dialysis	18.60

Table 5: Surgical management

Management	Primary procedure (%)	Secondary procedure (%)
Corneal tear repair	26 (60.46)	
Cortical matter removed	16 (37.20)	
Synechiolysis	16 (37.20)	5 (11.62)
Iridodialysis repair	12 (27.90)	4 (9.30)
FB removal	2 (4.6)	
ACIOL		1 (2.32)
Scleral fixation IOL		1 (2.32)
PCIOL	29 (67.44)	8 (18.60)
AC wash	15 (34.88)	
Vitrectomy	12 (27.90)	13 (30.23)

PCIOL: Posterior chamber intraocular lens, ACIOL: Anterior chamber intraocular lenses

comorbidities and severity of injury. Procedures required were undertaken as a primary or secondary procedure. Corneal tear repair (60.46%) was performed as a primary procedure. Cataract extraction with posterior chamber intraocular lens (67.44%), synechiolysis (37.20%), iridodialysis repair (27.90%), foreign body removal (4.6%), and vitrectomy (27.90%) was performed as a primary procedures.

The secondary procedure performed after primary corneal repair was synechiolysis (11.62%), iridodialysis repair (9.30%), anterior-chamber intraocular lenses (ACIOL) (2.32%), scleral-fixated IOL (2.32%), and vitrectomy (30.23%).

In Table 6, final visual outcome in relation to the type of injury was studied. Postoperatively, visual recovery was variable in different types of injuries. In 14 (56%) cases of penetrating, injury showed worst recovery of <1/60. Best visual gain was found in contusion type of injury with 6 (46.15%) improving to 6/36–6/18 and 4 (30.76%) improving to 6/12–6/6.

Table 7 lists the ocular comorbidities affecting final visual outcome. Patient with corneal scar, vitreous hemorrhage, retinal detachment, and aphakia had VA PL+/FCCF and patient with lesser comorbidities had good visual outcome up to 6/12–6/9.

DISCUSSION

Traumatic cataract management is always challenging as it is difficult to know and predict the final visual outcome.^[5] In such a situation it is very important to understand the predictors of visual outcome which helps to plan management strategy and to know visual prognosis.^[9] In our study, more of younger patients

with average age of 24 years was seen which was similar to Shah *et al.*^[10] Male dominance of 88.37% was seen similar to male dominance of 71% in Srivastava *et al.* study^[11] and 80% in Smith *et al.* study.^[12] The reason of the higher number of younger age cases with male predominance may be due to more exposure of outdoor activities such as playing or occupations related to the field.

The mean time interval between injury and presentation of the patient to institute was 6 days which was similar to observation made by Gogate *et al.*^[13] It was also noted that reporting of the patient was earlier in the severe grade of ocular injury which could be correlated to intolerable pain with gross diminution of vision.

It was helpful to classify patients accordingly to BETTS classification as it provides a clear definition for each type of injury. Open globe injuries were more common (67.44%) than closed globe injuries (32.55%) which was comparable with the study of Rizwan *et al.*^[14] (62.50% and 37.50%) and Gupta^[15] (52.77% and 47.23%). Among open globe injury, laceration injury (65.11%) was the most common. In closed globe injury, contusion injury (30.23%) was seen to be more common. Other studies have also used BETTS classification but had variable results.^[16]

It was observed by Thakkar *et al.*^[17] (RE - 46.43% and LE - 53.57%) and Greven *et al.*^[18] (RE - 45% and LE - 55%) that left eye injury was more than right eye may be due to physiological reflexes by which right (mostly dominant eye) escapes injuries, but in our study, such preponderance was not observed (RE - 55.81% and LE - 44.18%).

There was a direct correlation of the type of injury to the mode of injury. Mode of injury by the sharp or pointed object was the cause of open globe injury, while injury by blunt objects with considerable force such as iron rod and wooden stick was related to closed globe trauma. Of all modes of injury, close globe injury by iron rod (16.27%) and perforating injury by wooden chip (16.27%) was found to be the most common. Studies had different frequencies for modes of injury involved in traumatic cataract. In Gogate *et al.* study,^[13] wooden stick was found to be the most common mode of injury.

Mode of injury was found to be correlated to activity during trauma. In household injury, females and children were more commonly traumatized by objects such as scissors, pencil tip, and toys, resulting in penetrating injury. In outdoor injury, iron rod and wooden stick were the contributing factors. Most common activity leading to

Table 6: Final visual recovery in different types of injury

Type of injury	Parameters	Vision	After	Recovery
	<1/60	4/60–6/60	6/36–6/18	6/12–6/6
Penetrating	14 (56)	1 (4)	5 (20)	5 (20)
Perforating			1 (100)	
IOFB	2 (100)			
Rupture	1 (100)			
Lamellar laceration	1 (100)			
Contusion	1 (7.69)	2 (15.38)	6 (46.15)	4 (30.76)

Table 7: Final visual impairment in correlation with ocular comorbidity

Final visual outcome	Comorbidities
HM+, FC, PL+	Corneal scar (70.58%), Vitreous hemorrhage (29.41%), Retinal detachment (58.88%), Aphakia (23.52%), Foreign body (11.76%)
6/60–6/36	Corneal scar (66.66%), Vitreous hemorrhage (16.66%), Retinal detachment (16.66%)
6/24–6/18	Corneal scar (50%), Vitreous hemorrhage (12.5%), Retinal damage (12.5%)
6/12–6/9	Nebular corneal opacity (30%), CME (10%)

injury was outdoor activities such as occupational trauma at field (25.58%) and playing in ground (25.58%) which was similarly reported by Gogate *et al.*^[13]

Association of ocular tissue trauma along with traumatic cataract was a common observation. In our study, most commonly associated comorbidity was corneal tear (60.46%) followed by anterior chamber shallowing (27.9%), vitreous hemorrhage (6.9%), and hyphema (20.93%). Other associated ocular collateral damages were retinal detachment (9.3%), anterior capsule tear (6.9%), lens matter in the anterior chamber (6.9%), iridodialysis (6.9%), intraocular foreign body (4.6%), and hypopyon (2.3%). Other studies also have documented comparable association of ocular tissue injury with traumatic cataract.^[19,20] Corneal tear was the most common comorbidity in our study, causing corneal scar which was associated with poor visual outcome which was also observed in a study of Munndada *et al.*^[21]

We have managed the cases according to coexisting ocular comorbidities which helped in good visual outcome. Primary procedures were cortical matter removal (37.20%), anterior chamber wash (34.88%), vitrectomy (27.90%), and intraocular foreign body removal (4.6%). Synechiolysis was done as a primary procedure in 37.20% of cases and as secondary procedure in 11.62% of cases. Similarly, iridodialysis repair as the primary procedure was performed in 27.90% and as the secondary procedure in 9.30%. Secondary IOL implantation in the form of ACIOL (one case) and scleral fixated IOL (one case) was performed in cases who left aphakic due to the lack of support of capsular bag. Only one patient had poor VA of HM+ due to retinal detachment and was kept aphakic. One case with focal lenticular opacity not involving visual axis was treated with miotic, and refractive correction was given.

After 6 months of treatment, VA was compared on the basis of the type of injury. It was seen that 1/60 or less was achieved in 56% of cases of perforating type of injury, all cases of intraocular foreign body, and lamellar laceration. Contusion type of closed globe injury had visual recovery of 6/6 in 30.76% of cases. Hence, in our series, perforating visual outcome had poor visual outcome. Similarly, Shah *et al.*^[22] observed better visual gain in closed globe injury.

In our study, we tried to find the associated comorbidities which were responsible for decreased visual gain. We found that cases having VA of HM+/PL+ were related to corneal scar (70.58%), vitreous hemorrhage (29.41%), retinal detachment (58.88%), aphakia (23.52%), and intraocular

foreign body (11.76%). Cases with lesser ocular damage were having better VA acuity of >6/12.

Categorizing cases and managing them according to ocular comorbidities played important role in achieving better restoration of vision in our study.

We also observed that classifying different types of injury according to BETTS classification, evaluating mode of injury, associated ocular damage, initial vision, comorbidities affecting final visual outcome helps in assessing visual gain and realistic expectation in cases of traumatic cataract.

REFERENCES

1. Schein OD, Hibberd PL, Shingleton BJ, Kunzweiler T, Frambach DA, Seddon JM, *et al.* The spectrum and burden of ocular injury. *Ophthalmology* 1988;95:300-5.
2. Katz J, Tielsch JM. Lifetime prevalence of ocular injuries from the Baltimore eye survey. *Arch Ophthalmol* 1993;111:1564-8.
3. Shah MA, Shah SM, Applewar A, Patel C, Shah S, Patel U, *et al.* Ocular Trauma score: A useful predictor of visual outcome at six weeks in patients with traumatic cataract. *Ophthalmology* 2012;119:1336-41.
4. Meng Y, Yan H. Prognostic factors for open globe injuries and correlation of ocular trauma score in Tianjin, China. *J Ophthalmol* 2015;2015:345764.
5. Kuhn F. Traumatic cataract: What, when, how. *Graefes Arch Clin Exp Ophthalmol* 2010;248:1221-3.
6. Shah MA, Shah SM, Shah SB, Patel UA. Effect of interval between time of injury and timing of intervention on final visual outcome in cases of traumatic cataract. *Eur J Ophthalmol* 2011;21:760-5.
7. Kuhn F, Morris R, Witherspoon CD, Mester V. The Birmingham eye trauma terminology system (BETT). *J Fr Ophthalmol* 2004;27:206-10.
8. Kanski JJ. *Clinical Ophthalmology: A Systematic Approach*. London: Butterworths; 1989. p. 257-8.
9. Sharma AK, Aslami AN, Srivastava JP, Iqbal J. Visual outcome of traumatic cataract at a tertiary eye care centre in North India: A Prospective study. *J Clin Diagn Res* 2016;10:NC05-8.
10. Shah MA, Shah SM, Shah SB, Patel CG, Patel UA. Morphology of traumatic cataract: Does it play a role in final visual outcome? *BMJ Open* 2011;1:e000060.
11. Srivastava U, Lalramhluri R, Rawat P, Bhaire V. Clinical evaluation of post traumatic cataract in tertiary care hospital. *Int J Sci Res Publication* 2014;4:1-6.
12. Smith D, Wrenn K, Stack LB. The epidemiology and diagnosis of penetrating eye injuries. *Acad Emerg Med* 2002;9:209-13.
13. Gogate P, Sahasrabudhe M, Shah M, Patil S, Kulkarni A. Causes, epidemiology, and long-term outcome of traumatic cataracts in children in rural India. *Indian J Ophthalmol* 2012;60:481-6.
14. Cheema RA, Lukaris AD. Visual recovery in unilateral traumatic paediatric cataract treated with posterior chamber lens and anterior vitrectomy in Pakistan. *Int Ophthalmol* 1999;23:85-9.
15. Gupta RC, Vyas TN, Singh MP, Bihari V. Traumatic Cataract: P/C IOLs After Curette- Aspiration or Lensectomy. In: *Indian Ophthalmology today*. Proceedings 51st annual conference 1993. Aravali publishers. p. 235-7.
16. Shukla B, Agrawal R, Shukla D, Seen S. Systematic analysis of ocular trauma by a new proposed ocular trauma classification. *Indian J Ophthalmol* 2017;65:719-22.
17. Thakker MM, Ray S. Vision-limiting complications in open-globe injuries. *Can J Ophthalmol* 2006;41:86-92.
18. Greven CM, Collins AS, Slusher MM, Weaver RG. Visual results, prognostic indicators, and posterior segment findings following surgery

Aggarwal and Phalod: Predictors of Visual Acuity in Traumatic Cataract

- for cataract/lens subluxation-dislocation secondary to ocular contusion injuries. *Retina* 2002;22:575-80.
19. Pieramici DJ, Au Eong KG, Sternberg P Jr., Marsh MJ. The prognostic significance of a system for classifying mechanical injuries of the eye (globe) in open-globe injuries. *J Trauma* 2003;54:750-4.
 20. Cruvinel Isaac DL, Ghanem VC, Nascimento MA, Torigoe M, Kara-José N. Prognostic factors in open globe injuries. *Ophthalmologica* 2003;217:431-5.
 21. Munnada R, Shinde S, Pathan MS, Khaled M. Badaam observational study of ocular damage and visual loss associated with traumatic cataract patients at tertiary care hospital in Aurangabad Maharashtra. *Int Med J* 2014;1:35-6.
 22. Shah M, Shah S, Khandekar R. Ocular injuries and visual status before and after their management in the tribal areas of Western India: A historical cohort study. *Graefes Arch Clin Exp Ophthalmol* 2008;246:191-7.

How to cite this article: Aggarwal S, Phalod S. Predictors of Visual Acuity in Traumatic Cataract. *Int J Sci Stud* 2018;6(5):93-98.

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

Parents' Management of Acute Upper Respiratory Tract Infections in Children, Al Ahsa, Saudi Arabia

Zainab Al Shuhayb¹, Sukainah Al Haddad¹, Khalid Al Yahya², Rabel Khawaja³

¹Student, College of Medicine, King Faisal University, Al Ahsa, Saudi Arabia, ²Assistant Professor, Department of Otolaryngology, Head and Neck Surgery, College of Medicine, King Faisal University, Al Ahsa, Saudi Arabia, ³Assistant Professor, Department of Family & Community Medicine, College of Medicine, King Faisal University, Al Ahsa, Saudi Arabia

Abstract

Introduction: Although upper respiratory tract infections (URTIs) are usually self-limiting and numerous off-the-counter medications used have no effect on outcome (2), self-medication is quite common in the pediatric population, posing a great risk of inappropriate use and subsequently increasing the risk for mistreatment and adverse effects.

Purpose: This study aims to comprehensively investigate the prevalence, practices, and factors associated with medicine use in the management of symptoms of acute URTIs in children aging 12 years or younger in Al Ahsa, Kingdom of Saudi Arabia.

Methods: This is a cross-sectional study conducted among 344 randomly selected children. Data were collected from their caregivers using an online-based, self-administered questionnaire.

Results: 65% of children had 1–3 episodes of URTI per year, followed by 24% who had 4–6 episodes per year. Although 13% of parents had no idea what their child was going through, 72% of children received treatment for these symptoms, in which 77% were prescribed by the doctor, followed by 16% guardian suggestion and 14% pharmacist. The treatment given was 76% antipyretics, 39% antibiotics, 34% decongestant, and 26% cough suppressants and antihistamines. The majority (79%) children took the correct dose for full duration; however, 20% did not. 50% of participants used more than one medicine at one time to treat their children URTI. Most of the children (91%) improved on using the medicines prescribed. 79% of parents are aware of the risks associated with taking drug without prescription and 91% consider that certain drugs should not be given to children. Surprisingly, 94% would take their child to doctor if they develop URTI, but 34% will advise a relative/friend to use certain treatments.

Conclusion: The results obtained indicate good parents' knowledge and practice regarding proper management of URTIs for the majority of participants.

Key words: Al Ahsa, Children, Parents, Saudi Arabia, Self-medication, Upper respiratory tract infections

INTRODUCTION

Upper respiratory tract infections (URTIs) are one of the most commonly encountered diseases in both pediatric and adult populations.^[1] Although URTIs are rarely fatal, they compose a great economic burden on health systems.^[2] 20–30% of all hospital admissions and 30–60% of practitioner visits in the developing countries are related

to respiratory tract infections.^[3-5] URTIs have a high cost to society, leading to unnecessary absence from school and unnecessary medical care.^[1]

Although URTIs are usually self-limiting and numerous off-the-counter medications used have no effect on outcome,^[2] self-medication and use of medicines without a prescription are quite common.^[6-8] Self-medication is the taking of drugs, herbs, or home remedies on one's own initiative, or on the advice of another person, without consulting a doctor, as traditionally defined.^[9] Common sources of self-medication include friends, families, pharmacists, or even previously prescribed drugs.

When it comes to pediatric population, such decision is made by the caretaker and it is primarily influenced by

Access this article online



www.ijss-sn.com

Month of Submission : 06-2018
Month of Peer Review : 07-2018
Month of Acceptance : 08-2018
Month of Publishing : 08-2018

Corresponding Author: Zainab Al Shuhayb, College of Medicine, King Faisal University, AL Ahsa, Saudi Arabia. Phone: +91-966500642701. E-mail: Zainab.alshuhaib@icloud.com

parents' knowledge, beliefs, and attitude toward self-medication. Unfortunately, medicines used for disease management in pediatrics are commonly obtained without a prescription, posing a great risk of inappropriate use, and subsequently increasing the risk for mistreatment and adverse effects.^[10]

Since most published studies in the Kingdom of Saudi Arabia exclusively assessed antibiotics use and the role of parents' in the management,^[11-12] this study aims to comprehensively investigate the prevalence, practices, and factors associated with medicine use in the management of symptoms of acute URTIs in children aging 12 years or younger in Al Ahsa, Kingdom of Saudi Arabia.

METHODS

Study Type

This is a cross-sectional study conducted in Al Ahsa, Saudi Arabia, from Dec 1, 2017, to May 1, 2018.

Study Size and Population

A total of 344 parents of neonates, infants, and children from birth to 12 years old, who have a history of at least one episode of acute upper respiratory tract infection during their lifetime, were selected. Exclusion criteria include (1) children older than 12 years and (2) children having comorbidities that interfere with the parents' management of acute upper respiratory tract infection.

The sample size for the study was calculated through Open Source Epidemiologic Statistics for Public Health using $[(DEFF \cdot Np(1-p)) / ((d^2 / Z_{21-\alpha/2}^2 \cdot (N-1) + p \cdot (1-p)))]$ formula. It was estimated that 344 patients will be needed for the study. The prevalence of URTI was taken from a previous study^[13] with 95% confidence level, z corresponding to two-tailed significance level 1.96, and marginal error of 0.05.

Data Collection

The data were measured using a self-administered web-based questionnaire. The questionnaire is based on Ocan *et al.*^[14] study, which initially derived their questionnaire from the literature review and from articles by Morgan *et al.*^[15] and Ocan *et al.*^[16] and then further modified using the outcome of the pre-test. The study has three main measures which are: (1) Parent sociodemographic data, (2) children sociodemographic data and medical history, and (3) medicine use practice in the management of acute upper respiratory tract infection. The questionnaire was supplemented by new items not present in the original questionnaire (14), for suitability for the region, religion and culture in the area.

Statistical Analysis

Statistics were performed using the IBM SPSS Statistics version 22.0 software. Quantitative variables were presented as mean and standard deviation and number with a percentage for qualitative variables. For correlation with categorical variables, Chi-square test was used with the results presented in crosstabs tables and clustered bar graphs and t -test or one-way ANOVA for correlation with continuous variables, with the result presented in tables. P value of <0.05 was considered as statistically significant.

Ethical Statement

Ethical clearance was obtained from King Faisal University Research Ethics Committee. Written informed consent was obtained as well from the participants in the introduction web page before involvement in the study.

RESULTS

The results suggest that majority (37%) of the participants were between age 26 and 33 years followed by 29% who belonged to the age group of 34–41 years as shown in Table 1. More than half of the participants (60%) were females followed by 40% of males. Almost all the participants were Muslims and majority were married (96.5%). 29% of participants had more than 4 children followed by 24% who had 2 children, 23% who had 3 children and 23% who had 1 child only. 68% of the participants belonged to the urban area followed by 32% belonging to rural. Approximately 66% of the subjects had completed their graduation and 27% were secondary pass. However, 40% of them were unemployed and 32% were government employees. Majority of the participants had medium socioeconomic status followed by 12% belonging to lower class. Majority (83%) of them did not have any chronic illness.

Regarding demographics of a child, majority (53%) of them were between age 1 and 3 years, followed by 17% belonging to 4–8 years and 11% belonging to 9–12 years of age. Approximately 58% were male children and 42% were female children. However, 53% population of children in the study were the first child in their family and 65% at least have 1–3 episode of URTI per year, followed by 24% who have 4–6 episodes per year. Majority of the children (85%) were carrier of sickle cell disease with no chronic illness at all. Vaccine coverage was done in 94% of the children; however, 6% were not vaccinated.

Table 2 suggests the reported disease condition which was most common in the study population. Approximately 66% of children have cough, 61% had runny nose along with fever, and 45% had nasal blockage. The most probable cause for these symptoms as per perceived by parents was

Table 1: Demographics

Demographics	n (%)
Age of parent	
18–25 years	50 (14)
26–33 years	127 (37)
34–41 years	101 (29)
More than 41 years	66 (19)
Gender of parent	
Male	138 (40)
Female	206 (60)
Religion	
Muslim	343 (100)
Non-Muslim	1
Marital status	
Single	5 (1.5)
Married	332 (96.5)
Divorced	4 (1.2)
Widow	3 (0.9)
Number of children	
1	81 (23)
2	83 (24)
3	80 (23)
≥4	100 (29)
Residence	
Urban	233 (68)
Rural	111 (32)
Level of education	
Primary	3 (1)
Elementary	20 (6)
Secondary	93 (27)
Graduate	226 (66)
Occupation	
Student	32 (9)
Government employee	110 (32)
Private employee	65 (19)
Unemployed	137 (40)
Socioeconomic status	
Low	43 (12)
Medium	286 (83)
High	15 (4)
Chronic illness	
Yes	60 (17)
No	284 (83)
Age of child	
<1–3 years	142 (53)
4–8 years	133 (17)
9–12 years	69 (11)
Gender	
Male	198 (58)
Female	146 (42)
Ranking	
First child	181 (53)
Second child	58 (17)
Third child	37 (11)
Fourth and beyond	68 (20)
Episodes of acute upper respiratory tract infections per year	
1–3	223 (65)
4–6	82 (24)
7–9	24 (7)
10 or more	15 (4)
Sickle cell anemia	
Affected	14 (4)
Carrier	293 (85)
Not affected	37 (11)
Chronic illness	
Yes	294 (15)
No	50 (85)
Vaccine	
Yes	323 (94)
No	21 (6)

Table 2: Reported disease conditions of the children

Question	Description of answer	Proportion (%)
Symptoms the child usually have?	Runny nose	211 (61)
	Nasal blockage	156 (45)
	Sneezing	123 (36)
	Cough	229 (66)
	Throat pain	136 (39)
	Difficulty swallowing	70 (20)
	Fever	211 (61)
	Malaise	92 (27)
	Loss of appetite	114 (33)
	Rapid breathing	34 (10)
The most probable cause for these symptoms is?	Phlegm	134 (39)
	Common cold	260 (75)
	Rhinitis	45 (13)
	Pneumonia	24 (7)
	Asthma	30 (9)
	Rhinosinusitis	1 (1)
Does the child receive treatment for the symptoms?	I do not know	44 (13)
	Yes	248 (72)
If yes, who recommend this treatment?	No	93 (27)
	I do not know	4 (1)
What medicine does the child receive?	Guardian	57 (16)
	Doctor	265 (77)
	Pharmacist	48 (14)
	Family/friends	9 (3)
	Websites	7 (2)
	Social media	2 (1)
	Other	42 (12)
	Antihistamine	89 (26)
	Antipyretic	264 (76)
	Decongestant	119 (34)
From where you get the medicine?	Cough syrup	90 (26)
	Anti-phlegm	88 (25)
	Amoxicillin	136 (39)
	Azithromycin	
	Trimethoprim	
	Other	14 (4)
	Pharmacy	91 (26)
	Hospital	281 (81)
	Herbal remedy	1 (1)
	Home pharmacy	22 (6)
Home remedy	6 (2)	
Family/friends	1 (1)	
Other	16 (5)	

common cold (75%) followed by 13% rhinitis, and 13% of parents had no idea what their child was going through. However, 72% of children received treatment for these symptoms and 77% were prescribed by the doctor, followed by 16% guardian suggestion and 14% by pharmacist. The treatment given was 76% antipyretics, 39% antibiotics, 34% decongestant, and 26% cough suppressants and antihistamines.

The practice for drug use is summarized in Table 3, and the results suggest that majority (79%) children took the correct dose for full duration; however, 20% did not take proper dose of the prescribed medicine. Approximately 32% of participants discarded the leftover drug and 21% kept it as

left over. 50% of participants used more than one medicine at one time to treat their children URTI. Most of the children (91%) improved on using the medicines prescribed. 79% of parents are aware of the risks associated with taking drug without prescription, and 91% consider that certain drugs should not be given to children. Surprisingly, 94% would take their child to doctor if they develop URTI, but 34% will advise a relative/friend to use certain treatments.

For the association between demographic factors and drug use, age was significant ($P = 0.01$) for one components of 9 questions [Table 4]. Similarly, level of education had also shown significance toward one question $P = 0.03$.

Regarding marital status, two questions showed significant values, i.e., did the child receive more than one medicine at one time ($P = 0.04$) and would you advise a relative/friend to use certain treatments ($P = 0.02$). Whereas, occupation was significantly associated with three components, i.e., did you know the risks of taking drug without prescription in children ($P = 0.00$), do you think some medicines should not be used for children ($P = 0.01$), and would you advise a relative/friend to use certain treatments ($P = 0.00$).

DISCUSSION

Kunin *et al.* defined self-medication as self-administering inadequate doses of non-prescription medicines before doctors' diagnosis.^[17] Bi *et al.* found that the act of self-medication may lead to negative consequences to the

child such as growth retardation, drug resistance, and unbalanced bacteria distribution.^[18] Previous studies have been done to evaluate the extent of self-medication by parents to their children. Akici *et al.*, in Turkey, found that approximately 60% of parents had self-medicated their children before doctor visit.^[19] Likewise, Bi *et al.* found that 59% of children in China had been self-medicated by their parents.^[18] Moreover, Grigoryan *et al.* found that acute URTIs were the most common reason in Europe for parent's self-medication to their children.^[20] Self-medication is an important issue in Saudi Arabia^[21] and several adjacent countries such as Iran,^[22] Jordan,^[23,24] and Sudan.^[25] In our study, 72% of children received treatment for acute upper respiratory tract infection symptoms, of which 77% were prescribed by the doctor, followed by 16% guardian suggestion and 14% by pharmacist. Similarly, Alrafiaah *et al.* assessing Saudi parent's awareness of antibiotics role in upper respiratory tract infection in children reveal that the majority of parents identified their physicians as being their main source of information regarding antibiotic use,^[12] as well as Rousounides *et al.*,^[26] which stated that most of the parents acknowledged their pediatrician as the main source of information regarding use and misuse of antibiotics, showing parent's trust and confident in their doctors regarding their children health. Furthermore, Alrafiaah *et al.* stated that some participants would use antibiotics based on pharmacists' recommendations.^[12] Similarly, a Greek study showed that a substantial proportion of antibiotic outpatient use is attributed to over-the-counter purchase, while in another study involving pharmacists, it

Table 3: Drug use practices in the treatment of illnesses in children in household

Statements	Yes (%)	No (%)
The child takes the medicine in the correct dose and for full duration	260 (79)	70 (20)
Discard left over medicine	110 (32)	72 (21)
The child receives more than one medicine at one time?	162 (50)	162 (50)
Child improved on the medication	301 (91)	29 (9)
What did you do when child did not improve?		
Consult doctor	4 (1)	
Change medicines	1 (1)	-
Used same medicine	2 (1)	
Herbal remedies	2 (1)	
Other	335 (97)	
Do you know the risks of taking drug without prescription in children?	273 (79)	71 (21)
Risks associated with drug without prescription		
Drug overdose	23 (7)	
Complications	79 (23)	-
Fatigue	7 (2)	
Kidney failure	9 (3)	
Allergy	19 (5)	
Drug resistance	8 (2)	
GI disturbance	6 (2)	
Drug interaction	1 (1)	
Do you think some medicines should not be used for children?	313 (91)	31 (9)
Can you name some of the medicine that should not be used for children?	109 (32)	235 (68)
If the child has symptoms of upper respiratory tract infection in the future, would you like to visit a doctor	324 (94)	20 (6)
Would you advise a relative/friend to use certain treatments?	119 (34)	225 (65)

Table 4: Association between demographic factors and drug use

Age* drug use	Yes	No	P value
Would you advise a relative/friend to use certain treatments?	119	225	0.01
Marital status* drug use			
Did the child receive more than one medicine at one time?	162	162	0.04
Would you advise a relative/friend to use certain treatments?	119	225	0.02
Level of education* drug use			
Left over medicine discarded	110	72	0.03
Occupation* drug use			
Did you know the risks of taking drug without prescription in children?	273	71	0.00
Do you think some medicines should not be used for children?	313	31	0.01
Would you advise a relative/friend to use certain treatments?	119	225	0.00

was illustrated that over-the-counter purchase of antibiotics is easy.^[26]

Parent's knowledge, attitude, and behavior toward self-medication may show a significant variation in terms of geographical locations, social behaviors, cultural factors, and demographics such as age, educational level, employment, and marital status, all of which have been previously identified by other studies as important factors related to parent's self-medication and antibiotic consumption. Likewise, a recent study illustrates the significant association between demographics and parents KAPs toward management of symptoms of URTIs,^[26] in which older parental age and educational level significantly correlated with correct parental knowledge, attitudes, and practices on wise use of antibiotics during childhood URTIs. On the other hand, Bi *et al.* studied Chinese parent's self-medication and concluded that mothers with higher level of education are more likely to self-medicate their child, parental self-medication usually increases with the age of the child, and severity of disease was related to parental self-medication (i.e., when the diseases were not serious self-medication and antibiotics misuse are more likely to occur).^[18] Our results were in concordance with the study of.^[26] However, in which people with lower level of education had a tendency toward keeping drugs left over (66.77% of participants with primary school education compared to 22.1% of college degree holders), suggesting that people with higher level of education have a better practice toward leftover drug. Moreover, our study shows that 70.8% and 75.7% of the study population aging between 26 and 33 years of age and people aging more than 41 years, respectively, will not advice friends neither relatives of using certain treatment for their children to treat an URTI signifying a healthier practice as compared to other age groups.

Moreover, in our study, occupation was found to be significantly associated with parents' KAPs toward management of acute upper respiratory tract infection in their children, in which our results suggest that the private sector employees are the least knowledgeable about risks of using non-prescription drugs and drugs that should not be used in children.

Our study reveals that most common treatments given by parents to treat their child's illness were antipyretics (76%), antibiotics (39%), decongestant (34%), and cough suppressants and anti-histamines (26%). Ocan *et al.* study had similar outcomes for the use of antibiotics in treating acute URTIs in children accounting for 44.8%. Another study shows that 67.3% of the study population expected that the possible treatment suggested by the pediatrician for URTI in children would be antipyretics and analgesics, and 60.5% also chose antibiotics as the treatment that they anticipated would be recommended by their pediatrician. This can explain parents' choice of these medications to self-medicate their children.^[12]

Furthermore, Sorkhou *et al.* conducted a study in Kuwait to assess the factors encouraging the antibiotic misuse and found that physicians feel obliged to prescribe antibiotics to their patients assuming the patients' or guardians' desire for such medication.^[27] However, this irrational prescribing behavior may encourage parents' false idea of antibiotics to treat URTIs and its side effects. Self-medication with antibiotics is more common in the developing countries due to factors such as ready availability of antibiotics without prescription, the unrestricted access to antibiotics, lack of regulation over drugs, and physicians and pharmacists prescribing and dispensing antibiotics without regard to the cause of infection.^[18,21,28]

CONCLUSION

The results obtained indicate good parents' knowledge and practice regarding proper management of URTIs for the majority of participants. However, interventions are still needed. We suggest health education campaigns, professional education, and the implementation of new policies that will ideally help in raising awareness of the public about the proper management of URTIs and limit unnecessary use of medications. Since this study is the first of its own in the region, further studies must be conducted on a larger sample of the population to confirm the results.

ACKNOWLEDGMENT

We would like to thank Bayan AL Shuhayb and Sajjad AL Haddad for their work on data collection.

LIMITATIONS

The cross-sectional design of the study is susceptible to recall bias, which might affect the accuracy of the result.

REFERENCES

- Cotton M, Innes S, Jaspan H, Madide A, Rabie H. Management of upper respiratory tract infections in children. *S Afr Fam Pract* (2004) 2008;50:6-12.
- West J. Acute upper airway infections. *Br Med Bull* 2002;61:215-30.
- Yousif TK, Khaleq BA. Epidemiology of acute respiratory tract infections (ARI) among children under five years old attending Tikirit general teaching hospital. *Middle East J Fam Med* 2006;4:4-23.
- Ujunwa FA, Ezeonu CT. Risk factors for acute respiratory tract infections in under five children in Enugu Southeast Nigeria. *Ann Med Health Sci Res* 2015;4:95-9.
- Leowski J. Mortality from acute respiratory infections in children under 5 years of age: Global estimates. *World Health Stat Q* 1986;39:138-44.
- Saeed AA. Self-medication among primary care patients in Farazdak clinic in Riyadh. *Soc Sci Med* 1988;27:287-9.
- Vanden Eng J, Marcus R, Hadler JL, Imhoff B, Vugia DJ, Cieslak PR, *et al.* Consumer attitudes and use of antibiotics. *Emerg Infect Dis* 2003;9:1128-35.
- Borg MA, Scicluna EA. Over-the-counter acquisition of antibiotics in the Maltese general population. *Int J Antimicrob Agents* 2002;20:253-7.
- Hernandez-Juyol M, Job-Quesada JR. Dentistry and self-medication: A current challenge. *Med Oral* 2002;7:344-7.
- Cruz MJ, Dourado LF, Bodevan EC, Andrade RA, Santos DF. Medication use among children 0-14 years old: Population baseline study. *J Pediatr (Rio J)* 2014;90:608-15.
- Alumran A, Hurst C, Hou X. Antibiotics overuse in children with upper respiratory tract infections in Saudi Arabia: Risk factors and potential interventions. *Clin Med Diagn* 2012;1:8-16.
- Alrafiaah AS, Alqarny MH, Alkubedan HY, AlQueffie S, Omair A. Are the Saudi parents aware of antibiotic role in upper respiratory tract infections in children? *J Infect Public Health* 2017;10:579-85.
- Al-Khaldi YM, Diab MM, Al-Gelban KS, Al-Asmari AS, Al-Amin S, Al-Shahrani MS, *et al.* Prescribing patterns for acute respiratory infections in primary health care, Aseer region, Saudi Arabia. *J Family Community Med* 2005;12:121-6.
- Ocan M, Aono M, Bukirwa C, Luyinda E, Ochwo C, Nsambu E, *et al.* Medicine use practices in management of symptoms of acute upper respiratory tract infections in children (≤ 12 years) in Kampala city, Uganda. *BMC Public Health* 2017;17:732.
- Morgan DJ, Okeke IN, Laxminarayan R, Perencevich EN, Weisenberg S. Non-prescription antimicrobial use worldwide: A systematic review. *Lancet Infect Dis* 2011;11:692-701.
- Ocan M, Bwanga F, Bbosa GS, Bagenda D, Waako P, Ogwal-Okeng J, *et al.* Patterns and predictors of self-medication in northern Uganda. *PLoS One* 2014;9:e92323.
- Kunin CM, Lipton HL, Tupasi T, Sacks T, Scheckler WE, Jivani A, *et al.* Social, behavioral, and practical factors affecting antibiotic use worldwide: Report of task force 4. *Rev Infect Dis* 1987;9 Suppl 3:S270-85.
- Bi P, Tong S, Parton KA. Family self-medication and antibiotics abuse for children and juveniles in a Chinese city. *Soc Sci Med* 2000;50:1445-50.
- Akici A, Kalaça S, Uğurlu MU, Oktay S. Prescribing habits of general practitioners in the treatment of childhood respiratory-tract infections. *Eur J Clin Pharmacol* 2004;60:211-6.
- Grigoryan L, Burgerhof JG, Haaijer-Ruskamp FM, Degener JE, Deschepper R, Monnet DL, *et al.* Is self-medication with antibiotics in Europe driven by prescribed use? *J Antimicrob Chemother* 2007;59:152-6.
- Bawazir S. Prescribing pattern at community pharmacies in Saudi Arabia. *Int Pharm J* 1992;6:222-4.
- Sarahroodi S, Arzi A, Sawalha A, Ashtarinezhad A. Antibiotics self-medication among southern Iranian university students. *Int J Pharm* 2010;6:48-52.
- Al-Azzam SI, Al-Husein BA, Alzoubi F, Masadeh MM, Al-Horani MA. Self-medication with antibiotics in Jordanian population. *Int J Occup Med Environ Health* 2007;20:373-80.
- Al-Bakri AG, Bustanji Y, Yousef AM. Community consumption of antibacterial drugs within the Jordanian population: Sources, patterns and appropriateness. *Int J Antimicrob Agents* 2005;26:389-95.
- Awad A, Eltayeb I, Matowe L, Thalib L. Self-medication with antibiotics and antimalarials in the community of Khartoum state, Sudan. *J Pharm Pharm Sci* 2005;8:326-31.
- Rousounidis A, Papaevangelou V, Hadjipanayis A, Panagakou S, Theodoridou M, Syrogiannopoulos G, *et al.* Descriptive study on parents' knowledge, attitudes and practices on antibiotic use and misuse in children with upper respiratory tract infections in Cyprus. *Int J Environ Res Public Health* 2011;8:3246-62.
- Sorkhou I, Al-Qallaf B, Hajiah A, Al-Sheibani H, Bayoomi A, Mustafa A. Perceptions of patients attending primary care in Kuwait regarding upper respiratory tract infections. *Kuwait med J* 2002;34:272-5.
- Cebotarencu N, Bush PJ. Reducing antibiotics for colds and flu: A student-taught program. *Health Educ Res* 2007;23:146-57.

How to cite this article: Al Shuhayb ZA, Al Haddad S, Al Yahya K, Khawaja R. Parents' Management of Acute Upper Respiratory Tract Infections in Children, Al Ahsa, Saudi Arabia. *Int J Sci Stud* 2018;6(5):99-104.

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

Clinical Study on Prophylactic and Therapeutic Management of Thrombophilia in Adverse Pregnancy Outcome Patients

S Sooraj

Assistant Professor, Department of Obstetrics and Gynaecology, Government Medical College, Kozhikode, Kerala

Abstract

Background: There is a growing view that inherited and acquired thrombophilia may predispose to adverse pregnancy outcome (APO). APOs such as pregnancy loss, preeclampsia, and intrauterine growth retardation (IUGR) are associated with thrombotic mechanisms and thrombophilia, *vice versa*. The use of low-molecular-weight heparin (LMWH) has been studied in women with previous APO; however, the reports are inconsistent. This may be due to heterogeneity of the study groups and insufficient classification of the entire disease processes to guide the treatment guidelines. It is also due to the variation in gestational age at the start-up of LMWH treatment which is equally important. In the absence of other effective treatments and its accepted safety in pregnancy, LMWH was used in this study to analyze the results.

Aim of the Study: This study aims to evaluate the overall efficacy of LMWH and low-dose aspirin in the management of thrombophilia.

Materials and Methods: A total of 69 patients with a history of APO with thrombophilia were included to evaluate the overall efficacy of LMWH and low-dose aspirin in their management. Thrombophilic studies done: Anticardiolipin antibodies test, lupus anticoagulant test, protein C assay, protein S assay, activated protein C-resistant test, antithrombin assay, homocysteine estimation, prothrombin gene mutation test, anti- β -2 glycoprotein antibodies assay, proglobal C assay, and factor V Leiden mutation test. American College of Obstetricians and Gynecologists guidelines were applied in planning the treatment of patients consisting of dalteparin (fragmin) and low-dose aspirin. Both symptomatic (prophylaxis) and asymptomatic (therapeutic) patients with a history of previous APO were treated; dose was adjusted on regular evaluation of activated partial thromboplastin time, creatinine clearance (Cr Cl <30 mL/min), and an International Normalized Ratio 2.0–3.0. All the data were analyzed using standard statistical methods.

Observations and Results: A total of 69 patients with a history of APO were screened for inherited and acquired thrombophilia. The patients were enrolled over a period of 2 years from July 2006 to June 2008 from the OPD at the Department of Obstetrics and Gynaecology, AIIMS, New Delhi. Recurrent abortion in 32 (46.37%) patients was the most common APO in women screened for thrombophilia. Other indications were IUGR in 11 (15.94%), severe preeclampsia in 9 (13.04%), and unexplained intrauterine device in 17 (24.63%) patients. 45/69 patients were treated for thrombophilia. 2/45 patients had to undergo termination of pregnancy; hence, 43 cases were tabulated for analysis in this study. 21/43 (48.83%) were asymptomatic and 22/45 were (51.16%) symptomatic patients with active thrombophilic symptoms and signs. In asymptomatic type of thrombophilia, the live birth rate was 86.87%, and in symptomatic type, it was 90.97% and both the results were significant statistically with *P* value of 0.010 and 0.001, respectively (*P* taken as significant at *P* < 0.05). Continuation of pregnancy beyond 37 weeks in asymptomatic group was 76.19% and in symptomatic group 68.18%. The results were significant with *P* values at 0.024. In the asymptomatic group, 15/21 newborns weight (71.42%) was >2.5 kg compared to 4/21 (19.045) with weight <2.5 kg and *P* = 0.031, significant. Among the newborns of symptomatic group, 14/22 (63.63%) were >2.5 kg and 7/22 (31.81%) were below, with *P* = 0.040 and significant.

Conclusions: The management of thrombophilia in the setting of pregnancy remains controversial. LMWH and aspirin provide benefit, both as prophylactic and therapeutic treatment for asymptomatic and symptomatic thrombophilia. However, prophylactic anticoagulation should be addressed on a case-by-case basis taking into account the inherited and acquired thrombophilias and history of prior pregnancies and their outcomes. Women with acquired thrombophilia are more likely to benefit from anticoagulation and should be treated according to published guidelines.

Key words: Adverse pregnancy outcome, Heparin and low-molecular-weight heparin, Pregnancy, Thrombophilia, Thrombosis

Access this article online



www.ijss-sn.com

Month of Submission : 06-2018
Month of Peer Review : 07-2018
Month of Acceptance : 08-2018
Month of Publishing : 08-2018

Corresponding Author: Dr. S Sooraj, Department of Obstetrics and Gynaecology, Government Medical College, Kozhikode, Kerala, India.
E-mail: drsoorajsaiims@gmail.com

INTRODUCTION

Pregnancy is a physiological prothrombotic state. Venous thromboembolism is a leading cause of direct maternal death well described in the MBRACE reports.^[1] The various adverse pregnancy outcomes (APOs) such as recurrent abortions, intrauterine growth retardation (IUGR), preeclampsia, intrauterine death of fetus, and placental abruption collectively account to 15% of pregnancies.^[2] All these conditions share similar and overlapping micro- and macro-thrombotic pathogenic processes. Recurrent abortions are defined as three or more miscarriages before 20 weeks of gestation and remain an important problem in women of reproductive age affecting approximately 1–2% of all pregnancies;^[3] if they are sequential the incidence rises to 5%.^[4] The association between inherited thrombophilia and recurrent abortions was first reported by Sanson *et al.*, in 1996.^[5] The root cause of APO is inadequate placental perfusion due to hemostatic imbalance.^[6] The causes of inherited thrombophilia are deficiency of factor V Leiden (FVL), prothrombin (PT G20210A), methylenetetrahydrofolate reductase (MTHFR) C677T, and A1298 mutations (MTHFR), as well as protein C, protein S, and antithrombin III, whereas acquired cases of thrombophilia are due to the presence of antiphospholipid antibodies (APAs) such as lupus anticoagulant and anticardiolipin antibody.^[7] Restoration of sufficient uteroplacental circulation results in saving the pregnancy and from complications. Hence, antithrombotic prophylaxis has been used in the management of thrombophilia of APO.^[8] Review of one meta-analysis showed that thromboprophylaxis was helpful in antiphospholipid syndrome cases rather than inherited thrombophilia.^[9] The overall effectiveness of anticoagulant prophylaxis is controversial even though it is being used widely in patients with APO and poor obstetric history. The use of low-molecular-weight heparin (LMWH) in women with thrombophilic defects and recurrent miscarriage with significant improvement in live birth rates was recorded by the studies by Brenner,^[10] Tzafettas *et al.*,^[11] Grandone *et al.*,^[12] Brenner *et al.*^[13] In a subgroup, an association between recurrent miscarriages and APAs was well established; these antibodies were shown to play a role in recurrent fetal loss by producing a thrombophilic and inflammatory effect. In such patients, the use of LMWH with low-dose aspirin was shown to be efficient and promoted as a standard care.^[14] LMWH was demonstrated to have anti-inflammatory effects on the placental vasculature by preventing leukocyte activation by blocking P- and L-selectins.^[15] The present study is conducted to analyze the results of final outcome in the APO patients with thrombophilia.

MATERIALS AND METHODS

A total of 69 patients with a history of APO in previous pregnancies were included in this study to evaluate the overall efficacy of LMWH and low-dose aspirin in the management of thrombophilia. Ethical committee clearance was obtained before the commencement of the study. An ethical committee approved pro forma and consent forms were used while conducting the study.

Inclusion Criteria

Patients with a history of APO in previous pregnancies such as (1) severe preeclampsia <36 weeks; (a) blood pressure more than 160/110, (b) proteinuria >5 g/day, (c) hemolysis, (d) elevated liver enzymes, (e) platelets <1 lakhs/mm³, and (f) eclampsia; (2) placental abruption; (3) delivery of small for gestational age baby; (4) unexplained intrauterine deaths; and (5) recurrent abortions (>3) were included in the study.

Exclusion Criteria

Patients with chronic hypertension, diabetes mellitus, cardiovascular disease, renal disease, multiple pregnancies, maternal drug or alcohol abuse, intrauterine infections, suspected chromosomal abnormalities, congenital malformations detected by ultrasound, and on anticoagulation therapy, patients under progesterone therapy were excluded from the study.

Timing of Study

Patients with a history of APO fitting inclusion criteria were screened for thrombophilia in the preconception period, during pregnancy, and/or >6 weeks postpartum.

Method of Study

This was a prospective, cross-sectional, observational study. Detailed obstetric history was taken. Routine investigations such as hemogram and liver and renal function tests were done. Some special investigations such as thyroid-stimulating hormone, glucose tolerance tests with 75 g glucose, hysteroscopy, parental blood karyotyping, and TORCH screen if indicated were done to exclude other causes of APO. Various thrombophilic studies were undertaken using the blood samples of the patients. They included (1) anticardiolipin antibodies test, lupus anticoagulant test, protein C assay, protein S assay, activated protein C-resistant test, antithrombin assay, homocysteine estimation, prothrombin gene mutation test, anti- β -2 glycoprotein antibodies assay, proglobal C assay, and FVL mutation test. Based on the test results, the type of thrombophilia was diagnosed. American College of Obstetricians and Gynecologists guidelines were applied in planning the treatment of patients.^[16] It consisted of administering dalteparin (fragmin) which comes in prefilled syringes of 2500 units, 5000 units, 7500 units, 10,000 units,

and 12,500 units. Among the 69 patients included 45 who were positive for thrombophilia were treated in this study irrespective of their gestational age. Allergy to heparin and/or contraindications for heparin was strictly considered, but none of the screened patients needed to be excluded from the study. Patients included did not take progesterone. In symptomatic patients, therapeutic doses of dalteparin = 200 units/kg/day were used. In asymptomatic patients with a history of previous APO, prophylactic dalteparin = 2500–5000 units/day was used. The dose was adjusted based on regular evaluation of activated partial thromboplastin time, creatinine clearance (Cr Cl <30 mL/min), and an INR 2.0–3.0 is maintained. Patients with preeclampsia were avoided treatment with dalteparin and only low-dose aspirin (150 mg/day) was used. In addition, the treatment was continued for 6 weeks in postnatal period. All the patients were kept under consultation and supervision of the institutional hematologist for modification, stoppage, or treatment of adverse effects. Patients were monitored during the antenatal period with regular ultrasound examination of abdomen and Doppler study of major vessels for evidence of complications. All the data were analyzed using standard statistical methods. Simple arithmetic mean, standard deviation, and Student's *t*-test were used to analyze the statistical significance.

OBSERVATIONS AND RESULTS

A total of 69 patients with a history of APO were screened for inherited and acquired thrombophilia. The patients were enrolled over a period of 2 years from July 2006 to June 2008 from the OPD at the Department of Obstetrics and Gynaecology, AIIMS, New Delhi. Recurrent abortion in 32 (46.37%) patients was the most common APO in women screened for thrombophilia. Other indications were IUGR in 11 (15.94%), severe preeclampsia in 9 (13.04%), and unexplained intrauterine device (IUD) in 17 (24.63%) patients [Table 1 and Figure 1].

Age distribution

The mean age of the patients in this study was 27.34 ± 3.28 with a range of 20–36 years. The mean age of patients with recurrent abortion was 27.38 ± 2.25 with a range of

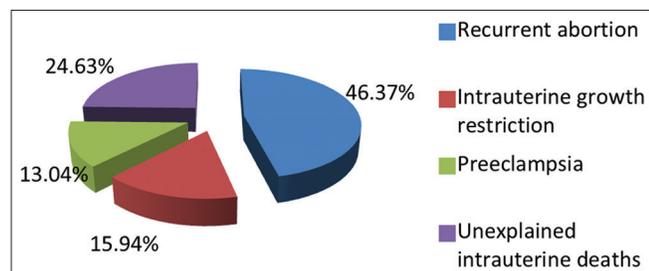


Figure 1: The incidence of adverse pregnancy outcome in the study (n = 69)

22–32 years while that for the patients with intrauterine deaths it was 27.70 ± 1.99 with a range of 24–31 years, with intrauterine growth restriction it was 27.81 ± 2.92 with a range of 24–34 years and preeclampsia it was 28.66 ± 3.35 with a range of 25–36 years [Table 2].

Distribution of Gravidity

The mean gravidity of the patients in the present study was 3.7 ± 1.25. The mean gestation of the patients with recurrent abortion was 3.81 ± 0.86, while that for patients with IUD was 3.41 ± 1.12, with IUGR it was 4 ± 0.89 and preeclampsia it was 4.33 ± 0.87 [Table 3].

Of 69 patients with APO, 45/69 (65.21%) were positive to the various thrombophilic tests. Among them, 9/45 (20%) were inherent type and 35/45 (77.77%) were acquired type of thrombophilia. 19/32 (59.37%) patients with a history of recurrent abortions were thrombophilic; among them, 3/19 (15.78%) were inherent and 16/19 (84.21%) were acquired type. Of 17 patients with IUD, 11/17 (64.70%) were thrombophilic; 2/11 (18.18%) were inherent and 10/11 (90.90%) were acquired type. Of 11 patients with IUGR, 7/11 were thrombophilic; 2/7 (28.57%) were inherent and 5/11 (45.45%) were acquired type. Among the 09 preeclampsia patients, 7/9 (77.77%) patients

Table 1: The incidence of adverse pregnancy outcome in the study (n=69)

Type of adverse pregnancy outcome	Number of patients n=69 (%)
Recurrent abortion	32 (46.37)
Intrauterine growth restriction	11 (15.94)
Preeclampsia	9 (13.04)
Unexplained intrauterine deaths	17 (24.63)

Table 2: The age distribution of patients with different adverse pregnancy outcome

Adverse pregnancy outcome	Age: Mean±SD (range in years)
All patients	27.34±3.28 (20–36)
Recurrent abortion	27.38±2.25 (22–32)
Unexplained intrauterine deaths	27.70±1.99 (24–31)
Intrauterine growth restriction	27.81±2.92 (24–34)
Preeclampsia	28.66±3.35 (25–36)

SD: Standard deviation

Table 3: The distribution of gravidity in the study group

Adverse pregnancy outcome	Mean gravidity±SD (range)
All patients	3.7±1.25 (1–8)
Recurrent abortion	3.81±0.86 (3–6)
Unexplained intrauterine deaths	3.41±1.12 (1–5)
Intrauterine growth restriction	4±0.89 (3–6)
Preeclampsia	4.33±0.87 (3–6)

SD: Standard deviation

were thrombophilic; 2/7 (28.7%) were inherent and 5/7 (71.42%) were acquired type [Table 4].

Thrombophilic tests positive in different types of APO in the present study are shown in Table 5. Anti- β -2 glycoprotein antibody was positive in 24/45 tests (53.33%). Protein C deficiency was observed in 1/45 (2.22%), (IUGR), patient. Protein S deficiency was observed in 1/45 (2.22%) (recurrent abortion) patient. Antithrombin III deficiency was observed in 2/45 (4.44%) (recurrent abortion and preeclampsia) patients, FVL mutation was observed in 4/45 (8.88%) (recurrent abortion, IUD, IUGR, and preeclampsia) patients, hyperhomocysteinemia was observed in 2/45 (4.44%) and LAC positive in 3/45 (6.66%) (two in IUD and preeclampsia) patients, and ACL test was positive in 9/45 (20%) [Table 5].

Of 45 patients, two patients had to undergo termination of pregnancy; hence, 43 cases were tabulated for analysis in this study. Among the 43 patients, 21 (48.83%) were asymptomatic and the remaining 22 (51.16%) were symptomatic patients with active thrombophilic symptoms and signs. Continuation of pregnancy beyond 37 weeks in patients with APO was considered as a good prognosis, and in the present study, the overall live birth rate following treatment was calculated. In asymptomatic type of thrombophilia, the live birth rate was 86.87%, and in symptomatic type, it was 90.97% and both the results were statistically significant with P value of 0.010 and 0.001, respectively (P taken as significant at $P < 0.05$). The percentage of patients with successful continuation of pregnancy beyond 37 weeks in asymptomatic group was 76.19%, and in symptomatic group, it was 68.18%. The results were significant with p values at 0.024. APGAR score and birth weight reflect the improved placental

circulation in APO with thrombophilias, and in this study, in the asymptomatic group, 15/21 newborns weight (71.42%) was >2.5 kg compared to 4/21 (19.045) with weight <2.5 kg and P value of 0.031, significant. Among the newborns of symptomatic group, 14/22 (63.63%) were >2.5 kg and 7/22 (31.81%) were below, with P value of 0.040 and significant. The APGAR score of asymptomatic group was >7 in 15/21 (71.42%), and in symptomatic group, it was 63.63; P value was statistically significant. The overall treatment result distribution of patients depending on their obstetrical diagnosis is shown in Table 5. In this study, the overall live birth rate in patients with thrombophilia with or without symptoms and signs was 88.92%.

The overall effect of the treatment of thrombophilia in symptomatic and asymptomatic types, in terms of live birth rate, continuation of pregnancy beyond 37 weeks, birth weight, and APGAR score was to be statistically significant; $P < 0.05$ in all the parameters mentioned above.

DISCUSSION

In this study, 69 pregnant women with APOs such as recurrent abortions, IUDs, IUGRS, and preeclampsia were investigated for evidence of thrombophilias with the help of thrombophilic tests. It was observed that 45/69 was positive to thrombophilia; inherent and acquired types. The patients were treated depending on whether the symptoms and signs of thrombophilia were present or not, using American College of Obstetricians and Gynecologists guidelines.^[16] Thrombophilia management during pregnancy consists of primary thromboprophylaxis in asymptomatic women, secondary prophylaxis of

Table 4: The incidence of types of thrombophilia in the study (n=69)

Thrombophilia patients (n=45)	Recurrent abortions (n=32)	IUD (n=17)	IUGR (n=11)	Preeclampsia (n=9)
Inherent (n=9)	3	2	2	2
Acquired (n=36)	16	10	5	5
Total	19	12	7	7

IUD: Intrauterine device, IUGR: Intrauterine growth retardation

Table 5: The positive thrombophilic tests in different types of APO in this study (n=69)

Thrombophilic tests positive (n=45)	Recurrent abortions (n=19)	IUD (n=12)	IUGR (n=7)	Preeclampsia (n=7)	Total n=45 (%)
Protein C deficiency (n=1)	-	-	1	-	4-8.88
Protein S deficiency (n=1)	1	-	-	-	1-2.22
Antithrombin III deficiency (n=2)	1	-	-	1	1-2.22
FVL mutation (n=4)	1	2	1	-	4-2.22
Hyperhomocysteinemia (n=2)	1	-	1	-	2-4.44
LAC (n=3)	-	2	-	1	2-4.44
ACL IgG (n=6)	3	1	1	1	6-13.33
ACL IgM (n=3)	3	-	-	-	3-6.66
Anti- β -2 glycoprotein antibody (n=23)	9	7	3	4	25-55.55

IUD: Intrauterine device, IUGR: Intrauterine growth retardation, APO: Adverse pregnancy outcome, FVL: Factor V Leiden

recurrences in women who have previously developed thrombosis, and the treatment of acute thrombotic episodes.^[17] The absence of well-controlled trials in the management of thrombophilia in pregnancy makes it difficult to establish clear cur guidelines. Hence, recommendations regarding prophylactic and therapeutic strategies in pregnancy are largely based on clinical trials in non-pregnant populations.^[18] In addition, assessing the therapeutic response to treatment is difficult as pregnancy remains a contraindication for repeated imaging procedures. Hence, the final outcome following delivery or completion of 6 weeks of postnatal period was taken in this study for therapeutic assessment. It is a well-established fact that pregnant women with previous history of fetal death, severe preeclampsia, IUGR, abruptio placenta, or recurrent miscarriage have an increased risk of recurrence in subsequent pregnancies.^[19-21] It may be as high as 46% with a history of two or more adverse outcomes, even before any thrombophilia is taken into account.^[22] Hence, the authors recommended prophylactic treatment which included low-dose aspirin with or without subcutaneous heparin, as well as folic acid and Vitamin B₆ supplements, according to the type of thrombophilia present as well as the nature of the previous adverse outcome. The most confirmative evidence of association between APO and pregnancy loss and thrombophilia was afforded by APAs. Women with APAs develop thrombosis, pregnancy loss, and preeclampsia.^[19,20] Currently, it has been postulated

that the recurrent abortions occurring especially after the week 12 of gestation may be due to interference with spiral artery remodeling during secondary trophoblastic invasion.^[21] Rai *et al.*^[22] using combined aspirin 75 mg and unfractionated heparin 5000 units every 12 h, in pregnant women with thrombophilia, precipitated by APAs, markedly improved the live birth rate of women to 71%. Farquharson *et al.*^[23] were unable to confirm a significantly better outcome after treatment with aspirin plus heparin. Life birth rate was 78% in 51 women treated with aspirin plus heparin and 72% in women treated with aspirin alone. A recent Cochrane collaboration^[24] reported a 15% reduction in the risk of preeclampsia and a 14% reduction in fetal and/or neonatal death. The combination of aspirin and heparin or LMWH was effective in recurrent fetal loss in APS syndrome and could be considered for women with inherited thrombophilias and history of severe preeclampsia, IUGR, abruptio placenta, or fetal loss, although no controlled studies on the subject are currently available. In this study, 7/9 patients with preeclampsia were positive for thrombophilia, and the final results showed a live birth rate of 100% among both the symptomatic and asymptomatic types [Table 6]. The role of LMWH and low-dose aspirin is well accepted in patients with antiphospholipids antibody-associated fetal loss. The live birth rate in these patients is about 10% if left untreated.^[25] It has been demonstrated that the live birth rate can be increased to about 80% using LMWH and low-dose aspirin.^[24,23,26] In the present

Table 6: Overall results of treatment with LMWH in patients with thrombophilia in the study (n=43)

Type of thrombophilia total (n=43)	Recurrent abortions (n=17)	IUD (n=12)	IUGR (n=7)	Preeclampsia (n=7)	Overall percentage	P value
Asymptomatic (n=21)	8-47.05%	5-41.66%	4-57.14%	4-57.14%		
Prophylactic treatment						
Delivered at gestation ≥37 weeks	6	4	3	3	76.19	0.024
Delivered at gestation ≤37 weeks	1	0	1	1	14.28	
Abortions ≥15 weeks gestation	1	0	0	0	04.76	
Abortions ≤15 weeks gestation	0	1	0	0	04.76	
Live birth rate	87.50%	80%	80%	100	86.87%	0.010
Birth weight ≥2.5 kg	5	4	3	3	71.42	0.031
Birth weight ≤2.5 kg	2	0	1	1	19.04	
APGAR score ≥7	6	3	3	3	71.42	0.028
APGAR score ≤7	1	1	1	1	19.04	
Postnatal DVT incidence	0	0	0	0	0	-
Symptomatic (n=22)	9-40.90%	7-31.81%	3-13.63%	3-13.63%		
Therapeutic treatment						
Delivered at gestation ≥37 weeks	7	5	2	1	68.18	0.024
Delivered at gestation ≤37 weeks	1	2	1	2	27.27	
Abortions ≥15 weeks gestation	1	0	0	0	04.54	
Abortions ≤15 weeks gestation	0	0	1	0	04.54	
Live birth rate	88.88%	100%	75%	100%	90.97	0.001
Birth weight ≥2.5 kg	6	5	2	1	63.63	0.040
Birth weight ≤2.5 kg	2	2	1	2	31.81	
APGAR score ≥7	6	5	2	1	63.63	0.041
APGAR score ≤7	2	2	1	2	31.81	
Postnatal DVT incidence	1	1	0	1	13.63	0.653

IUD: Intrauterine device, IUGR: Intrauterine growth retardation, DVT: Deep vein thrombosis, LMWH: Low-molecular-weight heparin

study, there were three patients with antiphospholipids antibody-associated fetal loss and following treatment [Table 6], such loss was averted. In a study by Brenner *et al.*^[27] who treated 50 women with recurrent miscarriage and thrombophilia in 61 subsequent pregnancies with enoxaparin (40–120 mg/day), a 75% of live birth could be achieved compared to 20% of previously untreated pregnancies in the same women. Similar study by Carp *et al.*^[28] showed 70% live births under 40 mg/day enoxaparin in 37 women with thrombophilia and recurrent abortions compared to 44% live births in 48 untreated women. A prospective multicenter study (the LIVE-ENOX study) on pregnant patients with thrombophilia and abortions compared 40 and 80 mg/day enoxaparin and found them to be equally effective resulting in live births in 81% and 77% compared to only 28% live births in previously untreated pregnancies of these women.^[13] Sarto *et al.*^[29] concluded from their study that live birth rate could be improved to 85% in women with recurrent abortions and thrombophilia under enoxaparin; before thrombophilia was diagnosed, only 15% of 105 untreated pregnancies of these women resulted in live births. In this study, the overall live birth rate in patients with thrombophilia with or without symptoms and signs was 88.92%. Monien *et al.*^[30] from their study concluded that the overall live birth rate was 87.50%, which was far higher than the live birth rate of 16.6% recorded in the same patients in earlier pregnancies without treatment.

CONCLUSIONS

Pregnancy is a prothrombotic state in the complex underlying physiology of pregnancy, leading to an increase of procoagulant factors; physical changes lead to increased stasis and the additional contribution in cases of inherited and acquired thrombophilias. The management of thrombophilia in the setting of pregnancy remains controversial. LMWH and aspirin provide benefit, both as prophylactic and therapeutic treatment for asymptomatic and symptomatic thrombophilia. However, prophylactic anticoagulation should be addressed on a case-by-case basis taking into account the inherited and acquired thrombophilias and history of prior pregnancies and their outcomes. Women with acquired thrombophilia are more likely to benefit from anticoagulation and should be treated according to published guidelines.

REFERENCES

1. Knight M, Kenyon S, Brocklehurst P. editors. On Behalf of MBRRACE-UK. Saving lives, Improving Mothers' Care: Lessons Learned to Inform Future Maternity Care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2009-12. Oxford: National Perinatal Epidemiology Unit, University of Oxford; 2014, Available from: <http://www.npeu.ox.ac.uk/mbrance-uk>. [Last accessed on 2018 Aug 01].
2. Wilcox AJ, Weinberg CR, O'Connor JF, Baird DD, Schlatterer JP, Canfield RE, *et al.* Incidence of early loss of pregnancy. *N Engl J Med* 1988;319:189-94.
3. Baek KH, Lee EJ, Kim YS. Recurrent pregnancy loss: The key potential mechanisms. *Trends Mol Med* 2007;13:310-7.
4. Carson A, Branch W. Management of Recurrent Early Pregnancy Loss, Compendium Selected Publications. Washington, DC: American College of Obstetricians and Gynecologists; 2001. p. 372-83.
5. Sanson BJ, Friederich PW, Simioni P, Zanardi S, Hilsman MV, Girolami A, *et al.* The risk of abortion and stillbirth in antithrombin-, protein C-, and protein S-deficient women. *Thromb Haemost* 1996;75:387-8.
6. Nadar S, Blann AD, Kamath S, Beevers DG, Lip GY. Platelet indexes in relation to target organ damage in high-risk hypertensive patients: A substudy of the anglo-scandinavian cardiac outcomes trial (ASCOT). *J Am Coll Cardiol* 2004;44:415-22.
7. John H. Antiphospholipid syndrome: An overview. *Can Med Assoc J* 2003;168:1675-82.
8. Kher A, Bauersachs R, Nielsen JD. The management of thrombosis in pregnancy: Role of low-molecular-weight heparin. *Thromb Haemost* 2007;97:505-13.
9. Pattison NS, Chamley LW, Birdsall M, Zanderigo AM, Liddell HS, McDougall J. Does aspirin have a role in improving pregnancy outcome for women with the antiphospholipid syndrome? A randomized controlled trial. *Am J Obstet Gynecol* 2000;183:1008-12.
10. Brenner B. Efficacy and safety of two doses of enoxaparin in pregnant women with thrombophilia and recurrent pregnancy loss. *Blood* 2002;100:2765-29.
11. Tzafettas J, Petropoulos P, Psarra A, Delkos D, Papaloukas C, Giannoulis H, *et al.* Early antiplatelet and antithrombotic therapy in patients with a history of recurrent miscarriages of known and unknown aetiology. *Eur J Obstet Gynecol Reprod Biol* 2005;120:22-6.
12. Grandone E, Brancaccio V, Colaizzo D, Sciannamè N, Pavone G, Di Minno G, *et al.* Preventing adverse obstetric outcomes in women with genetic thrombophilia. *Fertil Steril* 2002;78:371-5.
13. Brenner B, Hoffman R, Carp H, Dulitzky M, Younis J. Efficacy and safety of two doses of enoxaparin in women with thrombophilia and recurrent pregnancy loss: The LIVE-ENOX study. *J Thromb Haemost* 2005;3:227-9.
14. Girardi G, Redecha P, Salmon J. Heparin prevents antiphospholipid antibody-induced fetal loss by inhibiting complement activation. *Nat Med* 2004;10:1222-6.
15. Wang L, Brown JR, Varki A, Esko JD. Heparin's antiinflammatory effects require glucosamine 6-O-sulfation and are mediated by blockade of L- and P-selectins. *J Clin Invest* 2002;110:127-36.
16. American College of Obstetricians and Gynecologists. Hypertension in pregnancy. *Obstet Gynecol* 2013;122:1122-31.
17. Kupferminc MJ. Thrombophilia and pregnancy. *Reprod Biol Endocrinol* 2003;1:111.
18. Ginsberg JS, Hirsh J. Use of antithrombotic agents during pregnancy. *Chest* 1998;114:524-30.
19. Paidas MJ, De-Hui WK, Arkel YS. Screening and management of inherited thrombophilias in the setting of adverse pregnancy outcome. *Clin Perinatol* 2004;31:783-805.
20. Infante-Rivard C, Rivard GE, Yotov WV, Génin E, Guiguet M, Weinberg C, *et al.* Absence of association of thrombophilia polymorphisms with intrauterine growth restriction. *N Engl J Med* 2002;347:19-25.
21. Howley HE, Walker M, Rodger MA. A systematic review of the association between factor V Leiden or prothrombin gene variant and intrauterine growth restriction. *Am J Obstet Gynecol* 2005;192:694-708.
22. Rai RS, Clifford K, Cohen H, Regan L. High prospective fetal loss rate in untreated pregnancies of women with recurrent miscarriage and antiphospholipid antibodies. *Hum Reprod* 1995;10:3301-4.
23. Farquharson RG, Quenby S, Greaves M. Antiphospholipid syndrome in pregnancy: A randomized, controlled trial of treatment. *Obstet Gynecol* 2002;100:408-13.
24. Kutteh WH. Antiphospholipid antibody-associated recurrent pregnancy loss: Treatment with heparin and low-dose aspirin is superior to low-dose aspirin alone. *Am J Obstet Gynecol* 1996;174:1584-9.
25. Chamley LW, Duncalf AM, Mitchell MD, Johnson PM. Action of anticardiolipin and antibodies to Beta2-glycoprotein-I on trophoblast

Sooraj: Management of Thrombophilia in APO

- proliferation as a mechanism for fetal death. *Lancet* 1998;352:1037-8.
26. Rai R, Cohen H, Dave M, Regan L. Randomised controlled trial of aspirin and aspirin plus heparin in pregnant women with recurrent miscarriage associated with phospholipid antibodies (or antiphospholipid antibodies). *BMJ* 1997;314:253-7.
 27. Brenner B, Hoffman R, Blumenfeld Z, Weiner Z, Younis JS. Gestational outcome in thrombophilic women with recurrent pregnancy loss treated by enoxaparin. *Thromb Haemost* 2000;83:693-7.
 28. Carp H, Dolitzky M, Inbal A. Thromboprophylaxis improves the live birth rate in women with consecutive recurrent miscarriages and hereditary thrombophilia. *J Thromb Haemost* 2003;1:433-8.
 29. Sarto A, Rocha M, Geller M, Capmany C, Martinez M, Quintans C, *et al.* Treatment with enoxaparin adapted to the fertility programs in women with recurrent abortion and thrombophilia. *Medicina (B Aires)* 2001;61:406-12.
 30. Monien S, Kadecki O, Baumgarten S, Salama A, Dörner T, Kieseewetter H. Use of heparin in women with early and late miscarriages with and without thrombophilia. *Clin Appl Thromb/Hemost* 2009;15:636-44.

How to cite this article: Sooraj S. Clinical Study on Prophylactic and Therapeutic Management of Thrombophilia in Adverse Pregnancy Outcome Patients. *Int J Sci Stud* 2018;6(5):105-111.

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

A Comparative Study of Equi-concentration of Bupivacaine-Fentanyl and Ropivacaine-Fentanyl for Epidural Labor Analgesia

Gunda Shraavan Kumar¹, B Srinivas Rao², U Mahesh Kumar³

¹Associate Professor, Department of Anaesthesiology and Intensive Care, Kakatiya Medical College, MGM Hospital, Warangal, Telangana, India, ²Professor and Head, Department of Anaesthesiology, Kakatiya Medical College, MGM Hospital, Warangal, Telangana, India, ³Post Graduate, Department of Anaesthesiology, Kakatiya Medical College, MGM Hospital, Warangal, Telangana, India

Abstract

Introduction: Pain relief in labor has always been surrounded with myths and controversies and providing effective and safe analgesia during labor has remained an ongoing challenge. Neuraxial techniques were introduced for pain relief in labor in 1950. Modern neuraxial labor analgesia reflects a shift in obstetrical anesthesia, thinking away from a simple focus on pain relief toward a focus on the overall quality of analgesia.

Aims and Objectives: The present study is carried out to compare equi-concentration of low dose (0.125%) bupivacaine-fentanyl 2 µg/mL and (0.125%) ropivacaine-fentanyl 2 µg/mL in primigravid full-term parturients for epidural labor analgesia.

Materials and Methods: A prospective randomized double-blind controlled study was undertaken after obtaining Ethical Committee approval to compare the effect of equi-concentration of 0.125% bupivacaine with fentanyl 2 µg/mL and 0.125% ropivacaine with fentanyl 2 µg/mL in 60 parturients coming for delivery at Government Maternity Hospital, Hanamkonda.

Results: This study was undertaken to compare equi-concentration of bupivacaine-fentanyl and ropivacaine-fentanyl for epidural labor analgesia in primigravida patients. Providing excellent labor analgesia, statistically significant motor blockade produced by bupivacaine compared to ropivacaine does not change mode of delivery at lower concentrations.

Conclusion: In our study comparing equi-concentration (0.125%), bupivacaine-fentanyl 2 µg/mL and (0.125%) ropivacaine-fentanyl 2 µg/mL for epidural labor analgesia results indicate that both are equally effective clinically by intermittent epidural supplementation in providing excellent labor analgesia with hemodynamic stability, minimal motor blockade, mode of delivery, maternal satisfaction without serious maternal, or fetal side effects.

Key words: Bupivacaine, Epidural labor analgesia, Ropivacaine, Visual analog scores

INTRODUCTION

Pain relief in labor has always been surrounded with myths and controversies and providing effective and safe analgesia during labor has remained an ongoing challenge.

Neuraxial techniques were introduced for pain relief in labor in 1950. Modern neuraxial labor analgesia reflects a shift in

obstetrical anesthesia, thinking away from a simple focus on pain relief toward a focus on the overall quality of analgesia.^[1]

A study shows that, in India, the average incidence and practice of labor analgesia is only 11%. In our country, the awareness of regional analgesia for labor is still lacking and except a few centers that run a comprehensive labor analgesia program, the national awareness or acceptance of pain relieving options for women in labor virtually does not exist. Central neuraxial analgesia is the most versatile method of labor analgesia and the gold standard technique for pain control in obstetrics that is currently available.^[2] The satisfaction of birth experience is greater with neuraxial techniques. Epidural blockade is an effective means of providing analgesia during labor.

Access this article online



www.ijss-sn.com

Month of Submission : 06-2018
Month of Peer Review : 07-2018
Month of Acceptance : 08-2018
Month of Publishing : 08-2018

Corresponding Author: Dr. B. Srinivas Rao, H. No: 2-4-624/1, Ramnagar Hanamkonda Warangal - 506 001, Telangana, India.
Phone: +91-9390109191. E-mail: drsrinivasbathula@hotmail.com

Bupivacaine and ropivacaine are widely used to provide efficient epidural analgesia in labor. The value of bupivacaine is limited by the risks of motor blockade and toxicity. There have been conflicting comparisons of ropivacaine and bupivacaine for labor analgesia.^[3-5] Some studies have suggested that ropivacaine produces less motor block than bupivacaine while others found the drugs to be indistinguishable. Dilute solutions of epidural local anesthetics combined with opioids may be used to minimize unwanted motor block. The amount by which fentanyl reduces local anesthetic dose requirement depends on dose of fentanyl.^[6]

Present day epidural local anesthetic for labor is low concentration, minimal, dose, and volume with opioids. The present study is taken up to provide labor analgesia service to our patients and compare the analgesic requirement, hemodynamic effects, and mode of delivery of fetus with bupivacaine and ropivacaine.

Objectives of the Study

The present study is carried out to compare equi-concentration of low dose (0.125%) bupivacaine-fentanyl 2 µg/mL and (0.125%) ropivacaine-fentanyl 2 µg/mL in primigravid full-term parturients for epidural labor analgesia. The following parameters were compared:

- Analgesic efficacy
- Degree of motor blockade
- Hemodynamic parameters
- Mode of delivery
- Maternal satisfaction
- Total dose of local anesthetic used.

Sample size

Total sample size 60 patients, 30 patients in Group B - received bupivacaine (0.125%) with fentanyl (2 µg/mL) and 30 patients in Group R - received ropivacaine (0.125%) with fentanyl (2 µg/mL).

Expected result

Results expected to achieve in this study, equi-concentration (0.125%) bupivacaine-fentanyl 2 µg/mL and (0.125%) ropivacaine-fentanyl 2 µg/ml for epidural labor analgesia are equally effective in terms of highest sensory blockade, hemodynamics, patient satisfaction, and total dose used. Motor blockade produced by bupivacaine compared to ropivacaine does not change mode of delivery at low concentrations.

MATERIALS AND METHODS

A prospective randomized double-blind controlled study was undertaken after obtaining Ethical Committee approval

to compare the effect of equi-concentration of 0.125% bupivacaine with fentanyl 2 µg/ml and 0.125% ropivacaine with fentanyl 2 µg/ml in 60 parturients coming for delivery at Government Maternity Hospital, Hanamkonda, with the following inclusion and exclusion criteria.

Inclusion Criteria

The following criteria were included in the study:

1. ASA physical status I–II
2. Primigravida women with gestational age ≥ 36 weeks
3. Singleton pregnancy with vertex presentation
4. Uncomplicated pregnancy with normal fetal heart rate (FHR)
5. Cervical dilatation 3–5 cm.

Exclusion Criteria

The following criteria were excluded from the study:

1. ASA physical status III or IV
2. Multiple or preterm gestation
3. Allergy to any study drug
4. Contra indications or patients unwilling for labor analgesia
5. Cervical dilatation > 5 cm.

Method of Study and Collection of Data

After obtaining Ethical Committee approval, a written informed consent was obtained. A detailed examination of the patient was done, and the following parameters were recorded: Demographic data, parity and gestational age, condition of membranes, vital parameters, and FHR.

Patients were randomized into two groups based on a computer-generated randomization table.

- Group B - received 0.125% bupivacaine with 2 µg/mL fentanyl.
- Group R - received 0.125% ropivacaine with 2 µg/mL fentanyl.

Preparation of the Parturient

The parturient was prepared as per the routine preparations done for delivery. In addition, preparation of the back was done for performing the epidural block. The onset of active labor, degree of cervical dilatation and adequacy of the pelvis for vaginal delivery were all assessed by the attending obstetrician before institution of the epidural block.

An intravenous access was secured with an 18G cannula and the parturient was preloaded with 500 mL of Ringer's lactate solution. 3 lead electrocardiogram, pulse oximeter, and non-invasive blood pressure were connected, and baseline vitals were recorded.

All equipment needed for resuscitation of the mother and the fetus was kept ready before the institution of the block.

A disposable epidural set (BRAUN Perifix 18G) was used to perform the block. The parturient and anesthesiologist performing the technique and administering the study drug were blinded to the drug. Study solutions were prepared by an anesthesiologist not directly involved in the patient's care or data collection.

Under aseptic precautions epidural space was identified in sitting position with midline approach using 18 gauge Tuohy needle in L₃₋₄ or L₄₋₅ interspace with loss of resistance to air technique and catheter was threaded cephalad 3–4 cm into epidural space. After negative aspiration for blood and cerebrospinal fluid, a test dose of 3 mL of lignocaine 2% with 1:2,00,000 adrenaline was administered through the catheter. Intravascular spread of the drug was detected by a change in heart rate of > 30 beats per minute from baseline within 20–40 s. Intrathecal spread was detected by appearance of motor blockade within 3 min. Subjects with positive test dose response were excluded from the study. 3 min after administering the test drug, 10–15 ml of study drug of either 0.125% bupivacaine with fentanyl 2 µg/mL or 0.125% ropivacaine with fentanyl 2 µg/mL, depending on the height and weight of the patient, was given in 5 ml increments over 10 min. Patients not experiencing analgesia within 20 min of initial bolus were supplemented with additional 5 mL of the solution. Patients not experiencing analgesia within 20 min of drug administration were excluded.

Analgesia was maintained by intermittent bolus injections of 5 ml every 40–60 min. Patients who experienced inadequate analgesia (visual analog score [VAS] >4) during the process were supplemented with additional 5 mL of solution up to a maximum of 10 mL/h until the delivery of the baby. During the second stage of labor, additional supplementation of 5–10 mL was given in sitting position to maintain VAS <4.

After administration of bolus dose, the following parameters were noted:

1. Level of sensory block - assessed by loss of temperature discrimination to alcohol swab.
2. Degree of motor blockade was assessed using Bromage scale.
 - Grade 0 - Patient able to move at all the joints (hip, knee, and ankle)
 - Grade 1 - Unable to move at hip joint
 - Grade 2 - Unable to move at both hip and knee joint
 - Grade 3 - Unable to move at all the three joint hip, knee, and ankle.
3. Pain score - assessed using VAS 0–10, where 0- no pain and 10 - worst possible pain.



4. Oxygen saturation
5. Heart rate
6. Non-invasive blood pressure
7. FHR.

The level of sensory block and Bromage scale were assessed at 20 min after the initial bolus and every 30 min thereafter. All other parameters were monitored at 0, 5, 10, 20, 30, 45, and 60 min and every 30 min after that, until delivery.

Adverse effects such as hypotension, bradycardia, and arterial desaturation were noted and managed if necessary.

Hypotension is defined as fall of systolic blood pressure (SBP) >20% of base line or <90 mmHg. Bradycardia is defined as heart rate <60/min and was managed by injection atropine 0.6 mg.

After delivery, the following parameters were noted:

1. Patient's satisfaction - assessed as excellent, good, fair, or poor. Satisfaction was assessed based on a verbal numerical score from 0 to 10. 8–10 was taken as excellent, 5–7 was taken as good, 2–4 was taken as fair, and <2 was taken as poor.

[POOR]	[FAIR]	[GOOD]	[EXCELLENT]							
0	1	2	3	4	5	6	7	8	9	10
2. The mode of delivery - spontaneous, vaginal, instrumental vaginal, and cesarean section.
3. Total dose of local anesthetic used and number of additional supplementation in mL/h was recorded.

RESULTS

A total of 60 primigravida patients who were taken up for the study were randomized into two groups.

- Group B - received 0.125% bupivacaine with 2 µg/mL fentanyl.
- Group R - received 0.125% ropivacaine with 2 µg/mL fentanyl.

They were monitored continuously until the delivery of the baby. The following observations were made during the study:

Age

The mean age in Group B was 22.30 with SD 2.57 and in Group R was 23.33 with SD 1.95 with *P*-value of 0.085 which was statistically not significant.

Age Distribution

The patients were distributed into 3 age groups 19–21 years, 22–25 years, and >25 years. The percentage of patients in Group B was 36.6%, 50%, and 13.4%, and Group R was 13.3%, 76.7%, and 10%.

Height

The mean height in Group B was 153.26 cm with SD 3.609 and in Group R was 154.03 cm with SD 3.285 with *P* = 0.393 which was statistically not significant.

Weight

The mean weight in Group B was 64.86 with SD 5.21 and in Group R was 60.60 with SD 4.810 with *P* = 0.002 which was statistically significant.

Duration of Labor (Min)

The mean duration of labor in minutes was 251 ± 50.74 in Group B and $242 \text{ min} \pm 50.40$ in Group R, *P* value was 0.49 which was not significant.

Level of Sensory Block

In Group B, 23 patients (76.7%) achieved T_8 , 4 patients (13.3%) achieved a level of T_{10} , and 3 patients (10%) achieved a level of T_6 . In Group R, 21 patients (70%) achieved T_8 , 8 patients (26.7%) achieved T_6 , and 1 patient (3.3%) achieved T_{10} with *P* = 0.125 which was not significant.

DISCUSSION

Labor is a physiologic process but associated with the most severe of pains. The goal of labor analgesia is to provide adequate pain relief without causing any maternal and fetal jeopardy. Continuous/intermittent epidural analgesia depending on the situation is the most versatile and most commonly used technique, because it can be used for pain relief during labor and for subsequent vaginal delivery as well as analgesia and anesthesia for cesarean section if necessary.^[7]

Obstetricians and anesthesiologists have always feared that incidence of instrumental deliveries in women receiving epidural analgesia could be higher than in those who do not receive it.

Thus, it is intriguing to the obstetric anesthetist to strike a balance between patient satisfactions by providing good analgesia, reduces motor block thus making the parturient

participate in labor and decrease instrumental deliveries due to prolonged second stage.

Factors contributing to instrumental delivery include as follows:

- Diminished pain and sensation from uterine contraction leading to diminished Ferguson's reflex and of the perception of the need to push at full dilatation
- Reduced motor force due to weakened abdominal musculature and
- Inadequate rotation of the presenting part due to weakened pelvic floor musculature.

All these factors have generated intense interest in epidural analgesia in three forms: Decreased local anesthetic concentration, combining with opioids, and combined spinal epidural technique.

Effective pain relief with minimal motor block is the necessary ingredient of an ideal epidural block for labor analgesia. Bupivacaine is the most commonly used drug for providing reliable epidural analgesia during labor.^[8]

Epidural bupivacaine provides excellent pain relief during labor and delivery and is still the most widely used local anesthetic for obstetric analgesia. However, its potential for motor blockade and cardiac/central nervous system toxicity by accidental intravenous injection is clinically undesirable, especially for obstetric patients.^[9]

Therefore, dilute solutions of epidural bupivacaine (0.25%, 0.125%, and 0.0625%) combined with opioid are used to minimize the unwanted motor blockade. The amount by which fentanyl reduces the local anesthetic dose requirement depends on the dose of fentanyl. The optimal dose of fentanyl varies from 2 to 3 mg/mL. Most workers have used 2 mg/mL of fentanyl.

The new two S-enantiomer drugs, ropivacaine and levobupivacaine have purportedly lesser motor block and toxicity related to bupivacaine. They are theoretically advantageous in obstetric patients and may be good alternatives to bupivacaine for labor analgesia.

Many authors have tried relative analgesic potency of ropivacaine and bupivacaine for epidural labor analgesia. The studies on relative potencies of these local anesthetics are conflicting. A number of clinical labor studies comparing ropivacaine and bupivacaine in 0.2–0.25% have demonstrated differences in the motor block between these drugs. However, some studies suggest that the extent of epidural motor block produced by 0.125% ropivacaine was indistinguishable from 0.125% bupivacaine in laboring patients.

Epidural labor analgesia was initiated when cervical dilatation was 3–5 cm. There was no accidental intravascular/intrathecal injection in all the 60 patients. All patients experienced adequate analgesia within 20 min of the first bolus dose.

Study considered the mean of numerical data such as Bromage score, VAS score, and heart rate over the entire duration, and we have considered mode for the non-numerical data such as level of sensory block and mode of delivery.

Demographic Profile

Age

The age group of all the 60 patients was between 19 and 27 years. The mean age of all the 60 patients was 22.81. The mean age in Group B was 22.30 with SD of 2.57 and in Group R was 23.33 with a SD of 1.95 with $P = 0.085$ which was not statistically significant [Table 1]. Most of our patients (63.3%) were between 22 and 25 years age group. 25% were in the 19–21 years age group and 11.6% were above 25 years. The age distribution of the 2 groups was comparable with $P = 0.86$ which was statistically not significant [Table 2].

Height

The mean height in Group B was 153.26 cm with a SD 3.609 and in Group R was 154.03 cm with a SD of 3.285. Both groups were comparable with $P = 0.393$ [Table 3].

Weight

The mean weight in Group B was 64.86 kg with a SD of 5.21 and in Group R was 60.60 kg with a SD of 4.81. P -value was significant (0.002) [Table 4].

Regarding the demographics both the groups were comparable with respect to age and height, weight was statistically significant in our study which was due to random sampling.

Duration of Labor

The duration of labor is highly variable. We have considered the overall mean time duration in both the groups. In our study, the mean duration of labor was 251 ± 50.742 min in Group B and 242 ± 50.405 min in Group R. Both groups were comparable with P -value of 0.49 which was not significant [Table 5].

In the similar study conducted by Paddalwar *et al.*, duration of Stage I and II of labor and total duration in the ropivacaine with fentanyl and bupivacaine with fentanyl were comparable and showed no statistical significance, P -value was >0.01 . The total duration of labor between the two groups which was 196.07 ± 42.32 min and 186.33 ± 43.67 min in the ropivacaine and bupivacaine groups, respectively ($P = 0.380$).

Table 1: The mean age and SD in both the groups

Group	n	Mean±SD	P value
Bupivacaine	30	22.30±2.57	0.085 ^{NS}
Ropivacaine	30	23.33±1.95	

SD: Standard deviation

Table 2: The distribution of age in both the groups and P value

Age (years)	Bupivacaine (%)	Ropivacaine (%)	χ^2 (P-value)
19–21	11 (36.6)	4 (13.3)	0.086 ^{NS}
22–25	15 (50)	23 (76.7)	
More than 25	4 (13.4)	3 (10)	
Total	30 (100)	30 (100)	

Table 3: The mean height in cm and SD in both the groups

Group	n	Mean±SD	P value
Bupivacaine	30	153.26±3.609	0.393
Ropivacaine	30	154.03±3.285	

SD: Standard deviation

Table 4: The mean weight in kg and SD in both the groups

Group	n	Mean±SD	P-value
Bupivacaine	30	64.86±5.210	0.002
Ropivacaine	30	60.60±4.810	

SD: Standard deviation

Table 5: The mean duration of labor in both groups with SD and P value

Group	n	Mean±SD	P-value
Bupivacaine	30	251±50.74	0.49
Ropivacaine	30	242±50.40	

Level of Sensory Block

The level of sensory block achieved in each patient is variable and the dermatomal level achieved is a non-numerical variable. Therefore, we considered the most frequent value (mode) achieved in percentage in all the 60 patients and also separately in Group B and Group R.

A total of 60 patients, 44 patients (73.3%) achieved a level of T_8 , 11 patients (18.3%) achieved a level of T_6 , and 5 patients (8.3%) achieved a level of T_{10} .

In Group B, 23 patients (76.7%) achieved T_8 , 4 patients (13.3%) achieved a level of T_{10} , and 3 patients (10%) achieved a level of T_6 . In Group R, 21 patients (70%) achieved T_8 , 8 patients (26.7%) achieved T_6 , and 1 patient (3.3%) achieved T_{10} with P value 0.125 which was not significant.

In a similar study done by Meister *et al.*, the level of sensory block achieved in the bupivacaine-fentanyl group was T₈ (T_{6,9}) and in the ropivacaine-fentanyl group it was T₇ (T_{6,8}). They have considered the combined median (25–75th percentile).

In another study done by Kalra *et al.*, the level of sensory blockade achieved was expressed as number of patients who achieved T₆, T₈, and T₁₀, respectively, in fentanyl-bupivacaine group and sufentanyl-bupivacaine group. It was 2, 27, and 6 patients in the B - F Group and 2, 28, and 5 patients in B - SF Group.

Similar studies conducted by Polley *et al.* and Chua *et al.* also found that the most frequent sensory level achieved was T8.

Our results are concurring with the above studies.

Degree of Motor Block

The degree of motor blockade produced depends on the volume and concentration of drug used and also on the additional supplementation given from time to time. The degree of motor block was assessed at 20 min and every 30 min thereafter, until delivery. The degree of motor block was assessed using Bromage score. The degree of motor block in each patient varied from time to time. Results are expressed in various studies as a mean, median, and highest Bromage score achieved.

Our results were expressed as a trend of mean Bromage score in all 30 patients in both groups at 20 min and every 30 min thereafter for the entire duration of labor. Furthermore, the overall mean Bromage score was calculated for the entire duration in each group. In our study, the mean Bromage score in Group B was 0.65 with SD 0.42 and Group R was 0.35 with SD 0.27 and $P = 0.02$ which was statistically significant, but clinically, there was no difference with respect to mode of delivery. This is probably due to the low concentration (0.125%) of drug used for the study. A statistically significant difference in motor blockade in the groups may be attributable to the relative potencies of the drugs.

Since most of our patients had a Bromage score 0 or 1, we decided to test whether this statistically significant value had any clinical significance. Therefore, we considered the most frequent Bromage score reached in all patients in

both groups. We found that 46.6% of patients in Group B and 73.3% of patients in Group R had Bromage score 0, and 46.6% of patients in Group B and 26.6% of patients in Group R had Bromage score 1, and 6.6% patients in Group B had a Bromage score of 2, while this number was 0 in Group R.

In a similar study conducted by Paddalwar *et al.*, 2016, found in her study that no patient of 30 patients in group Ropivacaine developed motor block, whereas 5 patients in group bupivacaine developed Grade 2 (mild) motor block, which means the ability to weakly flex the knees (Bromage scale). P -value was 0.02, which was statistically significant, although the degree of block was mild. Distribution of Bromage scoring in both groups showed statistical significance ($P < 0.05$).

In a study conducted by Girard *et al.* comparing epidural bupivacaine versus ropivacaine (0.125%) both with 1 µg/mL fentanyl in laboring patients. They did not find any difference in the incidence of motor block between parturients receiving either ropivacaine or bupivacaine each at 0.125% with 1 µg/mL fentanyl for epidural labor analgesia. 15 parturients (45%) in the bupivacaine group and 17 (63%) in the ropivacaine group did not show any motor block (Bromage = 0) throughout labor. There were no differences in motor block between the two drugs (Chi-square = 1.84, $P = 0.4$). Indeed, there were more parturients without motor block in the ropivacaine group than in the bupivacaine group (45% vs. 63%). However, this difference was neither statistically significant nor clinically relevant.

In another study conducted by Merson *et al.* found that the incidence of motor blockade was 71% in the high (0.25%) bupivacaine group and 47% in the high (0.25%) ropivacaine group. It was 38% in the low (0.125%) bupivacaine group and only 0.06% in the low (0.125%) ropivacaine group. The overall odds ratio between higher and lower doses of either drug was 3.93. It was 9 for high doses of bupivacaine and ropivacaine. This indicates that overall there is a four-fold increase of motor blockade with bupivacaine and 9 times when higher doses are used. However, they did not find any clinically significant difference when mode of delivery was considered.

In the meta-analysis conducted by Guo *et al.* of epidural analgesia with bupivacaine and fentanyl versus ropivacaine and fentanyl for pain relief in labor, 15 randomized

Table 6: The number of patients who achieved most frequent sensory level in both the groups and all the patients over entire duration with P value

Number of Patients	Sensory level	Group B (%)	Group R (%)	Total (%)	χ^2 (P -value)
Number of patients (percentages)	T6	3 (10)	8 (26.7)	11 (18.3)	0.125
	T8	23 (76.7)	21 (70)	44 (73.3)	
	T10	4 (13.3)	1 (3.3)	5 (8.3)	
	Total	30 (100)	30 (100)	60 (100)	

controlled trials, recruiting 2097 parturient mothers overall, were selected for the meta-analyses showed 187 of 1015 women in ROPI-FEN group and 335 of 1022 women in BUPI-FEN group developed notable motor blocks as measured by modified Bromage scores. Both the odds ratio-based models revealed ROPI-FEN group to be significantly superior to BUPI-FEN combination.

Incidence of motor blocks was significantly lower in ROPI-FEN administered women, percent women who developed motor block measurable with Bromage scale were 18.4% in ROPI-FEN and 32.8% in BUPI-FEN treated groups. Incidence of motor blocks increased significantly with increasing concentration of bupivacaine but not significantly with ropivacaine. Overall, there was no significant relationship between fentanyl concentration and incidence of motor blocks.

Meister *et al.* in a similar study using 0.125% of both bupivacaine and ropivacaine with 2 µg/mL of fentanyl assessed the most intense motor blockade experienced by each patient at any assessment interval throughout labor. They found that 68% and 28% of patients had a Bromage score of 0, 32% and 68% had a Bromage score of 1.0%, and 4% had a Bromage score of 3 with ropivacaine and bupivacaine, respectively, indicating that bupivacaine produced a significant motor block when compared to ropivacaine.

Fernandez-Guisasola *et al.* who studied equipotent doses of bupivacaine (0.0625%) with fentanyl and (0.1%) ropivacaine with fentanyl found that the degree of motor blockade was similar at all-time intervals at which it was assessed. 5 (9.8%) patients in Group B and 3 (6.3%) in Group R had some degree of motor blockade which was not statistically significant.

In a study conducted by Bawadane *et al.* did not find any difference regarding motor blocks in the two groups of 0.1% ropivacaine versus 0.1% bupivacaine for extradural analgesia. This may be attributed due to lower concentration of local anesthetic used in it.

In all studies, the degree of motor blockade produced by bupivacaine is statistically significant when compared to ropivacaine, but clinically, there was no difference when compared with mode of delivery in all the studies.

VAS

After the initial bolus dose, analgesia was maintained by intermittent bolus injections of 5 mL every 40–60 min. Patients who experienced inadequate analgesia (VAS >4) during the process were supplemented with additional 5 mL of solution up to a maximum of 10 mL/h until the delivery of the baby.

Pain was assessed by VAS before initiating the epidural (zero time) and after 5, 10, 20, 30, 45, and 60 min and every 30 min after that, until delivery. The VAS score in each patient varied from time to time. Results are expressed in various studies as a mean or median (25–75th percentile) of VAS.^[7]

Our results were expressed as a trend of mean VAS score in all 30 patients of each group at 0, 5, 10, 20, 30, 45, and 60 min and every 30 min after that, until delivery. Before epidural injection, the mean score was 7.9 and 7.6 in Group B and Group R, respectively. After administration of the drug the mean VAS score in Group B was 1.53 with SD 0.46 and Group R was 1.54 with SD 0.46 and $P = 0.08$ which was statistically not significant. The trend of the mean VAS was similar and there was not much variation between the groups at different time intervals.

Paddalwar *et al.* in another similar study compared the analgesic potency of 0.125% bupivacaine and 0.125% ropivacaine, both with fentanyl 2 µg/mL. They measured pain by the VAS before initiating the epidural and at 5, 10, 15, 20, 30, 60, and 90 min and every 30 min after that, until delivery. The mean baseline VAS score in Group R was 9.60 ± 0.968 , whereas in Group B, it was 9.17 ± 0.98 . At 20 min, all the patients in both the groups were pain free with a VAS score of 0–2. Distribution of VAS at various intervals in both the groups was comparable and showed no statistical significance.

In a similar study done by Meister *et al.*, equi-concentration solutions (0.125%) of bupivacaine-fentanyl and ropivacaine-fentanyl were compared for their analgesic efficacy. They used the numeric rating scale (NRS) for grading of pain before initiating epidural and 60 min after initiation. They found that the mean NRS before epidural initiation was 9 with a SD of 1 in bupivacaine-fentanyl and 8 with a SD of 1 in ropivacaine-fentanyl groups. 60 min after initiation, it was 0.4 with SD 1 in bupivacaine-fentanyl group and 0.3 with SD of 1 in ropivacaine-fentanyl group. They found no statistical significance between the drugs.

Similar studies done by Kalra *et al.*, Fernandez-Guisasola *et al.*, and Guo *et al.* also found that there was no difference between the mean VAS scores between bupivacaine and ropivacaine at different time intervals and also the average scores over the entire duration.

Our results are concurring with the above studies.

Hemodynamics

During the procedure, the following hemodynamics such as oxygen saturation, heart rate, non-invasive blood pressure, and FHR were monitored. These parameters were

monitored at 0, 5, 10, 20, 30, 45, and 60 min and every 30 min after that, until delivery.

Oxygen Saturation

Our results were expressed as a trend of mean SPO₂ in both the groups for the entire duration and also the overall mean SPO₂ in the 2 groups. The mean SPO₂ in Group B was 98.7% with SD 0.57 and in Group R was 99.1% with SD 0.59 with $P = 0.009$ which was statistically significant. Changes in the SPO₂ between the two groups were statistically significant, but clinically, there was not much difference between the two groups. Trend diagram also shows that not much variation between two curves of Group B and Group R.

Heart Rate

Our results were expressed as a trend of mean HR in both the groups for the entire duration and also the overall mean HR in the 2 groups. The mean heart rate in Group B was 81.8 with SD 10.81 and in Group R was 83.40 with SD of 7.52 with P -value of 0.49 which was statistically not significant.

Similar results were found in the studies of Paddalwar *et al.*, Meister *et al.*, and Lacassie *et al.*

Non-Invasive Blood Pressure (SBP, Diastolic Blood Pressure [DBP], Arterial Pressure [MAP])

Our results were expressed as a trend of mean systolic, mean arterial, and diastolic pressure in both the groups for the entire duration and also the overall mean systolic, mean arterial, and diastolic pressure in the 2 groups.

The mean SBP in Group B was 116.6 with SD 6.91 and in Group R was 116.4 with SD of 7.13 with $P = 0.909$ which was statistically not significant.

The mean DBP in Group B was 74.40 with SD 4.41 and in Group R was 79.6 with SD of 3.77 with $P = 0.001$ which was statistically significant.

The mean MAP in Group B was 88.2 with SD 4.61 and in Group R was 91.5 with SD of 4.76 with $P = 0.0008$ which was statistically significant.

The changes in SBP, DBP, and MAP between the two groups were statistically significant, but clinically, there was not much difference between the two groups. The trend diagrams show that there is not much variation between the curves of Group B and Group R.

In many similar studies conducted by Paddalwar *et al.*, Meister *et al.*, and Polley *et al.*, etc., the changes in SBP, DBP, and MAP were not statistically significant between the two groups.

In our study, the significant statistical difference between the two groups may be attributed to differences in the sample sizes, variations in the doses and concentrations of drug used and method of supplementation. In our study, analgesia was maintained by intermittent bolus injections of 5 ml every 40–60 min. Patients who experienced inadequate analgesia (VAS >4) during the process were supplemented with additional 5 ml of solution up to a maximum of 10 mL/h until the delivery of the baby.

FHR

FHR was monitored using Doppler at 0, 5, 10, 20, 30, 45, and 60 min and every 30 min after that, until delivery. Our results were expressed as trend of mean FHR at regular time intervals and also the overall mean. The mean FHR in Group B was 140.9 with SD 5.22 and in Group R was 140.3 with SD of 2.63 with $P = 0.577$ which was statistically not significant.

Paddalwar *et al.* in a similar study compared the mean FHR at 0, 5, 10, 15, 20, and 30 min and every 30 min after that, until delivery. They found that the trend of mean FHR in both the groups were comparable with $P > 0.05$.

In a study done by Chua *et al.* FHR was monitored continuously throughout labor and they did not find any variation in FHR in both groups. The FHR was comparable with $P > 0.05$.

Finegold *et al.* in his study monitored FHR every hour from the initiation of epidural until the patient was 10 cm dilated. The mean FHR was 132 ± 16 bpm in bupivacaine group and 131 ± 21 in ropivacaine group. They found no difference existed between the groups ($P > 0.05$).

Adverse Effects

In our study, there were no clinically significant adverse effects such as bradycardia, hypotension, and desaturation which required active intervention.

CONCLUSION

In our study comparing equi-concentration (0.125%) bupivacaine-fentanyl 2 µg/mL and (0.125%) ropivacaine-fentanyl 2 µg/mL for epidural labor analgesia results indicate that both are equally effective clinically by intermittent epidural supplementation in providing excellent labor analgesia with hemodynamic stability, minimal motor blockade, mode of delivery, and maternal satisfaction without serious maternal or fetal side effects. The reported benefit of ropivacaine over bupivacaine such as lower motor blockade and lesser cardiotoxicity are more apparent when higher concentrations are used.

We conclude that there is clinically no significant difference between bupivacaine and ropivacaine for epidural labor analgesia when lower concentrations (0.125%) of the drug with fentanyl (2 µg/mL) as an adjuvant are used.

This study was undertaken to compare equi-concentration of bupivacaine-fentanyl and ropivacaine-fentanyl for epidural labor analgesia in primigravida patients.

- Group B - received 0.125% bupivacaine with 2 µg/mL fentanyl.
- Group R - received 0.125% ropivacaine with 2 µg/mL fentanyl.

With aseptic precautions epidural catheter was inserted and drug was given. Sensory level, motor blockade, VAS, hemodynamics, FHR, mode of delivery, patient satisfaction, and total dose of local anesthetic used were recorded.

Our results indicate that both are equally effective clinically in:

- Providing excellent labor analgesia,
- Hemodynamic stability,
- Maternal satisfaction without serious maternal or fetal side effects,
- Total local anesthetic dose used,
- Statistically significant motor blockade produced by bupivacaine compared to ropivacaine does not change mode of delivery at lower concentrations.

We conclude that lower concentration of bupivacaine or ropivacaine with opioids provide excellent analgesia for most obstetric patients.

REFERENCES

1. Wong CA. Advances in labor analgesia. *Int J Womens Health* 2009;1:139-54.
2. Hawkins JL. Epidural analgesia for labor and delivery. *N Engl J Med* 2010;362:1503-10.
3. Polley LS, Columb MO, Naughton NN, Wagner DS, van de Ven CJ. Relative analgesic potencies of ropivacaine and bupivacaine for epidural analgesia in labor: Implications for therapeutic indexes. *Anesthesiology* 1999;90:944-50.
4. Capogna G, Celleno D, Fusco P, Lyons G, Columb M. Relative potencies of bupivacaine and ropivacaine for analgesia in labor. *Br J Anaesth* 1999;82:371-3.
5. Owen MD, D'Angelo R, Gerancher JC, Thompson JM, Foss ML, Babb JD, *et al.* 1.25% ropivacaine is similar to 0.125% bupivacaine for labor analgesia using patient-controlled epidural infusion. *Anesth Analg* 1998;86:527-31.
6. Lyons G, Columb M, Hawthorne L, Dresner M. Extradural pain relief in labor: Bupivacaine sparing by extradural fentanyl is dose dependent. *Br J Anaesth* 1997;78:493-7.
7. Kalra S, Saraswat N, Agnihotri GS. Comparison of bupivacaine and fentanyl with *Bupivacaine* and sufentanil for epidural labor analgesia. *Saudi J Anaesth* 2010;4:178-81.
8. Sah N, Vallejo M, Phelps A, Finegold H, Mandell G, Ramanathan S. Efficacy of ropivacaine, bupivacaine, and levobupivacaine for labor epidural analgesia. *J Clin Anaesth* 2007;19:214-7.
9. Li-zhong W, Xiang-yang C, Xia L, Xiao-xia H, Bei-lei T. Comparison of bupivacaine, ropivacaine and levobupivacaine with sufentanil for patient-controlled epidural analgesia during labor: A randomized clinical trial. *Chin Med J* 2010;123:178-83.

How to cite this article: Kumar GS, Rao BS, Kumar UM. A Comparative Study of Equi-concentration of Bupivacaine-Fentanyl and Ropivacaine-Fentanyl for Epidural Labor Analgesia. *Int J Sci Stud* 2018;6(5):112-120.

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

Effect of Audio and Audiovisual Aids on Anxiety Level of Patients during First Appointment of Root Canal Treatment: An *In Vivo* Study

Sadashiv Daokar¹, Snehashree Pophli², Kalpana Pawar³, Kapil Wahane⁴, Rohit Tambake⁵, Laxmikant Late²

¹Professor, Head and PG Guide, Department of Conservative Dentistry and Endodontics, CSMSS Dental College and Hospital, Aurangabad, Maharashtra, India, ²Post Graduate Student, Department of Conservative Dentistry and Endodontics, CSMSS Dental College and Hospital, Aurangabad, Maharashtra, India, ³Professor and Post Graduate Guide, Department of Conservative Dentistry and Endodontics, CSMSS Dental College and Hospital, Aurangabad, Maharashtra, India, ⁴Reader and Post Graduate Guide, Department of Conservative Dentistry and Endodontics, CSMSS Dental College and Hospital, Aurangabad, Maharashtra, India, ⁵MDS, Department of Conservative Dentistry and Endodontics, CSMSS Dental College and Hospital, Aurangabad, Maharashtra, India

Abstract

Aim: The aim of this study is to compare the effect of audio and audiovisual aids on anxiety reduction of patients during the first visit of root canal treatment and to compare anxiety level between male and female patients.

Materials and Methods: A total of 90 patients were randomly divided into three groups depending on anxiety reduction method and again divided into subgroups depending on gender. Before starting endodontic treatment, the interviewer administered the Corah's Dental Anxiety Scale to the participants to assess the level of anxiety. Music and videos were played according to patient's preference. Before, during, and after endodontic procedures, the vital parameters (diastolic and systolic blood pressure, heart rate, and respiratory rate) were recorded. There are three groups: Group I ($n = 30$): Control group, Group II ($n = 30$): Audio aid, and Group III ($n = 30$): Audiovisual aid.

Statistical Analysis Used: Statistical analysis was performed using one-way Analysis of variance

Results: All measured vital signs decreased considering the overall period (during and after canal therapy) in audiovisual group.

Conclusions: Audio and audiovisual distraction techniques provided effective reduction in dental anxiety. Female patients showed greater anxiety than male patients.

Key words: Anxiety, Blood pressure, Heart rate

INTRODUCTION

Medical procedures almost always elicit a sense of loss of control, fear, helplessness, and feelings of stress and anxiety.^[1] Anxiety and fear of the dentist are common phenomenon, and it is universally recognized. Many patients fear to visit the dental clinic because of dental anxiety. Fear and anxiety toward the dentist and dental

treatment are both significant characteristics that contribute to the avoidance of dental care.^[2] Depending on the population and the measurement technique, 2.5–20% of people suffer high dental anxiety.^[3] Dental anxiety has been cited as the fifth most common cause of anxiety by Agras.^[2]

Dental anxiety is defined as patient's specific reaction toward stress related to the dental treatment in which the stimulus is unknown, vague or not present at that moment.^[3] Dental anxiety is a significant determinant whether people will make regular dental visits.^[4]

Anxiety and fear are often used interchangeably. Fear is a reaction to known or perceived threat or danger. Odontophobia is overwhelming and irrational fear

Access this article online



www.ijss-sn.com

Month of Submission : 06-2018

Month of Peer Review : 07-2018

Month of Acceptance : 08-2018

Month of Publishing : 08-2018

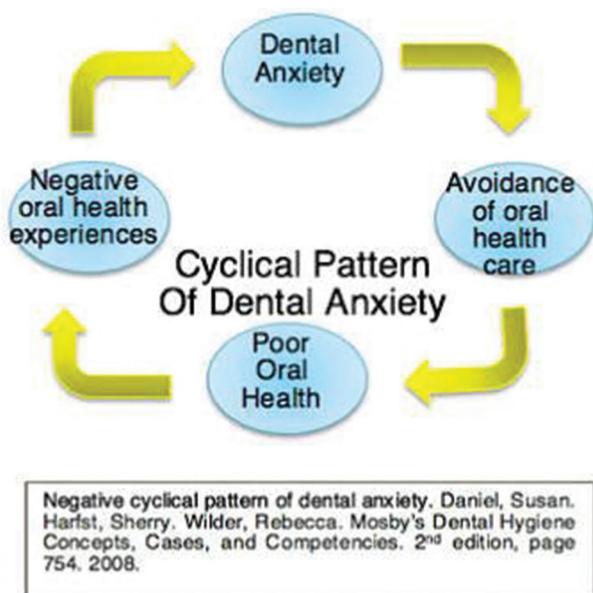
Corresponding Author: Dr. Snehashree Pophli, C/O Mr. Sanjay Pophli, Amrut Sai Sara City, Dwing Flat no 404, Kanchanwadi, Near Walmi Naka, Paithan Road, Aurangabad, Maharashtra, India. Phone: +91-9860994420. E-mail: snehashri.pophli88@gmail.com

of dentistry associated with devastating feelings of hypertension, terror, trepidation, and unease.^[2]

The first endodontic appointment, during which access will be gained and pulpal tissues removed, provides the greatest challenge to the endodontist. The primary obstacle to successful endodontic treatment is the presence of dual problems pain and fear.^[5] The effects of this anxiety associated with and exacerbated by the most frequent symptom in dentistry and dental pain are represented in the plane of the dental care, the hindering the cooperation with the dentist, extension of the duration, its medical benefits (on average about 20%), and subsequent trends postponing the presentation at the dental office.^[6] Peter Milgrom said “Deal with the fear first, then pain will be a minor problem.”^[5]

A study by Wong and Lytle showed that root canal therapy and oral surgery were found to be the most anxiety-provoking treatments.^[7] A woman tends to experience more root canal treatment (RCT)-associated anxiety and anticipates more pain than men.^[3]

Vicious Cycle of Dental Fear^[8]



Due to multifactorial etiology of dental anxiety, there is no monotherapy for management. Broadly, dental anxiety can be managed by psychotherapeutic interventions, pharmacological interventions, or a combination of both.^[2]

We should always try to reduce our patient anxiety by a non-pharmacologic manner. One option that has been shown to be a reliable alternative to pharmacologic methods is distraction.^[9]

Distraction, one of the psychobehavioral approaches used in medical and dental treatment situations, is defined as a non-aversive approach used to modify a patient's discomfort

by disrupting his/her attention away from the main task to accomplish successful treatment with a high quality.^[10]

Based on the theory by McCaul and Mallot, a patient's perception of pain is decreased when the patient is distracted from an unpleasant stimulus.^[9] Audiovisual aid is a new approach that has gained popularity to help relieve anxiety related to endodontics that incorporates a visual as well as an audio component.^[11]

In this study, we compared audio and audiovisual distraction techniques in managing anxiety during the first visit of endodontic appointment, and we also compared anxiety reduction between male and female patients.

This can be accomplished by having patients to listen music through JBL headphones in audio group and by having patients to watch an informative movie about the procedure or videos about dental and oral health by utilizing HP laptop and headphones to help better educate them.

SUBJECTS AND METHODS

Source of Data

A total of 90 patients requiring endodontic therapy were recruited for this study.

The selection of patients was made on the basis of the following criteria:

Inclusion Criteria

The following criteria were included in the study:

1. Age - 25 and 40 years.
2. Maxillary and mandibular molars with irreversible pulpitis or pulp necrosis

Exclusion Criteria

The following criteria were excluded from the study:

1. Uncooperative patients
2. Smokers and alcoholics
3. Individuals with any medical disorders and on anxiolytic and sedative medications
4. Patients who have undergone previous RCT
5. Pregnant women.

Patient's Preparation

All participants were informed about the aim of the present study. During the first visit, the ethical approval was requested and granted, and informed consent was obtained from each patient.

Randomization and Experimental Groups

The patients were randomly divided into three groups. Each group includes 15 males and 15 females.

- Group 1 (n = 30) control group
- Group 2 (n = 30) 432 Hz music
- Group 3 (n = 30) audiovisual aid.

Experimental Procedure

Patients were sitted in dental chair, and the patient was asked to complete a Corah’S Dental Anxiety Scale questionnaires. Upon completion of the questionnaires, vital parameters (diastolic blood pressure, Systolic blood pressure, heart rate, respiratory rate) were checked by Multipara monitor (Meditech MP 1200). Music or videos were played according to patient’s preference. All treatments were performed under local anesthesia using lignocaine hydrochloride without adrenaline (LOX 2%, NEON). The teeth were isolated with rubber dam. After rubber dam isolation, again vital parameters were checked. Access opening was performed by Airotor handpiece (Kavo 506c Extra Torque Handpiece) followed by pulp extirpation (Dentsply Barbed Broaches), irrigation (Prime Dental Sodium Hypochlorite), and intracanal medicament placement (RC CAL prime dental) and temporary filling material (Cavit W, 3M ESPE). Again vital parameters checked and compared after the removal of rubber dam. Music and videos were allowed to play throughout the RCT procedure. The subjects in the control group went through the same procedure, but without the evaluation of music and video preference and no music was played during the procedure. All vital parameters were recorded before local anaesthetic injection, at the treatment midpoint and after the removal of rubber dam with the help of Multipara monitor. Figure 1, Figure 2 and Figure 3 shows Corah’s Dental Anxiety Scale, Experimental procedure

and Armamentarium used in study (from left to right JBL Headphones, Multipara Monitor, HP Laptop respectively).

Selection of Audio and Audiovisual Aid

The music and videos selected for this study were according to the patient’s preference. The compositions were tuned to 432 Hz. The selection of music consisted of classical, environmental, new age, country-western, and general easy listening music. Audiovisual aid consists of informative movie about the procedure or videos about dental and oral health.

RESULTS

Statistical analysis was performed by one-way analysis of variance. Diastolic blood pressure, systolic blood pressure, heart rate, and respiratory rate were measured, and all parameters were analyzed and tabulated [Table 1]. Based on data obtained, comparison of estimated means between groups was recorded [Table 1]. Table 2 shows comparison of estimated means for point of time. The effect of audiovisual and audio aid was statistically significant (< 0.001) [Table 2]. Female patients showed more anxiety as compared to males [Graph 1].

DISCUSSION

In the present-day dentistry, endodontic procedures are among the most common dental therapies. Only a few studies have evaluated the level of anxiety and the different approaches available for the treatment of dental anxiety in adults although the demands for sedation in endodontics are high.^[12]

Table 1: Comparison of estimated means between the groups (with control)

Variable	Group	Mean difference	Standard error	P	Significant
Systolic blood pressure	Music	-4.377*	2.056	0.034	No
	Video	-6.194*	1.983	0.002	Yes
Diastolic blood pressure	Music	3.45*	1.395	0.014	Yes
	Video	5.68*	1.353	0.000	Yes
Heart rate	Music	-3.50*	0.937	0.000	Yes
	Video	-3.88*	0.909	0.000	Yes
Respiratory rate	Music	2.02*	0.219	0.000	Yes
	Video	2.21*	0.213	0.000	Yes

Table 2: Comparison of estimated means for the point of time

Variable	Time	Mean difference	Standard error	P	Significant
Systolic blood pressure	During	2.974	1.989	0.136	No
	After	2.121	1.989	0.287	No
Diastolic blood pressure	During	2.57	1.354	0.050	Yes
	After	1.93	1.354	0.156	No
Heart rate	During	0.79	0.910	0.387	No
	After	2.51*	0.910	0.006	Yes
Respiratory rate	During	0.79*	0.213	0.000	Yes
	After	1.26*	0.213	0.000	Yes

Corah's Dental Anxiety Scale, Revised (DAS-R)

Name _____ Date _____

Norman Corah's Dental Questionnaire

1. If you had to go to the dentist tomorrow for a check-up, how would you feel about it?
 - a. I would look forward to it as a reasonably enjoyable experience.
 - b. I wouldn't care one way or the other.
 - c. I would be a little uneasy about it.
 - d. I would be afraid that it would be unpleasant and painful.
 - e. I would be very frightened of what the dentist would do.
2. When you are waiting in the dentist's office for your turn in the chair, how do you feel?
 - a. Relaxed.
 - b. A little uneasy.
 - c. Tense.
 - d. Anxious.
 - e. So anxious that I sometimes break out in a sweat or almost feel physically sick.
3. When you are in the dentist's chair waiting while the dentist gets the drill ready to begin working on your teeth, how do you feel?
 - a. Relaxed.
 - b. A little uneasy.
 - c. Tense.
 - d. Anxious.
 - e. So anxious that I sometimes break out in a sweat or almost feel physically sick.
4. Imagine you are in the dentist's chair to have your teeth cleaned. While you are waiting and the dentist or hygienist is getting out the instruments which will be used to scrape your teeth around the gums, how do you feel?
 - a. Relaxed.
 - b. A little uneasy.
 - c. Tense.
 - d. Anxious.
 - e. So anxious that I sometimes break out in a sweat or almost feel physically sick.

Scoring the Dental Anxiety Scale, Revised (DAS-R)
(this information is not printed on the form that patients see)
a = 1, b = 2, c = 3, d = 4, e = 5 Total possible = 20

Anxiety rating:

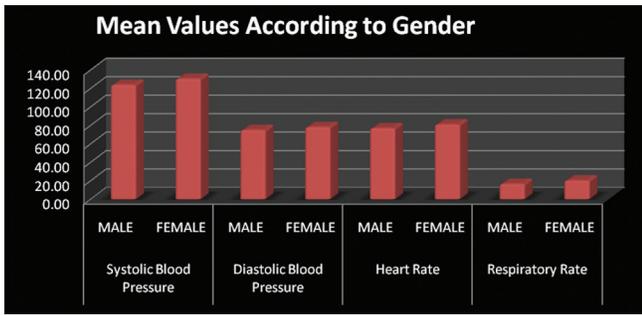
- 9 - 12 = moderate anxiety but have specific stressors that should be discussed and managed
- 13 - 14 = high anxiety
- 15 - 20 = severe anxiety (or phobia). May be manageable with the Dental Concerns Assessment but might require the help of a mental health therapist.

Figure 1: Corah's Dental Anxiety Scale

Patients who need endodontic treatment are often burdened by two main concerns, the length of the procedure and the pain.^[13] Pain causes an alarm reaction manifested by hypothalamic-oriented vasoconstriction and dilatation as well as the release of more epinephrine and norepinephrine. This results in increased heart rate and

cardiac output. In addition, pain may cause blood pressure to rise due to the release of endogenous catecholamine.^[14]

According to Georgelin, physiologic stress peaks early in a Root canal treatment appointment, around the time of local anesthesia delivery and initial instrumentation.^[15]



Graph 1: Mean values according to gender



Figure 2: Access opening procedure under experimental group



Figure 3: Armamentarium Used In Study

Etiology of dental anxiety is multifactorial such as previous negative experience, especially in childhood, vicarious learning from anxious family members or peers, individual personality characteristic such as neuroticism and self consciousness, lack of understanding, exposure to frightening portrayals of dentists in the media, the coping style of the person, perception of body image, and vulnerable position of lying back in the dental chair.^[2]

The initial interaction of the dentist with the patient can fairly reveal the presence of anxiety and fear, and in such situations, subjective evaluations using different multiple and single item self-reporting questionnaires and objective evaluations involving measurement of vital parameters can greatly enhance the diagnosis for successful management.^[2] The Corah's Dental Anxiety Scale (CDAS), modified DAS, and dental fear survey are the most commonly used questionnaires.^[2]

Various objective measures in measuring dental anxiety are an assessment of blood pressure, pulse rate, pulse oximetry, finger temperature, and galvanic skin response. An extremely accurate objective method used in various studies to measure dental anxiety is galvanic skin response.^[2]

This study evaluates the effect of audio and audiovisual aid on the anxiety level of patients during the first visit of endodontic treatment. The results obtained suggested that patients in audiovisual group showed more anxiety reduction because patients focus their attention on relaxation videos instead of anxiety-inducing dental equipment. It has been reported previously that such an audiovisual system is beneficial in the reduction of fear and pain for both adults and children undergoing dental prophylaxis and restorative procedures.^[16]

Measurement of Anxiety Level in this Study

We measured the anxiety level subjectively by CDAS and objectively by comparing their vital signs. In this study, the anxiety level of the subjects before treatment was measured by CDAS. It is considered reliable for its simplicity of application and the ease of translation into the patients' native languages.^[17] The scale consists of four questions about different dental situations. Hence, the range of possible score is from 4 to 20. The cutoff point of >15 indicates high anxiety level or possibly phobic.^[2]

Music and Anxiety

During dental treatments, music may elicit audio-analgesic responses due to different factors, including the masking of sound, distraction, and direct neurological suppression of pain.^[18] Music therapy can reduce anxiety and also have an analgesic effect by acting at psychological level. It acts by releasing intracerebral endorphins and distract the patient from painful and anxiogenic stimuli. It gives feeling of familiarity and comfort to patient in dental office.^[6] Music reduces activity in the neuroendocrine and sympathetic nervous systems, resulting in decreased anxiety, heart rate, respiratory rate, blood pressure, and better sleep.^[19]

The musical composition selected for this study tuned to 432 HZ instead of 440 Hz. Schumann resonance theory proposed that 432 Hz is the frequency at which earth beats. Hence, we should spent more time attuned to the natural electromagnetic

pulses of the earth at 432 Hz, and we would, in turn, feel more centered, balanced, conscious, and peaceful.^[20]

In this study, we also compared anxiety between male and female patients. Results showed greater anxiety in female patients as compared to male patients. One reason for this trend could be that males tend to hide their fears due to their orthodox gender role.^[3] In addition, it has been reported that, in general, females are more reactive to a specific stimulus than males, which could account for the higher anxiety levels reported by females.^[3]

Studies have shown that the average age at which reduction of fear begins is 40 years for both men and women.^[13] This may be explained by the increase of tolerance of frequent exposure to stressful situations over a prolonged period and life experience that shapes the behavioral characteristics of the individual.^[13]

Lai *et al.* studied the effect of music on state anxiety in patients undergoing root canal therapy. The subject's heart rate, blood pressure, and finger temperature were measured before treatment and during treatment. The results showed that subjects in the music group had a significant increase in finger temperature and a decrease in anxiety score over control group.^[19]

Prabhakar *et al.* compared audio and audiovisual device in reducing dental anxiety in pediatric patients. The results showed that audiovisual distraction technique is more effective in managing anxious patients than audio and normal dental setup.^[21]

Khotani *et al.* evaluated in their study effectiveness of viewing videotaped cartoons as an audiovisual distraction technique on behavior and anxiety of children receiving dental restorative treatment. Children using audiovisual distraction do not only report less distress during the procedure than control group but also show a more positive response after injection with local anesthesia.^[22]

CONCLUSIONS

Audio and audiovisual distraction techniques provided an effective reduction in dental anxiety. Female patients showed greater anxiety than male patients.

REFERENCES

1. Garbee DD, Gentry JA. Coping with the stress of surgery. *AORN J* 2001;73:946, 949-51.
2. Appukkuttan DP. Strategies to manage patients with dental anxiety and dental phobia: Literature review. *Clin Cosmet Investig Dent* 2016;8:35-50.
3. Wali A, Siddiqui TM, Gul A, Khan A. Analysis of level of anxiety and fear before and after endodontic treatment. *J Dent Oral Health* 2016;2:1-4.
4. Bashiru BO, Omotola OE. Prevalence and determinants of dental anxiety among adult population in Benin city, Nigeria. *Eur J Gen Dent* 2016;5: 99-103.
5. Ingle JI, Bakland LK, Baumgartner JC. Anxiety and Fear in the Endodontic Patient. *Endodontics*. 6th ed. Ch. 23. Lewiston, NY: BC Decker; 2008. p. 737-48.
6. Iorgulescu G. Musicotherapy in dental medicine. *Int J Music Perform Arts* 2015;3:19-24.
7. Wong M, Lytle WR. A comparison of anxiety levels associated with root canal therapy and oral surgery treatment. *J Endod* 1991;17:461-5.
8. Daniel SJ, Harfst SA, Wilder R. Mosby's Dental Hygiene Concepts, Cases, and Competencies. 2nd ed. St. Louis (MO): Mosby, Inc.; 2008. p. 754.
9. Lai HL, Hwang MJ, Chen CJ, Chang KF, Peng TC, Chang FM, *et al.* Randomised controlled trial of music on state anxiety and physiological indices in patients undergoing root canal treatment. *J Clin Nurs* 2008;17:2654-60.
10. Pinkham JR. Behavior management of children in the dental office. *Dent Clin North Am* 2000;44:471-86.
11. McCaul KD, Malott JM. Distraction and coping with pain. *Psychol Bull* 1984;95:516-33.
12. Huh YK, Montagnese TA, Harding J, Aminoshariae A, Mickel A. Assessment of patients' awareness and factors influencing patients' demands for sedation in endodontics. *J Endod* 2015;41:182-9.
13. Perković I, Romić MK, Perić M, Krmek SJ. The level of anxiety and pain perception of endodontic patients. *Acta Stomatol Croat* 2014;48:258-67.
14. Hondrum SO. Hypertensive episode in the dental office. *Gen Dent* 1985;33:134-9.
15. Georgelin-Gurgel M, Diemer F, Nicolas E, Hennequin M. Surgical and nonsurgical endodontic treatment-induced stress. *J Endod* 2009;35:19-22.
16. Frere CL, Crout R, Yorty J, McNeil DW. Effects of audiovisual distraction during dental prophylaxis. *J Am Dent Assoc* 2001;132:1031-8.
17. Di Nasso L, Nizzardo A, Pace R, Pierleoni F, Pagavino G, Giuliani V, *et al.* Influences of 432 Hz music on the perception of anxiety during endodontic treatment: A Randomized controlled clinical trial. *J Endod* 2016;42: 1338-43.
18. Standley JM. Music research in medical/dental treatment: Meta-analysis and clinical applications. *J Music Ther* 1986;23:56-122.
19. Lai HL, Good M. An overview of music therapy. *J Nurs* 2002;49:80-4.
20. Hz-Uneathing The Truth Behind Nature's Frequency. Available from: <http://www.binauralbeatsmeditation.com>.
21. Prabhakar AR, Marwah N, Raju OS. A comparison between audio and audiovisual distraction techniques in managing anxious pediatric dental patients. *J Indian Soc Pedod Prev Dent* 2007;25:177-82.
22. Al-Khotani A, Bello LA, Christidis N. Effects of audiovisual distraction on children's behaviour during dental treatment: A randomized controlled clinical trial. *Acta Odontol Scand* 2016;74:494-501.

How to cite this article: Daokar S, Pophli S, Pawar K, Wahane K, Tambake R, Late L. Effect of Audio and Audiovisual Aids on Anxiety Level of Patients during First Appointment of Root Canal Treatment: An *In Vivo* Study. *Int J Sci Stud* 2018;6(5):121-126.

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

A Comparative Study between Bupivacaine 0.5% and Ropivacaine 0.75% in Epidural Analgesia in Patients Undergoing Elective Lower Abdominal and Lower Limb Surgeries

G Shravan Kumar¹, R Shanthan Kumar², Laxmi Kanth³, M Srinath⁴

¹Associate Professor, Department of Anaesthesiology and Intensive Care, Kakatiya Medical College, Mahatma Gandhi Memorial Hospital, Warangal, Telangana, India, ²Associate Professor, Kakatiya Medical College, Warangal, Telangana, India, ³Junior Resident, Department of Anaesthesiology and Intensive Care, Kakatiya Medical College, Mahatma Gandhi Memorial Hospital, Warangal, Telangana, India

Abstract

Background: Regional anesthesia is noted for its simplicity, safety, and effectiveness. Although spinal anesthesia provides an efficient block, it has some limitations. Epidural anesthesia is one of regional techniques for lower abdominal and lower limb surgeries. Bupivacaine is the drug of choice for providing effective epidural analgesia. Ropivacaine is new long-acting local anesthetic with similar chemical structure but with less cardiotoxicity and central nervous system toxicity. We did a prospective randomized control study to compare between two groups - 20 ml of 0.75% ropivacaine (isobaric) and 20 ml 0.5% bupivacaine (isobaric) for epidural anesthesia in lower abdominal and lower limb surgeries in adults aged 18–60 years.

Aim: The study aimed to compare in two groups - 20 ml of 0.75% ropivacaine (isobaric) and 20 ml 0.5% bupivacaine (isobaric) for epidural analgesia in lower abdominal and lower limb surgeries in adults.

Design: This was a prospective randomized control study.

Methods: The study population was randomly divided into 2 groups with 30 patients in each group. Study Group R - received 20 ml of 0.75% ropivacaine (isobaric) by epidural route study Group B - received 20 ml of 0.5% bupivacaine (isobaric) by epidural route and compared (1) onset of sensory and motor block, (2) highest level of sensory block, (3) degree of motor blockade (using Modified Bromage scale), (4) duration of motor blockade, (5) duration of sensory analgesia, (6) hemodynamic changes heart rate, blood pressure, and respiratory rate, and (7) side effects if any

Results: Nearly 0.75% ropivacaine has a shorter duration of motor block when compared with 0.5% bupivacaine. The onset of sensory and motor blocks, highest level of sensory block, degree of motor block, and duration of sensory analgesia are similar to that of bupivacaine. The hemodynamic changes and side effect profile of ropivacaine are also not significantly different from that of bupivacaine.

Conclusion: Based on the present clinical comparative study, we conclude that ropivacaine can be used as a safe alternative to bupivacaine for epidural anesthesia in lower abdominal and lower limb surgeries. The shorter duration of motor block with ropivacaine suggest that it could be effectively used for early mobilization of patients in the post-operative period.

Key words: Bupivacaine, Epidural analgesia, Onset of motor block, Onset of sensory block, Ropivacaine

Access this article online



www.ijss-sn.com

Month of Submission : 06-2018

Month of Peer Review : 07-2018

Month of Acceptance : 08-2018

Month of Publishing : 08-2018

INTRODUCTION

Regional anesthesia is noted for its simplicity, safety, and effectiveness. Anesthesia with an efficient block, having least onset time and which can be prolonged with least complications is one of the challenges faced by the anesthesiologist.

Corresponding Author: : Dr. Repalle Shanthan Kumar, H. No: 5-12-22, Hanuman Nagar, University Road, Hanamkonda, Warangal-506 009, Telangana, India. , Telangana, India. Mobile: +91-9885054263. E-mail: shanthanrepalle@yahoo.com

Although spinal anesthesia provides an efficient block, it has some disadvantages such as height of block cannot be controlled, duration of block is constant and cannot be prolonged, and it is associated with complications such as post-dural puncture headache and neurological sequelae.

Epidural anesthesia is one of the regional techniques for lower abdominal, lower limb, pelvic, and vascular surgeries where complications are very less compared to spinal anesthesia. Furthermore, there is no limitation for the duration of surgery if an epidural catheter is in place. It can also be used as a modality for post-operative pain relief.

Bupivacaine has been the drug of choice in providing effective epidural anesthesia followed by post-operative analgesia for a considerable time.

Ropivacaine is a new, long-acting local anesthetic which is chemically homologous with bupivacaine and mepivacaine.^[1] It is similar to the “S” enantiomer of bupivacaine, except that a propyl group is present in place of butyl group on the piperidine ring’s tertiary nitrogen atom.^[2]

Ropivacaine exhibits less cardiotoxicity and central nervous system (CNS) toxicity. It produces effective analgesia as that of bupivacaine and that motor block appears to regress considerably more rapidly than sensory block.^[2] This makes ropivacaine potentially well suited for administration through the epidural route for epidural anesthesia.^[1]

Hence, this is prospective randomized control study to compare in two groups - 20 ml of 0.75% ropivacaine (isobaric) and 20 ml 0.5% bupivacaine (isobaric) for epidural anesthesia in lower abdominal and lower limb surgeries in adults aged 18–60 years.

Aims and Objectives of the Study

This was a prospective randomized control study to compare the following factors in two groups - 20 ml of 0.5% bupivacaine (isobaric) and 20 ml of 0.75% ropivacaine (isobaric) for epidural analgesia in lower abdominal and lower limb surgeries in adults aged 18–60 years, with respect to:

- Onset of sensory and motor block
- Highest level of sensory block
- Degree of motor blockade (using Modified Bromage scale)
- Duration of sensory analgesia
- Hemodynamic changes - heart rate, blood pressure, and respiratory rate at various time intervals
- Side effects if any.

METHODS

This study was conducted on patients undergoing elective lower limb and lower abdominal surgeries in M.G.M Hospital, attached to Kakatiya Medical College, Warangal, during the academic year from December 2012 to July 2014.

After Ethical Committee approval and written informed consent, 60 patients aged between 18 and 60 years undergoing elective lower limb and lower abdominal surgeries were selected.

Inclusion Criteria

The following criteria were included in the study:

- Age group of 18–60 years
- ASA Grade I or II
- Patients undergoing elective surgeries.

Exclusion Criteria

The following criteria were excluded from the study:

- ASA Grades III and IV
- Infection at the site of injection
- Coagulopathy or anticoagulation
- Congenital abnormalities of lower spine and meninges
- Active disease of CNS
- History of allergy to local anesthetics.

The selection of the patients was done randomly. A detailed preanesthetic evaluation including history, general physical examination, systemic examination, and spine examination for deformity was performed.

Routine investigations such as hemogram, total leukocyte cells, differential leukocyte cells, erythrocyte sedimentation rate, bleeding time, clotting time, random blood sugar, blood urea, serum creatinine, urine for albumin, sugar and microscopy, HIV and HBsAg, electrocardiogram, and chest X-ray (if required) were done. Patient’s weight and height was also recorded before surgery.

- The study population was randomly divided into 2 groups with 30 patients in each group.
- Study Group R - received 20 ml of 0.75% ropivacaine (isobaric) by epidural route
- Study Group B - received 20 ml of 0.5% bupivacaine (isobaric) by epidural route.

The following parameters were observed and recorded:

Onset of Sensory Block

The onset of sensory block was tested by pin-prick method using a 27 gauge hypodermic needle. The time of onset was taken from the time of injection of drug into epidural space to loss of pinprick sensation.

Onset of Motor Block

The time interval between administration of drug into epidural space and the patient's inability to lift the straight extended leg (Modified Bromage scale 1) was recorded as onset time for motor block.

Highest Level of Sensory Block

The highest level of sensory blockade was assessed by pinprick method using a hypodermic needle. The highest dermatomal level blocked was noted and recorded after the onset of motor block

Degree of Motor Block

This was assessed by Modified Bromage scale.

Modified Bromage Scale^[3]

- 0 - Able to raise leg straight, full flexion of knees and feet.
- 1 - Inability to raise leg, just able to flex knees, and full flexion of feet.
- 2 - Unable to flex knees, but some flexion of feet possible.
- 3 - Unable to move legs or feet.

Duration of Motor Block

The duration of motor block was taken from time of injection to complete regression of motor block (ability to lift the extended leg, i.e., Modified Bromage scale - 0).

Duration of Sensory Analgesia

Duration of sensory analgesia was noted and recorded from the onset of sensory block to complete return of sensation to pinprick.

Hemodynamic Changes

Patients were monitored for heart rate, blood pressure, and respiratory rate at 0, 5, 10, 15, 20, 25, 30, 45, 60, 90, 120, and 180 min after administration of epidural block.

Side Effects

Side effects such as nausea, vomiting, backache, retention of urine, and respiratory depression were observed for, recorded and treated accordingly.

Statistical Analysis^[4,5]

The following list of formulae was used for analyzing the data:

$$1. \text{Airthmetic mean} = \frac{\text{Sum of all the values}}{\text{No. of values}} = \frac{\sum x}{n}$$

$$2. \text{Standard deviation} = SD = \sqrt{\frac{\sum (X - \bar{X})^2}{n - 1}}$$

$$3. \text{Student's unpaired t-test, } t = \frac{\text{Difference of means}}{\text{S.E of difference of means}}$$

4. Fisher's exact test

Cases	T1	T2	Total
Abnormal	A	B	A+B
Normal	C	D	C+D
	A+C	B+D	N=A+B+C+D

$$\text{Fisher's test} = \frac{(A+B)! (C+D)! (A+C)!(B+D)!}{N!A!B!C!D!}$$

OBSERVATIONS AND RESULTS

The study sample comprised 60 patients aged between 18 and 60 years belonging to ASA Grade I and II, posted for elective lower abdominal and lower limb surgeries. 30 of them (Group R) received 20 ml of 0.75% ropivacaine (isobaric), and the others (Group B) received 20 ml of 0.5% bupivacaine (isobaric) for epidural anesthesia.

The demographic data such as age, gender, and weight were compared, and there was no statistically significant difference between the two groups as shown in Tables 1-3

Age

Table 1: Mean age

Age (Years)	n (%)	
	0.75% ropivacaine (Group R)	0.5% bupivacaine (Group B)
18-29	6 (20)	6 (20)
30-39	12 (40)	9 (30)
40-49	8 (27)	7 (23)
50-59	4 (13)	8 (27)
	30 (100)	30 (100)
Mean±SD	36.3±10.0	39.2±11.8
P* value, significance	0.29 NS	

*Student's unpaired

Sex Distribution

Table 2: Sex distribution

Sex	n (%)	
	0.75% ropivacaine (Group R)	0.5% bupivacaine (Group B)
Male	15 (50)	17 (57)
Female	15 (50)	13 (43)

Weight

Table 3: Weight distribution

Parameter	Mean±SD		Mean difference	P* value, Sig.
	0.75% Ropivacaine (Group R)	0.5% Bupivacaine (Group B)		
Weight (kg)	53.8±5.6	54.6±5.8	0.80	0.59 NS

*Student's unpaired t-test

Onset of Sensory Block

The mean time for onset of sensory block in ropivacaine group (Group R) was 10.2 ± 1.6 min and 10.8 ± 1.5 min in bupivacaine group (Group B) [Table 4]. The onset of sensory block in Group B was delayed by only few seconds than Group R ($P = 0.30$), so the difference was not statistically significant.

Onset of Motor Block

The mean time for onset of motor block in ropivacaine group (Group R) was 29.5 ± 3.0 min and in bupivacaine group (Group B) it was 28.9 ± 3.4 min [Table 5]. There was no significant difference between the groups ($P = 0.44$).

Highest Level of Sensory Block

In patients of ropivacaine group (Group R), 60% attained T6 level, 33% attained T7 level, and 7% attained T10 levels. In bupivacaine group (Group B) also, 60% attained T6 levels, followed by 27% attaining T7 level and 10% attaining T10 level [Table 6]. This implied that there was no difference in the highest level of sensory block achieved in both groups. ($P = 0.7$)

Degree of Motor Block

The degree of motor block was tested by Modified Bromage scale. On comparison, it was found that in ropivacaine group (Group R) there were 4 patients (13%) who had Grade 2 block and 26 patients (87%) who had Grade 3 block. In bupivacaine group (Group B), 3 patients (10%) had Grade 2 block, and 27 patients (90%) had Grade 3 block [Table 7]. The percentage distribution of patients who had Grade 2 and Grade 3 block was similar in both the groups.

Duration of Motor Block

The mean duration of motor block in ropivacaine group (Group R) was 241.7 ± 22.8 min, whereas in bupivacaine group (Group B) it was 282.3 ± 21.0 min. $P < 0.001$, indicating that the difference was highly significant [Table 8]. This implied that the duration of motor blockade

in ropivacaine Group R was significantly lower than the bupivacaine Group B.

Duration of Sensory Analgesia

The mean duration of sensory analgesia in ropivacaine group (Group R) was 389.7 ± 16.5 min. In bupivacaine group (Group B), the mean duration was 391.1 ± 15.1 min [Table 9]. The duration of sensory analgesia in Group B was prolonged by only a few minutes than Group R ($P = 0.72$), so the difference was not statistically significant.

Hemodynamic Parameters

Hemodynamic parameters such as pulse rate, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were compared at 0, 5, 10, 15, 20, 25, 30, 45, 60, 90, 120, and 180 min and found no statistically significant difference between the two groups with respect to changes in the mean PR, mean systolic blood pressure SBP, and DBP.

Pulse Rate

The mean pulse rate was compared between the two groups at 0, 5, 10, 15, 20, 25, 30, 45, 60, 90, 120, and 180 min [Table 10]. There was no significant difference between the ropivacaine and bupivacaine group with respect to pulse rate when recorded at these time intervals.

SBP

The mean SBP changes over the time intervals between the Ropivacaine (Group R) and bupivacaine group (Group B) were compared. It was found that the SBP did not differ between the two groups [Table 11].

DBP

As with the SBP, the mean DBP changes over the time intervals between ropivacaine (Group R) and bupivacaine (Group B) groups were similar. The difference was not statistically significant [Table 12].

Respiratory Rate

The mean respiratory rate at 0, 5, 10, 15, 20, 25, 30, 45, 60, 90, 120, and 180 min in ropivacaine group was compared

Table 4: Time of onset of sensory block

Parameter	Mean \pm SD		Mean difference	P* value, Sig.
	0.75% Ropivacaine (Group R)	0.5% Bupivacaine (Group B)		
Onset of sensory block (min)	10.2 \pm 1.6	10.8 \pm 1.5	0.57	0.30 NS

*Student's unpaired t-test

Table 5: Time of onset of motor block

Parameter	Mean \pm SD		Mean difference	P* value, Sig.
	0.75% ropivacaine (Group R)	0.5% bupivacaine (Group B)		
Onset of motor block (min)	29.5 \pm 3.0	28.9 \pm 3.4	0.63	0.44 NS

*Student's unpaired t-test

to that of bupivacaine group. The difference was not statistically significant at any of the time intervals with respect to respiratory rate [Table 13].

Side Effects

In ropivacaine group (Group R), 7% patients had hypotension, 3% had nausea, and 3% had vomiting. In bupivacaine group (Group B), 10% patients had hypotension, 7% had nausea, and 3% had vomiting. There was no significant difference between the two groups with regard to these side effects [Table 14].

DISCUSSION

Epidural anesthesia is widely practiced regional anesthesia technique for many lower abdominal and lower limb surgeries. When compared to spinal anesthesia, advantages of epidural anesthesia lie in its decreased frequency of hypotension, no limitation on duration of surgery, and effective post-operative analgesia.

Table 6: Highest level of sensory block

Highest level of sensory block	n (%)	
	0.75% ropivacaine (Group R)	0.5% bupivacaine (Group B)
T6	18 (60)	18 (60)
T7	10 (33)	8 (27)
T8	0 (0)	1 (3)
T10	2 (7)	3 (10)

$\chi^2=1.4, P=0.7$ NS

Table 7: Degree of motor block

Degree of motor block	n (%)	
	0.75% Ropivacaine (group R)	0.5% Bupivacaine (Group B)
Grade 0	0 (0)	0 (0)
Grade 1	0 (0)	0 (0)
Grade 2	4 (13)	3 (10)
Grade 3	26 (87)	27 (90)

$\chi^2=0.48, P=0.6$ NS

Table 8: Duration of motor block

Parameter	Mean±SD		Mean difference	P* value, sig.
	0.75% Ropivacaine (group R)	0.5% Bupivacaine (Group B)		
Duration of motor block (min)	241.7±22.8	282.3±21.0	40.600	<0.001 HS

*Student's unpaired t-test

Table 9: Duration of sensory analgesia

Parameter	Mean±SD		Mean difference	P* value, sig.
	0.75% Ropivacaine (Group R)	0.5% Bupivacaine (Group B)		
Duration of sensory analgesia (min)	389.7±16.5	391.1±15.1	1.433	0.72 NS

*Student's unpaired t-test

The local anesthetic drugs currently available for epidural anesthesia offer a varied degree of efficacy, from drugs of low potency such as Procaine to much potent drugs such as etidocaine and bupivacaine. Unfortunately, as the potency of local anesthetics increases so does their toxicity. Bupivacaine, one of the most widely utilized local anesthetics, has been the subject of intense investigation because of reports of sudden cardiovascular collapse in some patients.^[6-8]

Ropivacaine (LEA-103) is a new amino-amide local anesthetic agent similar in structure to bupivacaine. Ropivacaine is prepared as the s-isomer rather than a racemic mixture such as bupivacaine. Previous studies involving the isomers of local anesthetics suggest that the systemic toxicity of the S-isomer of various compounds may be less than that of racemic preparations. Pharmacologic studies in isolated nerves^[9] and intact animals have indicated that ropivacaine possesses an anesthetic profile similar to that of bupivacaine but with less potential for cardiotoxicity than bupivacaine.^[10,11]

This study aimed to compare the effects of 0.75% ropivacaine (isobaric) with that of 0.5% bupivacaine (isobaric) for epidural anesthesia in elective lower abdominal and lower limb surgeries. Our study design consisted of 60 patients aged between 18 and 60 years, ASA physical Status I and II undergoing epidural anesthesia for lower abdominal and lower limb surgeries. They were randomly divided into two groups. Group R (ropivacaine group) patients received 20 ml of 0.75% ropivacaine and Group B (bupivacaine group) received 20 ml of 0.5% bupivacaine through the epidural route. The following parameters were observed:

1. Sensory and motor blockade - Onset, duration, and highest level of sensory blockade
2. Degree of motor blockade
3. Recovery parameters - Time for complete sensory and motor recovery
4. Hemodynamic changes over various time intervals.

Table 10: Pulse rate comparison

Pulse rate	Mean±SD		Mean difference	P* value	Sig.
	0.75% Ropivacaine (group R)	0.5% Bupivacaine (Group B)			
0 min	74.6±4.8	75.6±5.1	0.97	0.46	NS
5 min	86.8±5.5	87.9±5.2	1.03	0.46	NS
10 min	89.9±4.0	92.4±4.2	2.43	0.03	NS
15 min	90.1±4.1	91.6±5.0	1.57	0.19	NS
20 min	83.4±5.1	86.4±6.0	2.93	0.05	NS
25 min	79.6±4.1	80.2±5.6	0.67	0.60	NS
30 min	77.8±3.6	78.9±4.9	1.07	0.34	NS
45 min	77.5±3.3	78.5±4.4	1.00	0.32	NS
60 min	76.7±1.9	77.0±2.5	0.30	0.60	NS
90 min	76.0±1.7	76.1±2.3	0.13	0.80	NS
120 min	75.3±1.7	75.6±2.3	0.33	0.53	NS
180 min	74.5±2.1	75.3±2.5	0.83	0.17	NS

Student's unpaired t-test

Table 11: SBP comparison

SBP (mm/Hg)	Mean±SD		Mean difference	P* value	Sig.
	0.75% Ropivacaine (group R)	0.5% Bupivacaine (Group B)			
0 min	119.6±7.4	118.7±7.8	0.93	0.63	NS
5 min	113.5±7.6	111.6±6.4	1.87	0.31	NS
10 min	110.4±8.5	107.4±6.5	3.00	0.13	NS
15 min	105.8±8.1	102.5±8.0	3.30	0.12	NS
20 min	107.5±7.7	103.5±7.1	4.07	0.06	NS
25 min	108.6±7.6	105.1±6.7	3.53	0.06	NS
30 min	110.3±7.0	107.5±6.7	2.87	0.11	NS
45 min	111.5±6.8	108.7±6.7	2.73	0.12	NS
60 min	112.3±6.8	110.2±7.1	2.13	0.24	NS
90 min	113.9±7.2	111.3±6.9	2.57	0.16	NS
120 min	114.4±6.0	112.3±6.7	2.07	0.22	NS
180 min	115.5±5.7	113.6±6.9	1.93	0.24	NS

Student's unpaired t-test. SBP: Systolic blood pressure

Table 12: DBP comparison

DBP (mm/Hg)	Mean±SD		Mean difference	P* value	Sig.
	0.75% Ropivacaine (group R)	0.5% Bupivacaine (Group B)			
0 min	74.9±6.1	75.3±5.8	0.47	0.76	NS
5 min	70.9±5.5	70.9±4.8	0.07	0.96	NS
10 min	68.2±5.5	68.9±5.3	0.67	0.63	NS
15 min	65.5±6.4	65.4±6.3	0.13	0.94	NS
20 min	65.7±4.6	65.6±5.3	0.13	0.92	NS
25 min	65.9±5.0	66.3±4.7	0.40	0.75	NS
30 min	68.3±5.5	67.8±5.7	0.53	0.71	NS
45 min	69.6±6.1	69.0±6.3	0.60	0.71	NS
60 min	71.0±5.7	70.1±5.7	0.87	0.56	NS
90 min	72.4±6.1	71.7±5.9	0.73	0.64	NS
120 min	73.7±5.3	72.5±5.9	1.20	0.41	NS
180 min	72.9±5.3	72.1±5.7	0.73	0.61	NS

DBP: Diastolic blood pressure

In the present study, the patients studied in both the groups did not vary much with respect to age, sex, or weight. Majority of patients were in the age group between 18 and 60 years, with mean age of 36.3 ± 10.0 years in Group R and 39.2 ± 11.8 years in Group B. The mean sex distribution and the mean weight in both groups were also identical. These parameters were matched in both the

groups to avoid changes in the intraoperative and post-operative outcome of patients.

Onset of Sensory and Motor Blockade

In our study, the mean time for onset of sensory block in the ropivacaine group was 10.2 ± 1.6 min and 10.8 ± 1.5 min in bupivacaine group. The mean time for onset of

Table 13: Respiratory rate comparison

Respiratory rate	Mean±SD		Mean difference	P* value	Sig
	0.75% Ropivacaine (group R)	0.5% Bupivacaine (Group B)			
0 min	14.3±1.3	14.1±1.1	0.13	0.67	NS
5 min	14.4±1.2	14.4±1.2	0.03	0.92	NS
10 min	15.1±1.3	15.1±1.3	0.03	0.92	NS
15 min	14.8±1.2	14.9±1.2	0.10	0.75	NS
20 min	15.0±0.8	15.0±0.9	0.07	0.77	NS
25 min	14.8±0.8	14.9±0.9	0.07	0.76	NS
30 min	14.4±1.1	14.5±1.1	0.10	0.72	NS
45 min	15.0±1.0	15.0±1.0	0.03	0.90	NS
60 min	15.0±1.1	14.9±1.0	0.13	0.62	NS
90 min	15.0±0.9	14.9±0.8	0.10	0.65	NS
120 min	14.6±0.9	14.6±0.9	0.07	0.78	NS
180 min	14.5±0.9	14.5±0.9	0.00	1.00	NS

Table 14: Side effects

Side effects	n (%)		P* value, sig.
	0.75% Ropivacaine (group R)	0.5% Bupivacaine (Group B)	
Nausea	1 (3)	2 (7)	NS
Vomiting	1 (3)	1 (3)	-
Hypotension	2 (7)	3 (10)	NS

*Fisher, exact test

motor block in ropivacaine group was 29.5 ± 3.0 min, and in bupivacaine group, it was 28.9 ± 3.4 min. There was no statistically significant difference with regard to onset of sensory and motor block between the groups.

Brockway *et al.*,^[2] who conducted a study comparing 0.5%, 0.75%, and 1% ropivacaine with 0.5% and 0.75% bupivacaine found no significant differences in the onset time of sensory or motor block.

Finucane *et al.*^[12] found no clinical difference in the onset of sensory or motor block when comparing 0.5%, 0.75%, and 1% ropivacaine with 0.5% bupivacaine for epidural anesthesia in patients undergoing an abdominal hysterectomy.

Katz *et al.*^[13] also conducted a double-blind comparison study of 0.5% bupivacaine with 0.75% ropivacaine administered epidurally. They found no difference in the onset of sensory or motor blockade similar to our results.

Wolff *et al.*^[14] found no difference in onset of sensory or motor block when comparing 0.5%, 0.75%, and 1.0% ropivacaine or 0.5% bupivacaine administered extradurally in patients undergoing elective hip surgery.

Brown *et al.*^[15] designed a randomized, double-blind study to compare the clinical effectiveness of ropivacaine and bupivacaine in patients undergoing lower-extremity surgery. They also found no difference in onset of sensory or motor block.

The above findings were similar to that of our study. Thus, we can conclude that there is no variation in the onset of sensory or motor blockade between 0.75% ropivacaine and 0.5% bupivacaine when administered through epidural route.

Highest Level of Sensory Block

Highest level of sensory block was assessed by pinprick method using a blunt needle after the onset of motor block. In our study, patients of ropivacaine group attained the following level of sensory block: 60% attained T6 level, 33% attained T7 level, and 7% attained T10 levels. In bupivacaine group also 60% attained T6 levels, followed by 27% attaining T7 level, and 10% attaining T10 level. This implied that the sensory block level achieved by both groups was similar.

Brockway *et al.*^[2] conducted a study comparing 0.5%, 0.75%, and 1% ropivacaine with 0.5% and 0.75% bupivacaine. They found the mean upper limit of sensory block to be T6.

Katz *et al.*^[13] conducted a double-blind comparison study of 0.5% bupivacaine with 0.75% ropivacaine administered epidurally. They found the median sensory block height to be between T4 for bupivacaine and T5 for ropivacaine. The higher block compared to our study could be related to the higher volume of the drug used in their study.

From the above studies, we can conclude that the highest level of sensory block is similar between ropivacaine and bupivacaine. These findings are similar to our study.

Degree of Motor Blockade

The degree of motor block was tested by Modified Bromage scale. In our study, there was no difference in the degree of the motor block between the two groups.

Brockway *et al.*,^[2] Finucane *et al.*,^[12] Katz *et al.*,^[13] and Wolff *et al.*^[14] found the degree of motor blockade assessed by Modified Bromage scale to be Grade 3 in both the ropivacaine and bupivacaine group. This finding was similar to our study.

Duration of Motor Block

Duration of motor blockade was assessed from the time of administration of the drug to complete motor recovery (Bromage scale - 0). In our study, the mean duration of motor block in ropivacaine group was 241.7 ± 22.8 min, whereas in bupivacaine group it was 282.3 ± 21.0 min. This difference was statistically significant ($P < 0.001$)

Brockway *et al.*,^[2] compared 0.5%, 0.75%, and 1% ropivacaine 15 ml with 0.5% and 0.75% bupivacaine 15 ml in 110 patients and found no a significant difference in onset, spread or duration of the sensory block when similar concentrations were compared. However, ropivacaine produced a slower onset, shorter duration, and less intense motor block than bupivacaine.

Wolff *et al.*^[14] studied 126 patients undergoing elective hip surgery; they received 20 ml of 0.5%, 0.75%, and 1.0% ropivacaine or 0.5% bupivacaine extradurally in a double-blind design. Similar to our study, they found that return of motor function was earlier with ropivacaine compared to bupivacaine.

From the above studies, we can conclude that the duration of motor block is shorter with ropivacaine than bupivacaine.

Duration of Sensory Analgesia

In our study, the mean duration of sensory analgesia in ropivacaine group was 389.7 ± 16.5 min. In bupivacaine group, the mean duration was 391.1 ± 15.1 min, indicating that there was no difference in the duration of sensory analgesia among the two groups.

In studies conducted by Brockway *et al.*^[2] Finucane *et al.*,^[12] Katz *et al.*^[13] Wolff *et al.*,^[14] and Brown *et al.*^[15] it was found that there was no significant difference in duration of sensory analgesia when comparing ropivacaine with bupivacaine.

Hemodynamic Changes (Heart Rate and Blood Pressure)

In our study, the two groups did not differ significantly with respect to heart rate at any time interval. There were

no episodes of bradycardia in either group. The changes in mean SBP and DBP at any time interval were statistically and clinically insignificant. 2 patients in ropivacaine group experienced hypotension, whereas 3 patients experienced hypotension in bupivacaine group. Hypotension was corrected by small doses of inj. ephedrine.

In the study conducted by Brockway *et al.*,^[2] the SBP and DBP decreased by about 20% from the baseline values over the first 20 min, whereas the heart rate tended to increase over first 15 min and thereafter decrease to slightly less than the baseline. This was similar to our study. There was no significant difference between the two groups.

A study by Wolff *et al.*^[14] comparing extradural ropivacaine and bupivacaine in hip surgery showed that systolic and diastolic arterial pressures decreased in all groups. Treatment with ephedrine or atropine was required more often in the 0.75% ropivacaine group and in the 1% ropivacaine group compared with the 0.5% ropivacaine group and the 0.5% bupivacaine group.

Finucane *et al.*^[12] and Brown *et al.*^[15] found that the cardiovascular changes with respect to heart rate and blood pressure were similar in both bupivacaine and ropivacaine group.

From the above discussion, we can conclude that epidural administration of ropivacaine produces similar changes in hemodynamic parameters as that of bupivacaine. These findings are similar to our study

Respiratory Rate

None of our patients experienced respiratory depression, and the mean RR between both the groups was statistically insignificant.

Our study found no changes in the respiratory rates between the two groups which corroborated with the other studies conducted by Brockway *et al.*,^[2] Finucane *et al.*,^[12] Katz *et al.*,^[13] Wolff,^[14] and Brown *et al.*^[15]

Side Effects

In ropivacaine group, 7% patients had hypotension, 3% had nausea, and 3% had vomiting. In bupivacaine group, 10% patients had hypotension, 7% had nausea, and 3% had vomiting, indicating no significant difference between the two groups with regard to these side effects.

Brockway *et al.*^[2] found similar number of side effects in each group, the most common being backache (23%) followed by nausea (14%) and vomiting (2%).

The most common adverse events reported in the study conducted by Finucane *et al.*^[12] were nausea, vomiting, hypotension, headache, and backache.

The reported side effects in the above studies were similar in both groups as were noticed into our study.

CONCLUSION

Based on the present clinical comparative study, we conclude that isobaric 0.75% ropivacaine, when administered through epidural route, provides adequate anesthesia for lower abdominal and lower limb surgeries and has a shorter duration of motor block when compared with 0.5% bupivacaine.

The onset of sensory and motor blocks, highest level of sensory block, degree of motor block, and duration of sensory analgesia are similar to that of bupivacaine, with no significant differences between the two groups with respect to hemodynamic changes.

Hence, ropivacaine can be used as a safe alternative to bupivacaine for epidural anesthesia in lower abdominal and lower limb surgeries. The shorter duration of motor block with ropivacaine suggest that it could be effectively used for early mobilization of patients in the post-operative period.

REFERENCES

1. Whitehead E, Arrigoni B, Bannister J. An open study of ropivacaine in extradural anaesthesia. *Br J Anaesth* 1990;64:67-71.
2. Brockway MS, Bannister J, McClure JH, McKeown D, Wildsmith JA. Comparison of Extradural ropivacaine and bupivacaine. *Br J Anaesth* 1991;66:31-7.
3. Vincent JC, editor. Spinal anesthesia-principles. *Principles of Anesthesiology*. 3rd ed. USA: Lea and Febiger; 1993. p. 1514-5.
4. Kaplans. *Biostatistics*. 3rd ed. Florida: Kaplans; 1999.
5. Park K. *Preventive and Social Medicine*. 24th ed. Madhya Pradesh: Banarsidas Bhanot Publishers; 2017.
6. Concepcion M, Arthur GR, Steele SM, Bader AM, Covino BG. A new local anesthetic, ropivacaine: Its epidural effects in humans. *Anesth Analg* 1990;70:80-5.
7. Edde RP, Deutsch S. Cardiac arrest after interscalene brachial plexus block. *Anesth Analg* 1977;56:446-7.
8. Albright G. Cardiac arrest following regional anesthesia with etidocaine or bupivacaine. *Anesthesiology* 1979;51:285-7.
9. Rosenberg PH, Heinonen E. Differential sensitivity of A and C nerve fibres to long acting amide local anaesthetics. *Br J Anaesth* 1983;55:163-7.
10. Akerman B, Hellberg IB. Primary evaluation of the local anaesthetic properties of the amino amide agent ropivacaine (LEA-103). *Acta anaesthesiol scand* 1988;32:571-8.
11. Moller RA, Covino BG. Cardiac electrophysiological effects of a new long-acting local anaesthetic agent (LEA-103). *Anesthesiology* 1986;65:3A-A183.
12. Finucane BT, Sandler AN, McKenna J, Reid D, Milner AL, Friedlander M, *et al.* A double blind comparison of ropivacaine 0.5%, 0.75%, 1% and bupivacaine 0.5%, injected epidurally in patients undergoing abdominal hysterectomy. *Can J Anaesth* 1996;43:442-9.
13. Katz JA, Jefferey AK, Donna K. A double blind comparison of 0.5% Bupivacaine and 0.75% ropivacaine administered epidurally in humans. *Reg Anesth* 1990;15:250-2.
14. Wolff AP, Hasselstrom L, Kerkkamp HE, Gielen MJ. Extradural ropivacaine and bupivacaine in hip Surgery. *Br J Anaesth* 1995;74:458-60.
15. Brown DL, Carpenter RL, Thompson GE. Comparison of 0.5% ropivacaine and 0.5% bupivacaine for epidural anesthesia in patients undergoing lower-extremity surgery. *Anesthesiology* 1990;72:633-6.

How to cite this article: Kumar GS, Kanth L, Srinath M. A Comparative Study between Bupivacaine 0.5% and Ropivacaine 0.75% in Epidural Analgesia in Patients Undergoing Elective Lower Abdominal and Lower Limb Surgeries. *Int J Sci Stud* 2018;6(5):127-135.

Source of Support: Nil, **Conflicts of Interest:** None declared

Clinical and Epidemiological Evaluation and Assessment of Various Modes of Therapeutic Management of Locally Advanced Carcinoma of Breast in a Tertiary Care Hospital: An Observational Study

Gaddam Padmasree

Professor and Head, Department of Surgery, ACSR Government Medical College, Nellore, Andhra Pradesh, India

Abstract

Background: Worldwide breast cancer is the most frequent cancer in women and represents the second leading cause of cancer death among women (after lung cancer). Higher incidence in developing countries is due to lack of active screening, and early detection programs, low awareness of breast cancer, poor access to health care due to poverty, and cultural issues are other contributory factors for late presentation. The locally advanced breast cancer (LABC) is characterized by varying clinical presentations of tumors belonging to Stages IIIA, IIIB, IIIC, and inflammatory breast cancer and the aim of this study is to evaluate the epidemiologic characteristics such as age distribution, clinical presentation, stage at presentation, and various modalities of treatment.

Methodology: The present study is a descriptive hospital-based study conducted in the department of general surgery in a tertiary care hospital during the period of November 2013–October 2015. All patients presenting to the hospital with Stage IIIA, IIIB, IIIC, and inflammatory carcinoma were included in the study. The multimodality treatment approach of LABC commenced in the majority of cases with neoadjuvant chemotherapy (NACT), followed by local therapy in the form of modified radical mastectomy (MRM) (Auchincloss modification). The patients were then subjected to consolidating radiotherapy to locoregional area.

Statistical Analysis: Descriptive statistics were done. Data were expressed as absolute numbers and percentage.

Results: Observations were made regarding demographics, quadrants involved, menstrual status, tumor size, and fixity to chest wall, lymph node status, stage of the disease, inoperability, chemotherapy regimen, receptor status, and complications of surgery.

Conclusion: Patients administered NACT showed a good response with 13.2% and 65.8% of the patients showing clinically complete and partial response, respectively. 92% of inoperable tumors became operable confirming that NACT is an effective method of downstaging the tumor.

Key words: Chemotherapy, Locally advanced breast carcinoma, Metastasis, Radiotherapy, Surgical treatment

INTRODUCTION

Worldwide breast cancer is the most frequent cancer in women and represents the second leading cause of cancer

death among women (after lung cancer).^[1,2] Hippocrates of the 5th century B.C. has considered cancer of the breast incurable and a classic description of a woman succumbing of late breast cancer appears in his volume “diseases of women.”

At present, 75,000 new cases occur in Indian women every year. Locally advanced breast cancer (LABC) constitutes more than 50–70% of the patients presenting for treatment.^[3] Higher incidence in developing countries is due to lack of active screening, and early detection programs, low awareness of breast cancer, poor access to health care

Access this article online



www.ijss-sn.com

Month of Submission : 06-2018
Month of Peer Review : 07-2018
Month of Acceptance : 08-2018
Month of Publishing : 08-2018

Corresponding Author: Dr. Gaddam Padmasree, D/No: 4-23-4, Sanjay Gandhi Colony 1st Line, Opp Men's Medical Hostel, Guntur - 522 007, Andhra Pradesh, India. Phone: +91-9440383316. E-mail: padmasri155155@gmail.com

due to poverty, and cultural issues are other contributory factors for late presentation.^[4,5] The LABC is characterized by varying clinical presentations such as presence of a large primary tumor (>5 cm), associated with or without skin or chest-wall involvement or with fixed (matted) axillary lymph nodes or with disease spread to the ipsilateral internal mammary or supraclavicular nodes in the absence of any evidence of distant metastases. These are tumors belonging to Stages IIIA, IIIB, IIIC, and inflammatory breast cancer.

Although the clinical features at presentation and prognosis among women with LABC vary, there are two common problems in the treatment. Achieving local control and prolonging survival by preventing or delaying distant metastasis.

Today treatment of LABC requires a combination of systemic and local/regional therapies.^[6,7] The most common approach for treating LABC in developed countries consists of neoadjuvant chemotherapy (NACT) with anthracyclines and taxanes followed by surgery and radiation therapy; hormonal treatment is added for receptor-positive disease, and patients with HER2/neu-positive disease receive trastuzumab therapy.^[8,9] Most patients have good clinical responses to induction chemotherapy in both the primary tumor and regional lymph nodes.

An attempt is made in this study to evaluate the epidemiologic characteristics such as age distribution, clinical presentation, stage at presentation, and various modalities of treatment.

Aims and Objectives

The objectives are as follows:

- To study the clinical presentation of locally advanced breast carcinoma
- Age distribution of locally advanced breast carcinoma
- To study the various modes of management
- Neo-adjuvant chemotherapy
- Surgery and immediate post-operative complications
- Commonly used chemotherapy regimens and immediate adverse effects, i.e., cyclophosphamide, methotrexate and 5-fluorouracil (CMF) doxorubicin and cyclophosphamide (AC), and other modalities such as hormonal therapy and radiotherapy.

MATERIALS AND METHODS

The present study is a descriptive hospital-based study conducted in the department of general surgery in a tertiary care hospital during the period of November 2013–October 2015.

Sample size: The sample size was 50 patients.

Method of Collection of Data

Inclusion criteria

All patients presenting to the hospital with Stage IIIA, IIIB, IIIC, and inflammatory carcinoma were included in the study.

Exclusion criteria

Patients who were clinically diagnosed as having LABC (i.e., Stage IIIA, IIIB, IIIC, and inflammatory carcinoma) but on investigations found to have distant metastasis were excluded from the study.

Fine needle aspiration cytology and other investigations that were available in the hospital were utilised for the diagnosis of Breast cancer.

Routine investigations such as complete blood count, urine analysis, random blood sugar, blood urea, and serum creatinine and electrocardiogram were obtained.

For patients to be put on doxorubicin echocardiography were done and ejection fraction noted.

Investigations to rule out metastasis were obtained. Ultrasonography abdomen and pelvis liver function test, chest X-ray, and skeletal X rays were done.

The multimodality treatment approach of LABC commenced in the majority of cases with NACT, followed by local therapy in the form of modified radical mastectomy (MRM) (Auchincloss modification). Chemotherapy was resumed to complete a total of 6 cycles.

The patients were then subjected to consolidating radiotherapy to locoregional area. The patients with inoperable tumors who showed no change in the size of tumors, which showed no decrease in the size of a tumor following NACT were subjected to radiotherapy as local therapy and followed up further.

Measure of response to neoadjuvant (induction) chemotherapy:

- Clinical complete response (CR) is defined as no palpable tumor in the breast and axilla.
- >50% reduction in the size of tumor was taken as a partial response (cPR).
- <50% reduction in the size of tumor was taken as stable disease (SD).

In certain cases of Stage IIIA disease considered operable at presentation (Stage T3N1) treatment is initiated with local therapy, i.e., MRM (Auchincloss modification) followed by adjuvant chemotherapy with a standard chemotherapy regimen. Furthermore, hormonal modality and regional radiotherapy are used as mentioned earlier.

The response to NACT was studied by serial clinical examination noting the regression in the size of the lump (or ulcer) and change in the lymph node status of axilla:

- <50% of reduction in size was taken as SD.
- The patients who had no change in size of tumor following NACT were subjected to radiotherapy and followed up.

OBSERVATIONS AND RESULTS

Proportion of Cases

The total number of patients with carcinoma breast admitted during the study period was 136. Out of these 60 patients were identified as patients of LABC based on the accepted definition. Thus, 44% of patients admitted with carcinoma breast presenting for treatment were identified as patients with LABC as represented in Figure 1.

Age Distribution

The age of the presenting patients ranged from 27 to 65 years. The highest number of patients was in the age group of 41–50 years age group with 17 (34%), followed by 31–40 years age group with 13 (26%). The mean age of patients was 45.1 years as represented in Table 1 and Figure 2.

Duration of Symptoms

The highest number of patients had symptoms for 3–6 months, i.e., 19 (38%). The duration of symptoms ranged from 1 to 28 months. The mean duration of symptoms was found to be 8.84 months as represented in Table 2 and Figure 3.

Symptoms at Presentation

Lump is the most consistent symptom and presented in all the patients. 8 (16%) of these patients presented with an ulcer over the lump. Pain was the complaint in 13 (26%)

of the patients. 6 (12%) patients complained of lump in the ipsilateral axilla as represented in Table 3 and Figure 4.

Quadrants Involved

The upper outer quadrant is the most common predominantly involved quadrant with a total of 29 (58%) cases. Since most of the lumps were large, they spanned more than one quadrants as represented in Figure 5 and Table 4.

Menstrual Status

30 (60%) of the patients were premenopausal and 20 (40%) were postmenopausal [Table 5 and Figure 6].

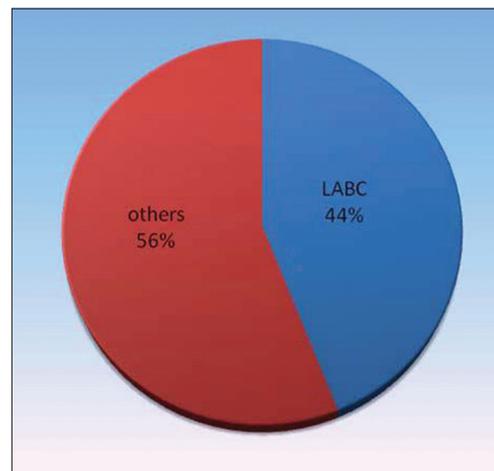


Figure 1: Proportion of cases

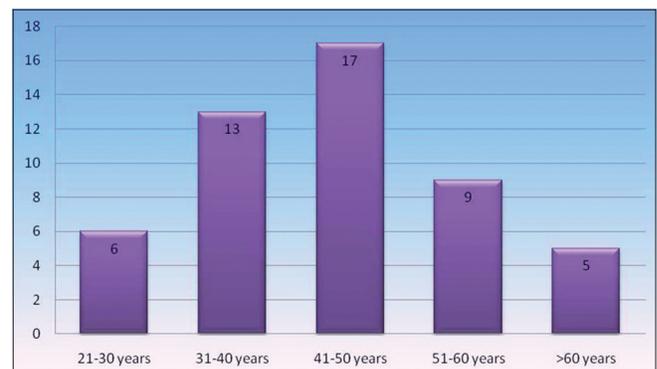


Figure 2: Age distribution

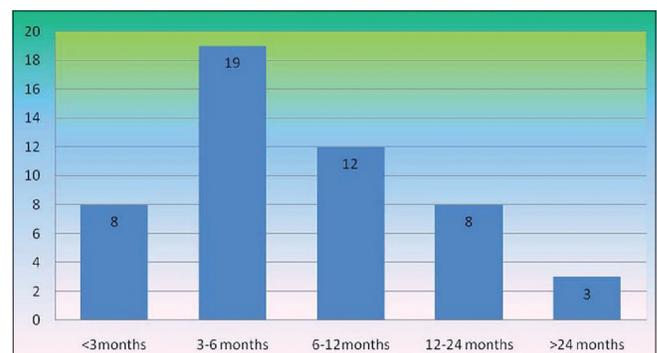


Figure 3: Duration of symptoms

Table 1: Age distribution

Age group (years)	Number of patients (%)
21–30	6 (12)
31–40	13 (26)
41–50	17 (34)
51–60	9 (18)
>60	5 (10)

Table 2: Duration of symptoms

Duration of symptoms	Number of patients (%)
<3 months	8 (16)
3–6 months	19 (38)
6–12 months	12 (24)
12–24 months	8 (16)
>24 months	3 (6)

Tumor Size

The tumor size ranged from 4 to 12 cm in the highest dimension. The smallest tumor measured 4 * 3 cm while the largest 12 * 10 cm. Majority of the tumors were 5–8 cm size. The mean size of the tumors is 6.6 cm. As represented in Table 6 and Figure 7.

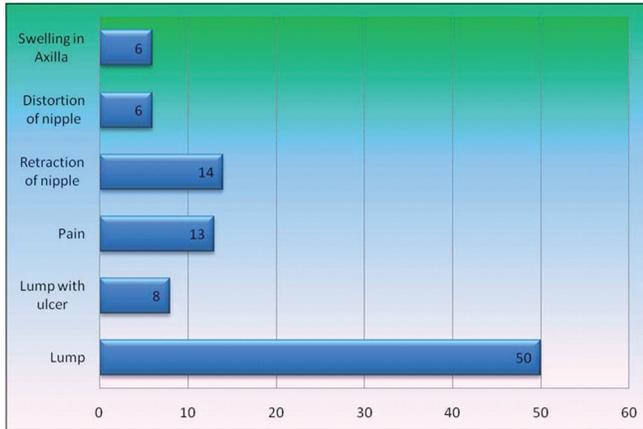


Figure 4: Symptoms on presentation

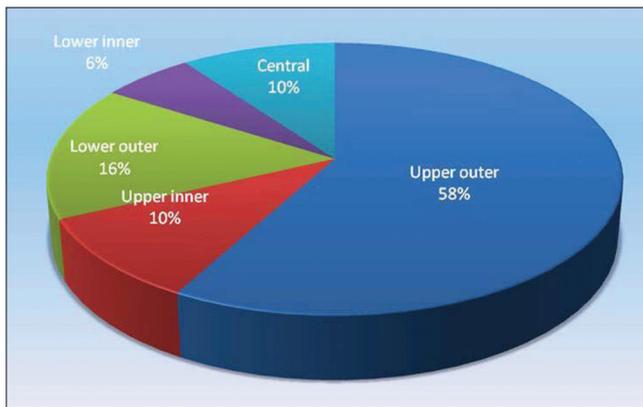


Figure 5: Quadrants involved

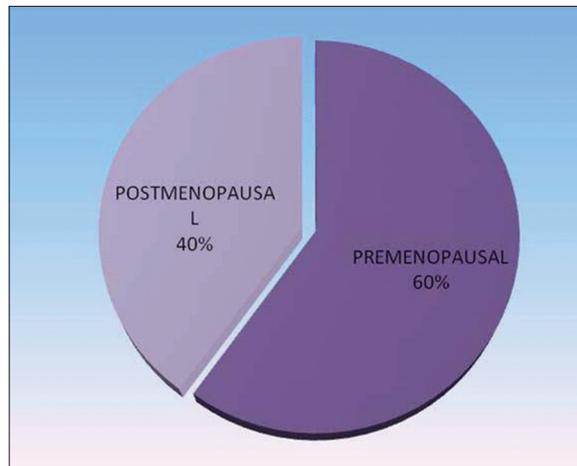


Figure 6: Menstrual status

One patient presenting with inflammatory carcinoma had a diffuse lump.

Fixity to Skin and Chest Wall

24 (48%) of 50 cases were found to have fixity skin. Highest number 12 (24%) were found to have peau d' orange implying skin fixity and 8 (16%) had ulcer over the lump. Chest wall fixity was found in 5 (10%) cases as represented in Table 7 and Figure 8.

Lymph Node Status

The axillary node status seen in the study is depicted in the following Table 8 and Figure 9.

Stage of the Disease

24 of the 50 cases studies 23 (46%) were of Stage IIIA, 24 (48%) are Stage IIIB, 2 cases (4%) are Stage IIIC, and

Table 3: Symptoms at presentation

Symptom	Number of cases (%)
Lump	50 (100)
Ulcer with lump	8 (16)
Pain	13 (26)
Retraction of nipple	14 (28)
Nipple discharge	6 (12)
Swelling in axilla	6 (12)

Table 4: Quadrants involved

Predominantly involved quadrant	Number of cases (%)
Upper outer	29 (58)
Upper inner	5 (10)
Lower outer	8 (16)
Lower inner	3 (6)
Central	5 (10)

Table 5: Menstrual status

Menstrual status	Number of patients (%)
Premenopausal	30 (60)
Postmenopausal	20 (40)

Table 6: Tumor size

Tumor size (cm)	Number of patients
<5	7 (14.2)
5–8	37 (75.5)
8–10	0 (8.2)
>10	1 (2)

Table 7: Fixity to skin and chest wall

Fixity	Feature	Number of patients (%)
Skin	Peau d' orange	12 (24)
	Ulcer	8 (16)
	Sat nodule	4 (8)
Chest wall		5 (10)

1 case (2%) is inflammatory carcinoma as represented in Table 9 and Figure 10.

Proportion of Inoperable Cases

A total of 38 (76%) cases were considered to be inoperable. These include 24 cases of IIIB, 2 IIIC, and one inflammatory cancer with 11 cases of IIIA which had fixed or matted nodes [Table 10 and Figure 11].

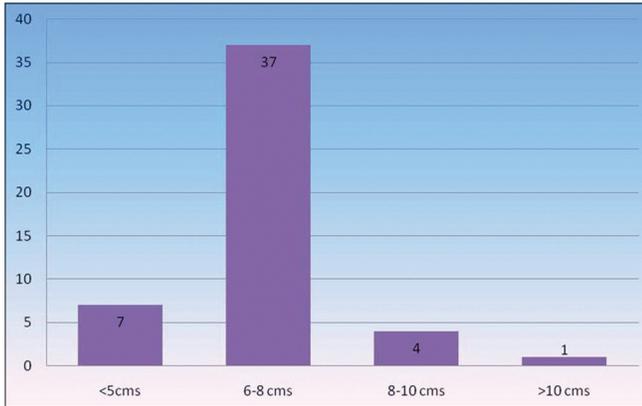


Figure 7: Tumour size

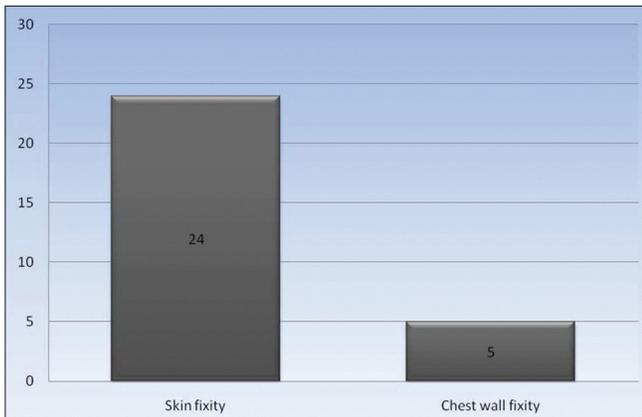


Figure 8: Skin and chest wall fixity

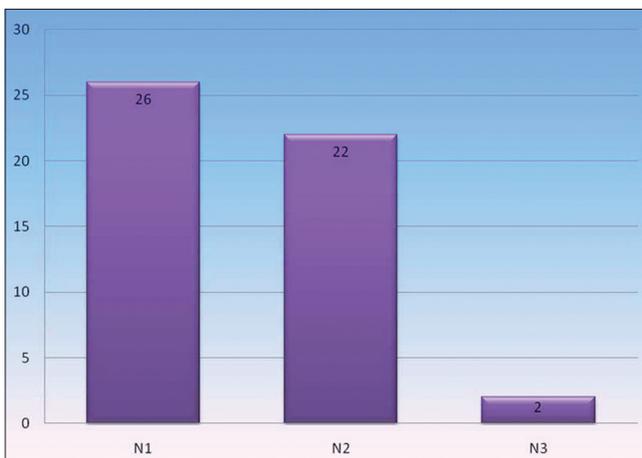


Figure 9: Lymph node status

Sequencing of Treatment

A total of 12 (24%) patients presenting inoperable stages (T3N1) were treated with MRM and adjuvant chemotherapy. 7 cases were later subjected to radiotherapy. 38 (76%) cases presenting in inoperable stages were subjected to NACT, and 35(92%) that were converted into operable stages were subjected to MRM followed by completion of chemotherapy and radiotherapy [Table 11 and Figure 12].

Chemotherapy Regimen

Standard regimen was used in the study. CMF was used the most in 26 (52%) of the patients. AC regimen was used in 24 (48%) as represented in Table 12 and Figure 13.

Table 8: Lymph node status

Lymph node status	Number of patients (%)
N1	26 (52)
N2	22 (44)
N3	2 (4)

Table 9: Stage of the disease

Group stage	TNM stage	Number of patients	Number of patients (%)
IIIA	T3N1M0	12	23 (46)
	T3N2M0	10	
	T2N2	1	
IIIB	T4aN1M0	1	24 (48)
	T4aN2M0	4	
	T4bN1M0	13	
	T4bN2M0	6	
IIIC	T3N3M0	2	2 (4)
Inflammatory Ca	T4d	1	1 (2)

Table 10: Operability of tumors

Operability	Number (%)
Operable	12 (24)
Inoperable	38 (76)

Table 11: Sequencing of treatment

Sequencing	Number of cases (%)
NC+S+C+R	33 (66)
NC+S+C	2 (4)
NC+R	3 (6)
S+C+R	7 (14)
S+C	5 (10)

Table 12: Chemotherapy regimen

Regimen	Number of patients (%)
CMF	26 (52)
AC	24 (48)

CMF: Cyclophosphamide, methotrexate and 5-fluorouracil, AC: Doxorubicin and cyclophosphamide

Response to Neoadjuvant Chemotherapy

Response to neoadjuvant chemotherapy was assessed by calculating the percentage decrease in the volume of the tumor. The response is classified according to the stage and depicted in Table 13 and Figure 14.

One case of inflammatory carcinoma had no response to therapy.

In our study of the 38 patients who received neoadjuvant chemotherapy, 5 (13.2%) patients had complete clinical

response, 25 (65.8%) patients had clinical partial response (pCR), and 8 (21%) had SD [Figure 15].

Proportion of inoperable tumors converted to operable stages:

A total of 38 (76%) cases presenting as inoperable were subjected to NACT, of these 35 were converted to operable, and only 3 remained inoperable. These tumors which remained inoperable were subjected to radiotherapy.

Receptor Status

Both ER and PR were positive in 23 (46%) of the cases, both ER/PR were negative in 20 (40%). ER positivity with

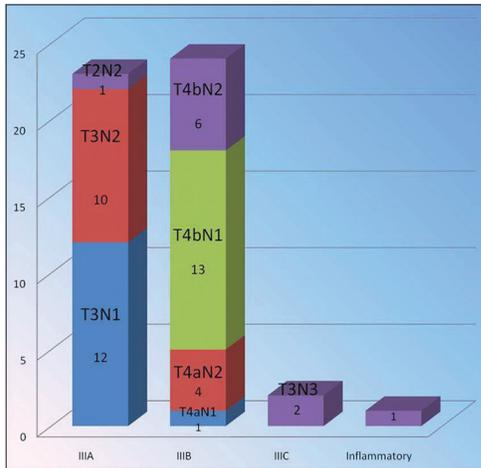


Figure 10: Stage of disease

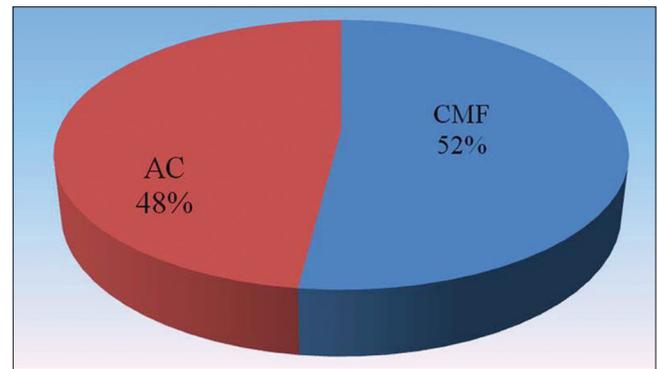


Figure 13: Chemotherapy regimen

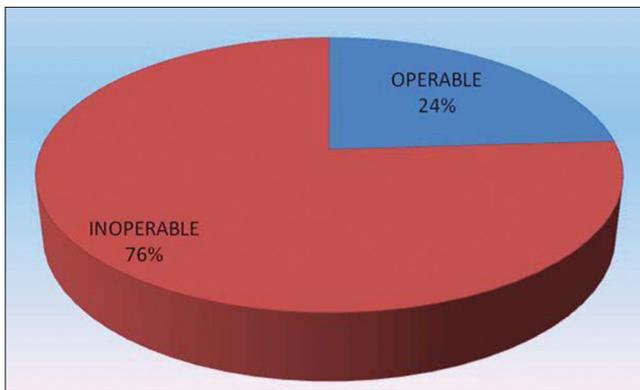


Figure 11: Operability of tumors

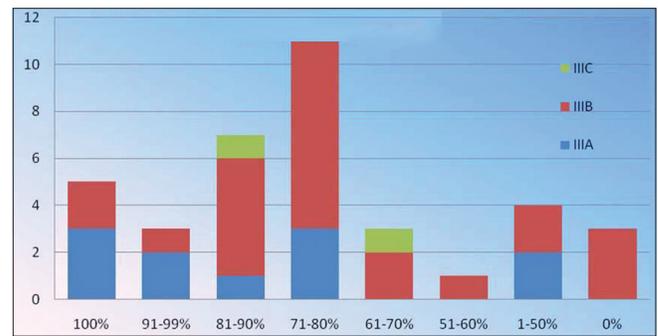


Figure 14: Response to neoadjuvant chemotherapy

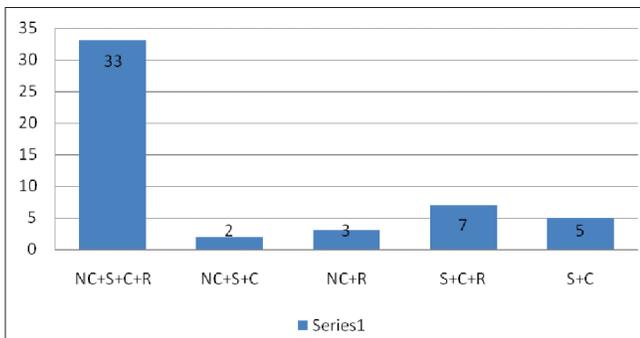


Figure 12: Sequencing of treatment

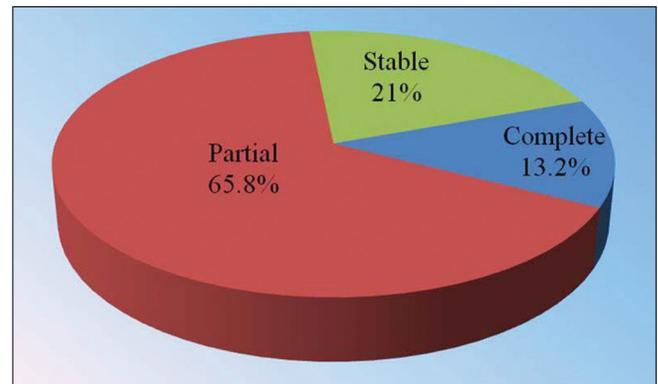


Figure 15: Clinical response to neoadjuvant chemotherapy

PR negativity was seen in 5 (10%). ER negativity with PR positivity was seen in 2 (4%). Overall, receptor positivity is seen in 30 (60%) patients. Tamoxifen 20 mg O.D for 5 years was advised to all patients with hormone receptor positive status [Table 14 and Figure 16].

Histopathology

Infiltrating intraductal carcinoma was the predominant type seen in 46 (92%) of the patients. Other types seen were 1 (2%) each of medullary, colloid, lobular, and inflammatory types [Table 15 and Figures 17-18].

Complications of Surgery (MRM)

Of the 47 patients who underwent MRM the following complications were seen. Seroma in 4 (8.5%), edema of the arm in 4 (8.5%), wound infection in 3 (6.3%), and wound dehiscence is seen in 2 (4.2%) of the patients [Table 16].

Table 13: Response to neoadjuvant chemotherapy

Clinical response	IIIA	IIIB	IIIC
cCR			
100%	3	2	-
cPR			
91-99%	2	1	-
81-90%	1	5	1
71-80%	3	8	-
61-70%	-	2	1
51-60%	-	1	-
SD			
1-50%	2	2	-
0%	-	3	-

One case of inflammatory carcinoma had no response to therapy. SD: Stable disease, cPR: Partial clinical response, cCR: Complete clinical response

Table 14: Receptor status

Receptor status	Number of patients (%)
Both ER/PR positive	23 (46)
ER-positive PR negative	5 (10)
ER-negative PR positive	2 (4)
Both ER/PR negative	20 (40)
Overall receptor positive	30 (60)

Table 15: Histopathology

Histopathology type	Number of patients (%)
Infiltrating intraductal	46 (92)
Medullary	1 (2)
Colloid	1 (2)
Lobular	1 (2)
Inflammatory	1 (2)

Table 16: Complications of surgery

Complication	Number of patients
Seroma	4 (8.5)
Edema of the arm	4 (8.5)
Wound infection	3 (6.3)
Wound dehiscence	2 (4.2)

Toxicity of Chemotherapy

It was noted that toxicity is, in general, more common in AC regimen. Most common toxicity noted is alopecia followed by anemia. Life-threatening toxicities are rare, with neutropenia being noted in one patient on AC other toxicities noted are nausea in 3.8% and 20.8% of patients of CMF and AC, emesis in 11.5% and 37.5%, mucositis noted in 15.4% and 12.5% of patients on CMF and AC, respectively [Table 17].

Radiotherapy

Among 45 patients who received radiotherapy, only one patient (2.2%) developed local recurrence. Radiotherapy was tolerated by all patients. Only 7 (15.5%) of 45 patients reported to have nausea. No other toxicity was reported.

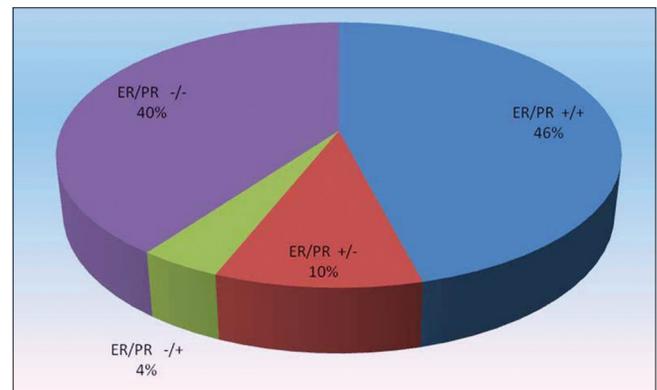


Figure 16: Receptor status

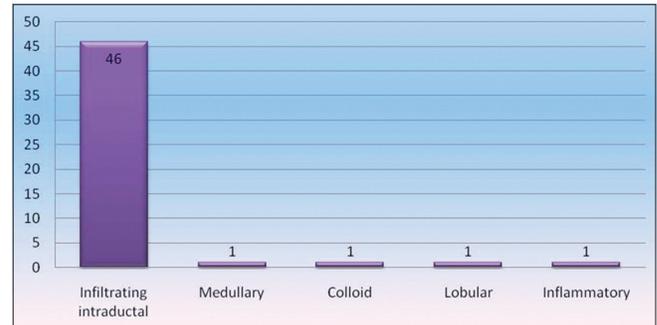


Figure 17: Histopathology

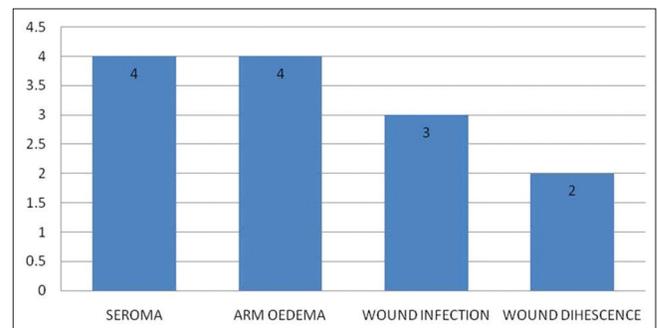


Figure 18: Surgery complications

Table 17: Chemotherapy toxicity

Toxicity	Number (%)	
	CMF	AC
Allopecia	10 (38.46)	20 (83.33)
Anemia	5 (19.2)	6 (25)
Mucositis	4 (15.4)	3 (12.5)
Nausea	1 (3.8)	5 (20.8)
Emesis	3 (11.5)	9 (37.5)
Fatigue	2 (7.7)	4 (16.6)
Neutropenia	0 (0)	1 (4.1)

CMF: Cyclophosphamide, methotrexate and 5-fluorouracil, AC: Doxorubicin and cyclophosphamide

Outcome

The patients were regularly followed up, and at the end of the study, 35 (70%) of the patients were doing well. 4 (8%) of the patients developed distant metastasis and 3 (6%) of the patients developing local recurrence. 8 (16%) of the patients were lost to follow-up.

DISCUSSION

Proportion of Cases

In our hospital, 44% of the patients admitted for the treatment of breast cancer were locally advanced. Chopra R states the proportion of LABC to the total number of reported breast cases to be 28.9%, 40.5%, and 52% in Mumbai, Trivandrum, and Chennai, respectively.^[10] The proportion of LABC is very high in developing countries compared to the western countries. LABC is a very common clinical scenario especially in developing countries (30–60%) possibly due to various factors such as lack of education and poor socioeconomic status.^[11]

The patients ignore the mass as it is commonly painless and does not interfere with the regular lifestyle of the patient. There is also a considerable delay in presenting to the hospitals due to ignorance allowing the lump to attain larger proportions.

Late diagnosis is a major factor for increased mortality as the majority of the patients present in the advanced or metastatic stage. This is primarily attributed to lack of access to medical facilities, virtually non-existent breast cancer screening programs, lack of awareness, and social-cultural attitudes

Age Distribution

The age incidences are compared in the Table 1 above. The highest number of cases is seen in the age group of 41–50 years in all the studies including ours except in Goel *et al.*, the peak is seen in 31–40 years age group.^[12]

The mean age is 46.5 years and 47.39 years in Aggarwal *et al.* and Sandhu *et al.*; series, respectively.^[13,14] The mean age in our study, i.e., 45.1 years matches closely with the above-mentioned studies.

In general, breast cancer has been reported to occur a decade earlier in Indian patients compared to their western counterparts. While the majority of breast cancer patients in western countries are postmenopausal and in their 60s and 70s, the picture is quite different in India with premenopausal patients constituting about 50% of all patients.^[15]

Symptoms at Presentation

The presenting features are compared with the percentages of presenting features in some of the similar series from India. The most consistent symptom is that of a lump and is seen in all cases in our study and 87.9%, 74%, and 96.5% in Sandhu *et al.*, Gang *et al.*, and Raina *et al.* series, respectively.^[16,17]

Quadrants Involved

In all the series, the percentage in the upper outer quadrant by far exceeds the percentage of location in other quadrants. The percentages of lump in the upper outer quadrants are 58%, 47%, 49%, and 48% in the current, Sandhu *et al.*, Sen and Dasgupta *et al.*, and Fields *et al.* series, respectively.^[18,19]

The possible explanation is that the upper outer quadrant has a relatively larger volume of breast tissue.

Duration of Symptoms

Most of the cases present with 3–6 months duration. The percentage of patients in this range was 38% and 32.9% in our study and Sandhu *et al.* series, respectively. The cases with <3 months duration were higher in Sandhu *et al.* series compared to our study.

Menstrual Status

In our study, more patients were premenopausal 30 (60%) than postmenopausal 20 (40%). Similar profile can be seen in Aggarwal *et al.* series.

In Sandhu *et al.* study 42.27% of the patients were premenopausal and 55.76% of the patients were postmenopausal. Karlson *et al.* reported 41% premenopausal patients versus 59% postmenopausal patients to be affected with carcinoma breast. Compared to the west, the percentage of premenopausal patients affected with breast carcinoma is reported to be more in India.

Tumor Size

The tumor sizes in our study are compared with Chintamani *et al.* and Aggarwal Himanshu *et al.* studies.^[21,22] Maximum

tumors are in the range of 5–8 cm. The percentage of tumors in that range is considerably higher in our study.

Lymph Node Status

Vishambaran *et al.* reported N1 stages to be 93% and N2 stages to be 7%.^[23] Compared to this study, our patients showed a higher incidence of N2 disease.

However, results similar to ours were seen in series of Chintamani *et al.* and Himanshu *et al.*

Stage of the Disease

In the present study, more percentage of cases were of Stage IIIB (48%), than Stage IIIA (46%). 4% and 2% of cases were of Stage IIIC and inflammatory carcinoma

Vishambaran *et al.* have reported 70% Stage IIIA and 30% Stage IIIB stages among their patients.

The percentages for IIIA were 24%, 55%, and 27.2%, respectively, in Yadav *et al.*, William *et al.*, and Nolen *et al.*^[24-26]

Stage IIIB cases were 33%, 27%, and 36.4%, respectively, in Yadav *et al.*, William *et al.*, and Nolen *et al.*

Stage IIIC cases were reported in Yadav *et al.* and William *et al.* with 25% and 2% of cases, respectively.

Sequencing of Therapy

In the present study, the inoperable tumors were treated with NACT. A majority of these cases the treatment was sequenced as NACT followed by surgery and completion of the remaining cycles of chemotherapy if any. This was followed by consolidation radiotherapy. This compares well with studies conducted by various authors who treated the patients with the same sequence and is also in sync with the current guidelines. The operable cases underwent surgery followed by adjuvant chemotherapy and radiotherapy in our study as in the study of Loprinzi *et al.*^[27]

The cases which presented inoperable stages are subjected to NACT to downstage the tumor and facilitate surgery, for local control of the disease. The patients undergoing surgery are then advised radiotherapy to prevent local recurrence.

Response to NACT

A total of 38 (76%) patients who presented inoperable states were subjected to neoadjuvant chemotherapy. CMF and an anthracycline-based regimen AC were used.

The primary objectives of NACT are to downstage the tumors and in cases of inoperable tumors to convert them into operable ones.

It was observed that the maximum number of cases in all the studies is under the category of pCR. In our study also a maximum number of cases 25 of 38 (65.8%) had partial response.

The rates of partial response were 45.45%, 65%, 73%, and 56.3% in Nolen *et al.*, Yadav *et al.*, Vishambaran *et al.*, and Aggarwal *et al.*, respectively. CR in our experience was seen in 13.2%, comparing closely with 22.7%, 22%, 13%, 16.3%, and 5% seen in Nolen *et al.*, Yadav *et al.*, Vishambaran *et al.*, Aggarwal *et al.*, and Karlsson *et al.*

In their article Raut and Chordiya present data related to response rates of various trials.^[28]

Our data relates closely with the results mentioned in the article of Raut and Chordiya.

Conversion rates of inoperable tumors.

Out of 38 inoperable tumors treated with NACT, 35 were rendered operable. Thus, 92% of inoperable tumors were converted to operable ones. This data show that in our study fairly good objective response to NACT was seen and that NACT downstages a good number of tumors and make them operable and give better locoregional control.

Receptor Status

Receptor status of our study compares closely with the results of receptor status study by Shet *et al.* conducted at Tata memorial hospital, Mumbai from 1999 to 2006.^[29] The receptor positivity is 60% in our population and 55.8% in Shet *et al.* study. It matches with the incidence in Indian population which is about 10% less than western population. All the patients with hormone receptor positive status were put on tamoxifen 20 mg O.D for 5 years. It was also noted that receptor status tended to be negative in younger patients.

Histopathology

Intraductal carcinoma is overwhelmingly common in all the studies mentioned below and account for more than 90% of cases.

Complications of Therapy

Toxicity of chemotherapy regimen

The toxicities of chemotherapy noted in our study are compared with study conducted by Kurapathy *et al.*^[30] In both the studies, overall the toxicity rates are higher in anthracycline-based regimen like AC than in CMF. Most common adverse effect noted is alopecia followed by emesis and anemia in AC regimen and anemia and mucositis in CMF regimen. Neutropenia was noted in only one patient on the AC regimen. The rates of toxicity are comparable to the above-mentioned study.

Surgical Complications

The complications noted were edema of the arm and seroma in 4 (8.5%) patients each. Wound infection was seen in 3 (6.3%) cases and wound dehiscence was seen in 2 (4.2%) of the patients.

The overall rate of complications was <30%.

Effects of Radiotherapy

Local recurrence was seen in about 2% of patients who received radiotherapy. It is an effective modality against local recurrence but still longer follow-up is required to conclusively prove the same. The only reported adverse effect of radiotherapy was nausea, seen in 7 (15.5%) of the 45 patients who underwent radiotherapy. No other toxicity was reported. Radiotherapy was well tolerated among our patients.

Outcome

Majority of the patients, 35 (70%) of the patients were doing well at the end of the study. The most distressing outcome was the development of distant metastasis in 4 (8%) of the patients. These cases included one inflammatory carcinoma, and other three were Stage IIIB, two of which had not responded to NACT and had remained inoperable.

Local recurrence was seen in 3 (6%) of the patients. Two of these cases were of Stage IIIA and were not on radiotherapy. One case belonged to Stage IIIB and had completed radiotherapy.

8 (16%) of the cases were lost to follow-up.

CONCLUSION

- About half of the cases presenting with breast cancer are in locally advanced stages.
- Lump in the breast is the most common symptom, upper outer quadrant being its most common location.
- Highest number of cases presented in 5th decade, followed by 4th decade indicating the presentation is a decade earlier in Indian patients compared to the west.
- Fixity to skin was seen in about 48% of the cases and was the most common cause of inoperability.
- Only a quarter of the cases were operable rest inoperable.
- Patients administered NACT showed a good response with 13.2% and 65.8% of the patients showing clinically complete and partial response, respectively. 92% of inoperable tumors became operable confirming that NACT is an effective method of downstaging the tumor.
- Chemotherapy was well tolerated in most patients, alopecia being the most common adverse effect followed by anemia and emesis.

- Surgical complications were seen in <30% of the cases.
- Hormone receptor positivity was seen in 60% of the patients and tamoxifen was advised in hormone receptor-positive patients.
- Infiltrating ductal carcinoma is the common histological variant seen.

Multimodality therapy is the effective treatment of locally advanced carcinoma of breast, but distant metastasis seen in 4 patients and local recurrence in 3 patients shows that management is a challenge and improvement in therapies are needed to further reduce disease-free interval and overall survival period.

SUMMARY

- A very high number of cases 44% presented in locally advanced stage of breast cancer in tune with trend in developing countries
- Highest incidence was seen in the fifth decade with 17 (34%) of patients presenting in this age group followed by the fourth decade with 13 (26%) of patients. Mean age being 45.1 years
- Lump in the breast is the common presentation and the most common location of the tumor being upper outer quadrant 29 (58%)
- Most of the patients 19 (38%) present with duration of symptoms from 3 to 6 months with mean duration being 8.8 months
- 60% of patients were premenopausal
- Size of 75% of tumors were in the range of 5–8 cm with mean size 6.6 cm.
- Fixity to skin and chest wall was seen in 38% and 10% of cases 24% of cases were operable at presentation and 76% inoperable.
- 46% presented in Stage IIIA, 44% presented in Stage IIIB, and 4% in Stage IIIC, and 2% of inflammatory breast cancer.
- NACT was administered to these all inoperable cases converting 92% these to operable stages. Clinical CR was seen in 13.2%, clinical partial response seen in 65.8% and 21% had SD.
- Chemotherapy was well tolerated in patients with alopecia being most common side effect.
- Surgical complications were seen in <30% of patients.
- Radiotherapy is effective in preventing local recurrence and well tolerated.
- 60% of patients are hormone receptor positive.

REFERENCES

1. Dumitrescu RG, Cotarla I. Understanding breast cancer risk-where do we stand in 2005? J Cell Mol Med 2005;9:208-21.

2. Chandra AB. Problems and prospects of cancer of the breast in India. *J Indian Med Assoc* 1979;72:43-5.
3. Halsted WS. The results of radical operation for the cure of cancer of the breast. *Trans Am Surg Assoc* 1907;25:61.
4. Agarwal G, Ramakant P. Breast cancer care in India: The current scenario and the challenges for the future. *Breast Care (Basel)* 2008;3:21-7.
5. Favourable and Unfavourable Effects on Long-term Survival of Radiotherapy for Early Breast Cancer: An overview of the randomised trials. Early breast cancer trialists' collaborative group. *Lancet* 2000;355:1757-70.
6. Warren SL. Roentgenologic study of the breast. *AJR Am J Roentgenol* 1930;24:113-24.
7. Baclesse F. Roentgen therapy alone in cancer of the breast. *Acta Un Int Contra Cancrum* 1959;15:1023.
8. Agarwal G, Pradeep PV, Aggarwal V, Yip CH, Cheung PS. Spectrum of breast cancer in Asian women. *World J Surg* 2007;31:1031-40.
9. Conte PF, Alama A, Bertelli G, *et al.* Chemotherapy with oestrogenic recruitment and surgery in LABC, clinical and cytokinetic results. *Int J Cancer* 1987;40:49.
10. Chopra R. The Indian scene. *J Clin Oncol* 2001;19:S106-11.
11. Rustogi A, Budrukkar A, Dinshaw K, Jalali R. Management of locally advanced breast cancer: Evolution and current practice. *J Can Res Ther* 2005;1:21-30.
12. Goel A, Bhan CM, Srivastava KN. Five year clinico pathological study of breast cancer. *Indian J Med Sci* 2003;57:347-9.
13. Agarwal G, Pradeep PV, Aggarwal V, Yip CH, Cheung PS. Spectrum of breast cancer in Asian women. *World J Surg* 2007;31(5):1031-40.
14. Sandhu DS, Sandhu S, Karwasra RK, Marwah S. Profile of breast cancer patients at a tertiary care hospital in North India. *Indian J Cancer* 2010;47:16-22.
15. Surakasula A, Nagarjunapu GC, Raghavaiah KV. A comparative study of pre- and post-menopausal breast cancer: Risk factors, presentation, characteristics and management. *J Res Pharm Pract* 2014;3:12-8.
16. Gang RK, Bothra VC, Pande K. Cancer of the breast. *Ind J Sur* 1982;1:347-50.
17. Raina V, Bhutani M, Bedi R, Sharma A, Deo SV, Shukla NK, *et al.* Clinical features and prognostic factors of early breast cancer at a major cancer center in North India. *Indian J Cancer* 2005;42:40-5.
18. Sen AK, Das Gupta TK. Cancer of the breast and its treatment. *Ind J Sur* 1962;6:833-47.
19. Fields KK, Goldstein SC, Clark RA, Sullivan DM, Djulbegovic B. *Decision Making in Oncology*. New York: Churchill Livingstone; 1997. P. 253-65.
20. Karlsson YA, Malmstrom PO, Hatschek T, Fornander TG, Söderberg MM, *et al.* Multimodality treatment of 128 patients with LABC in the era of mammography screening using standard polychemotherapy with 5-FU, epirubicin and cyclophosphamide- prognostic and therapeutic implications. *Cancer* 1998;83:936-47.
21. Chintamani, Singh JP, Mittal MK, Saxena S, Bansal A, Bhatia A, *et al.* Role of p-glycoprotein expression in predicting response to neoadjuvant chemotherapy in breast cancer- a prospective clinical study. *World J Surg Oncol* 2005;3:61.
22. Aggarwal H, Lubana PS, Jain DK, Mathur RK. Estimation of BCL-2 protein in carcinoma of the breast and its clinical correlation in locally advanced breast cancer. *J Cancer Res Ther* 2007;3:207-10.
23. Viswambharan JK, Kadambari D, Iyengar KR, Srinivasan K. Feasibility of breast conservation surgery in locally advanced breast cancer downstaged by neoadjuvant chemotherapy: A study in mastectomy specimens using simulation lumpectomy. *Indian J Cancer* 2005;42:30-4.
24. Yadav BS, Sharma SC, Singh R, Singh G. Patterns of relapse in locally advanced breast cancer treated with neoadjuvant chemotherapy followed by surgery and radiotherapy. *J Cancer Res Ther* 2007;3:75-80.
25. Cance WG, Carey LA, Calvo BF, Sartor C, Sawyer L, Moore DT, *et al.* Long-term outcome of neoadjuvant therapy for locally advanced breast carcinoma: Effective clinical downstaging allows breast preservation and predicts outstanding local control and survival. *Ann Surg* 2002;236:295-302.
26. Nolen BM, Marks JR, Ta'san S, Rand A, Luong TM, Wang Y, *et al.* Serum biomarker profiles and response to neoadjuvant chemotherapy for locally advanced breast cancer. *Breast Cancer Res* 2008;10:R45.
27. Loprinzi CL, Carbone PP, Tormey DC, Rosenbaum PR, Caldwell W, Kline JC, *et al.* Aggressive combined modality therapy for advanced locoregional breast carcinoma. *J Clin Oncol* 1984;2:157.
28. Raut NV, Chordiya N. NEO adjuvant chemotherapy in breast cancer: What have we learned so far? *Indian J Med Paediatr Oncol* 2010;31:8-17.
29. Shet T, Agrawal A, Nadkarni M, Palkar M, Havaldar R, Parmar V, *et al.* Hormone receptors over the last 8 years in a cancer referral center in India: What was and what is? *Indian J Pathol Microbiol* 2009;52:171-4.
30. Kuraparthi S, Reddy KM, Yadagiri LA, Yutla M, Venkata PB, Kadainti SV, *et al.* Epidemiology and patterns of care for invasive breast carcinoma at a community hospital in Southern India. *World J Surg Oncol* 2007;5:56.

How to cite this article: Padmasree G. Clinical and Epidemiological Evaluation and Assessment of Various Modes of Therapeutic Management of Locally Advanced Carcinoma of Breast in a Tertiary Care Hospital: An Observational Study. *Int J Sci Stud* 2018;6(5):136-146.

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

To study Incidence of Coronary Artery Disease in Asymptomatic Chronic Smokers by Using Exercise Stress Test

Mohd Suhel Siddiqui¹, Lalit Jain², Arpita Shrivastav³, Shivesh Thakur³

¹Associate Professor and Head Cardiology Unit, Department of Medicine, Netaji Subhash Chandra Bose Medical College and Hospital, Jabalpur, Madhya Pradesh, India, ²Assistant Professor, Department of Medicine, Netaji Subhash Chandra Bose Medical College and Hospital, Jabalpur, Madhya Pradesh, India, ³Senior Resident, Department of Medicine, Netaji Subhash Chandra Bose Medical College and Hospital, Jabalpur, Madhya Pradesh, India

Abstract

Introduction: Identification of coronary artery disease (CAD) in asymptomatic individuals is helpful in preventing future coronary events. The electrocardiographic exercise test is an easy, non-invasive, and reliable method for the diagnosis of latent CAD.

Purpose: The purpose of the study was to study the incidence of CAD in asymptomatic chronic smokers using exercise stress test, relationship between CAD risk and duration of smoking and to study the effect of smoking as an independent risk factor for CAD.

Materials and Methods: This study was conducted on 82 asymptomatic chronic smokers (duration of smoking at least 10 years and number of bidis/cigarettes >5 per day). Persons having history of angina pectoris, history of myocardial infarction, family history of IHD, significant abnormalities in the resting electrocardiogram, history of diabetes mellitus, history of hypertension, hypercholesterolemia, and severe non-cardiac disease were excluded from the study. Smoking history was taken with reference to years of smoking, type of smoking, and number of bidis/cigarettes per day. Study patient underwent exercise stress test as per modified Bruce protocol and other relevant blood investigations.

Results: In non-smoker group, only 7.3% subjects observed with positive treadmill test (TMT) but in bidi and cigarette smoker group positive TMT was observed in 33.3% and 39.1%, respectively. Inadequate exercise was noted in about 40% in smokers group while negative TMT was noticed in 20% in this group. The positive finding of TMT was strongly associated with smokers group ($P < 0.0001$). The study revealed that about 80% of non-smokers achieved the target heart rate while only 24.39% of smokers could achieve that and this is statistically highly significant ($P < 0.00001$). Non-smoker group has good exercise effort tolerance with an average of 10.74 ± 4.18 METS while smokers reported to have intermediate exercise effort tolerance with an average of 7.79 ± 4.55 METS. Among the chronic smokers and non-smokers, no subject developed any arrhythmias or cardiac decompensation during or after TMT. The mean pack-year (1 pack of bidi/cigarette = 10 bidis/cigarettes) of negative and positive cases was 24.12 ± 20.55 and 64.61 ± 15.45 ($P < 0.001$) and it was statistically significant.

Conclusion: This study concluded that chronic heavy smoking is an independent major risk factor for CAD and is about 5 times more frequently associated with the positive TMT and incidence of positive TMT is directly proportional to years of smoking ($P < 0.001$). Exercise electrocardiography is an important non-invasive tool for detection of latent CAD.

Key words: Coronary artery disease, Treadmill test, Target heart rate

Access this article online



www.ijss-sn.com

Month of Submission : 06-2018

Month of Peer Review : 07-2018

Month of Acceptance : 08-2018

Month of Publishing : 08-2018

INTRODUCTION

Coronary artery disease (CAD) is common heart disease in the developing as well as developed countries and accounts for large number of sudden cardiac death. It is the major cause of morbidity and mortality in the western world. patients of acute myocardial infarction or sudden cardiac

Corresponding Author: Mohd Suhel Siddiqui, Head Cardiology Unit, Department of Medicine, Netaji Subhash Chandra Bose Medical College and Hospital, Jabalpur – 482 003, Madhya Pradesh, India. Phone: +91-9424680834. E-mail: drsuhelsiddiqui@gmail.com

death may not have any related clinical manifestations before their illness. Reports indicate that many apparently healthy persons have silent C.A.D.^[1]

Smoking constitutes one of the definite and foremost preventable risk factors for the development of CAD.^[2] It has been found that in men who smoke >20 cigarettes per day, the risk of myocardial infarction was about 3 times higher than those who do not smoke. Sudden cardiac deaths are much more frequently associated with heavy smokers than in non-smokers. In women smoking >35 cigarettes per day, the incidence of myocardial infarction was estimated 20 folds higher than those who had never smoked.

Therefore, identification and quantification of such asymptomatic individual with this risk factor can be much helpful in preventing future coronary events. The electrocardiographic exercise test is an easily applicably non-invasive and reliable method for the diagnosis of latent CAD.^[3]

Stress testing was started in 1928 by Feil and Seigal,^[4] to assess the latent CAD modern stress was started in 1956 by Bruce. The basic aim of exercise test is to increase the oxygen demand of myocardium so as to unmask relatively reduced coronary blood flow. Treadmill exercise test is now an established non-invasive diagnostic, prognostic and evaluative technique in Cardiovascular Medicine. Although various other techniques are also available, for the developing countries such as India testing are economical and convenient methods to identify “at-risk” population.

This study was, thus, carried out to assess the relationship between asymptomatic chronic smokers and treadmill exercise test response as an indicator of latent CAD.

MATERIALS AND METHODS

This study was conducted on 82 asymptomatic males 28–60 years of age (mean 46 years) at the Department of Medicine, Netaji Subhash Chandra Bose Medical College Hospital, Jabalpur (M.P.), from June 2017 to May 2018. The study group consisted of 41 chronic smokers (having no other major risk factor for CAD) and 41 non-smokers (without any major risk factor for CAD). The smokers smoked Either bidis or cigarettes. The length of bidi or cigarette, whether filtered or non-filtered was not taken into consideration.

Criteria for Chronic Smoker (Arbitrary)

1. Duration of smoking: At least 10 years
2. Number of bidis/cigarettes: >5 per day.

Following persons were not included in the study:

1. Those having history of anginal chest pain
2. History of acute coronary syndrome

3. Family history of CAD
4. Abnormal resting electrocardiogram (ECG)
5. History of diabetes mellitus
6. History of hypertension
7. Hypercholesterolemia
8. Severe comorbid condition.

A detailed clinical history was taken from each individual. Family history of CAD, occupational history, and other risk factors for CAD were enquired. Smoking history was taken with reference to years of smoking, type of smoking, and number of bidis/cigarettes used per day.

A thorough physical examination was done with special reference to cardiovascular system. Any evidence of cardiac enlargement or failure such as S3-S4 and lungs for basal crackles was observed.

Criteria for Positive Treadmill Test (TMT)

(Based on Goldschlager and Seizers classification sept.1976)^[5]

Type Ia positive response: 1 mm or more of J-point depression with downsloping ST segment.

Type Ib positive response: 1 mm or more of 1-point depression with flat/horizontal St segment.

Type II positive response: 1.5 mm or more slowly upsloping ST-segment depression at 80 ms after i-point.

(Slow upsloping: ST slope <1.25mV/s)

Next, they are subjected to the following investigations:

1. Blood sugar
2. Fasting lipid profile
3. Renal function test: Blood urea and serum creatinine
4. Resting ECG.

The following instructions were given to each individual:

1. To have a light dinner on the night before the test and a light breakfast at least 4 h before the test.
2. To shave anterior chest wall and abdominal wall to facilitate proper placement of electrodes.
3. To bring at least one attendant with him.

Table 1: TMT result

TMT result	Groups		
	Non-smokers	Bidi's	Cigarettes
Positive	3 (7.3)	6 (33.3)	9 (39.1)
Inadequate	5 (12.2)	7 (38.9)	9 (39.1)
Negative	33 (80.5)	5 (27.8)	5 (21.7)
Total	41	18	23

TMT: Treadmill test

Table 2: Distribution of pack-years and positive TMT

Pack-years	Bidi Smokers			Cigarette smokers		
	Negative	Inad	Positive	Negative	Inad	Post.
5–40	3	1	0	4	4	0
41–80	2	3	3	1	4	8
81–20	0	2	3	0	1	1
<120	0	1	0	0	0	0
Total	5	7	6	5	9	9
Mean±SD	37.40±25.16	71.80±35.66	78.34±11.86	24.12±20.55	40.79±19.63	64.64±15.45

SD: Standard deviation, TMT: Treadmill test

Table 3: Workload attained during treadmill test

METS	Groups		
	Non-smokers	Bidi's	Cigarettes
<4	1 (2.4)	3 (16.7)	3 (13.0)
4–7	6 (14.6)	6 (33.3)	2 (8.7)
7–10	13 (31.7)	4 (22.2)	12 (52.2)
10–13	9 (22.0)	2 (11.1)	3 (13.0)
13+	12 (29.3)	3 (16.7)	3 (13.0)
Total	41 (100.0)	18 (100.0)	23 (100.0)
Mean±SD	10.74±4.18	7.79±4.55	7.82±4.51

SD: Standard deviation

- To abstain from smoking at least 2 h before the test.
- To wear comfortable clothes and foot wears to facilitate proper test.

Procedure

Height and weight of all individuals were recorded. The skin over the anterior chest wall at the site of application of the electrodes was cleaned with spirit and abraded until it becomes hyperemic, and the patient was asked to lie down, and the resting blood pressure was recorded followed by a pre-test 12 lead ECG was recorded. Now the patient was asked to stand up, and again the blood pressure and ECG changes were recorded. Now the patient was advised to hyperventilate for 30 s. After 30 s of hyperventilation blood pressure and ECG changes if any were recorded.

After demonstration and explanation regarding the procedure, the patient was subjected to exercise stress test according to Bruce protocol.

The blood pressure was recorded every 3 min. Test continued till patient reached target heart rate (THR= 220- age in years) or terminated prematurely due to some other reasons.

After completion of the test, the patient was asked to lie down on bed and was re-examined for signs of cardiac decompensation, i.e., S3, S4, or basal crypts. Blood pressure was recorded at 2 min interval from onset of recovery and then at least every 3 min. ECG monitoring was done until ECG changes return to normal or for at least 4 min in recovery phase.

RESULTS

This study was conducted in 82 asymptomatic males 28–30 years (mean 46.44 ± 9.43). The study groups consisted of 41 chronic smokers, of which 23 smoked cigarettes and 18 smoked bidis and 41 non-smokers. Each individual performed symptoms limited treadmill exercise following Bruce protocol on a case 12 system “UNI-EM TREADMILL SYSTEM” until the termination criteria were achieved.

In our study we found in non-smoker group, 7.3% subjects observed with positive TMT. In bidi and cigarette smoker group positive TMT was observed in 33.3% and 39.1%, respectively. Inadequate exercise was noted in 38.9% and 39.1%, respectively, for bidi and cigarette group while both of these groups showed negative TMT by 27.8% and 21.7%, respectively. The positive finding of TMT was observed strongly associated with smoker group (either bidi or cigarette) ($P < 0.0001$).

It is also obvious in this study that total 33 of 41 (80.5%) non-smokers achieved the THR while only 24.39% of smokers 5 bidi and 5 cigarette smokers could achieve that. It is statistically very highly significant ($P < 0.00001$).

The ST criteria (with positive TMT) were met with 3 non-smokers (7.3%) while it was met in 15 smokers with 6 (33.3) of bidi smokers and 9 (39.1%) of cigarette smokers. It was also statistically highly significant ($P < 0.001$).

Majority of cases in non-smoker group (51.3%) achieved >10 METS with an average of 10.74 ± 4.18 METS. While the bidi smokers reported 16.3% cases with <4 METS, 71.8% of the bidi smokers could achieve only up to 10 METS with an average of 7.79 ± 4.55 METS. A similar observation was noted among the cigarette smokers with the mean of 7.82 ± 4.51. The control group showed significantly higher amount of workload as compared with overall case group ($P < 0.05$). The cigarette and bidi smokers were almost comparable and showed equal amount of workload, i.e., METS ($P > 0.05$) but definitely significantly different with the non-smokers ($P < 0.05$).

Among the chronic smokers and non-smokers, no subject developed any arrhythmias during or after TMT, and none of the persons among both the groups developed any signs of cardiac decompensation during or just after exercise.

This study describes the correlation between number of bidi's and cigarettes smoking in terms of pack-years of smoking in relation with the TMT findings (1 pack of bidi/cigarette = 10 bidis/cigarettes). In bidi smokers, the negative TMT was confined to 5–80 pack-years, while the cases found positive on TMT showed the observation of 41–120 pack-years with the mean of 37.40 ± 25.16 and 78.34 ± 11.86 pack-years, respectively. The positive cases showed a significantly higher amount of bidi smoking compared to non-smokers. In cigarette smoker group, the negative TMT cases were primarily concentrated in 40–120 pack-years. The mean pack-year of negative and positive cases was 24.12 ± 20.55 and 64.61 ± 15.45 ($P < 0.001$). It is statistically significant [Tables 1-3].

DISCUSSION

Coronary heart disease is the chief single cause of death in developed as well as developing countries. 40% or more of patients of acute myocardial infarction or sudden death due to CAD have no previous clinical manifestations.^[1] This occurs as the results of advanced coronary atherosclerosis which has evolved slowly over many years without notable clinical manifestations.

In light of these considerations, a simple objective means of detecting latent coronary heart disease is of the utmost importance. A considerable number of such coronary prone subjects can be identified by exercise testing. The predictive value, i.e. probability of developing coronary heart disease in patients with an abnormal test in three careful follow-up studied in healthy men of a wide age group ranged from 13.6 to 23.0%.^[6]

Exercise electrocardiography is one of the most important and valuable non-invasive diagnostic tests for patients suspected or known to be having cardiovascular disease, particular CAD.

Doan *et al.*^[7] claimed that maximum exercise (treadmill) increase the sensitivity of the electrocardiographic exercise test nine folds in comparison to the double two-step test.

The positive ischemic ST-segment changes, produced by treadmill exercise test, are more sensitive and specific (75–90%) as compared to Master's two-step test (50%). It is because of this reason we preferred to do treadmill exercise test rather than Master's two-step in the present study.

In the asymptomatic population where the incidence of CAD is expected to be low, the chance of a positive results being false positive is obviously higher than in a population with typical anginal discomfort due to CAD. In this asymptomatic population^[6] found 44% and Borer *et al.* (1975) found 37% of positive test to be true positive tests.

A positive exercise results indicates that the likelihood of CAD is 98% in patients with typical angina, 88% in patient with atypical pain, 44% in patients with non-anginal chest pain, and only 33% in asymptomatic persons (Braunwald 1989).

Many retrospective studies have been conducted to determine the association between smoking and coronary heart disease, but few studies have been conducted in asymptomatic healthy persons to find out the incidence of latent heart disease among those having risk factors. The number of risk factors is protean, but we have restricted to only one, i.e. chronic-smoking (>5 cigarettes per day for at least 10 years) in this study.

We studied 82 asymptomatic subjects, 41 were non-smokers without any clinical or electrocardiographic features suggestive of CAD and chronic smokers, of which 18 were smoking bidis, and 23 were smoking cigarettes. All cases were males. In the present study, among 41 chronic smokers, total 15 (36.58%) had positive TMT whereas only 3 (7.3%) persons in the non-smokers group had positive test. Among the smokers total 6 of 18 (33.33%) had positive results whereas in cigarette smoker Group 9 of 23 (39.1%) had positive TMT. The incidence of positive TMT was >5 times in chronic smokers than in non-smokers. The difference between these groups is statistically significant ($P < 0.05$). There was no significant difference found among bidi and cigarette smokers. Our observations are quite consistent with those of Nayak *et al.* (1989) 136 where they found incidence by 4.3 times more in chronic smokers. They found no significant difference between bidi and cigarette smokers.

In a study by Pais *et al.* (2001) found that smoking 10 or more bidis or cigarettes per day carries an independent four-fold increase risk of AMI. Odds ratio for cigarette was 3.58 ($P < 0.08$) and bidis was 4.36 ($P < 0.001$). The results are very close to our observations. They studied the incidence among the AMI cases, but we studied it in asymptomatic patients.

Other published reports, however, were not quite comparable with the present study as they were either on unselected healthy persons or with multiple risk factors.

Bellet and Roan^[3] found 2.7% positive exercise tests in normal persons without any risk factors while in our study it is 7.1%; however, his study group was large. Of 710 persons 19 were having positive test. Cumming *et al.* (1981) used maximum exercise as bicycle ergometer in asymptomatic men found 12% positive exercise tests.

Agarwal *et al.*^[1] studied 50 middle-aged subjects with important coronary risk factors and yielded 22% positive tests.

Jayant *et al.* (1983) in the case–control study in India shown that cigarette smokers are more than twice as likely to develop coronary heart disease and 3 times more likely to develop myocardial infarction than non-smokers.

In our study, the incidence of positive stress testing in chronic smokers shows an increasing trend with the rise in age, i.e., 12.19% in age group below 50 years while 24.39% in subject >50 years. Statistically, it is just significant ($P < 0.1$).

Bellet and Roan^[3] screened 1390 subjects for latent CAD using treadmill exercise test. The results were as follows:

Age group	Positive TMT (%)
20–29 years (253)	8 (3.2)
30–39 years (563)	31 (5.5)
40–54 years (574)	101 (17.6)

In the present study, the incidence of positive test in chronic smokers is directly proportional to the total amount of smoking, i.e., duration and number of cigarettes smoked represented as pack-years. Prevalence positive TMT was 66.6% in those who had >40.30 pack-years cigarette smoking compared to only 1% in those who had for 5–40 pack-years and the difference is statistically highly significant. These observations are consistent with those of Kannel (1976, 1981) 87 and Nayak *et al.* (1989) 136. In their study out 10 cases of heavy smokers (>20 cigarettes per day), 5 were having positive tests.

The interpretation of a positive exercise test is beset with many difficulties, particular when performed in asymptomatic persons.

Bellet and Roan^[3] found 2.7% positive stress tests in normal healthy persons. A positive test may be due to various reasons:

- Unmasking of latent CAD
- False positivity
- A direct consequence of heavy smoking.

It has been reported in literature (Chung *et al.* 1979) that exercise test may be positive if one smoked shortly before performing a stress test, which might suggest that it may be a pharmacologic action since no details are available.

CONCLUSION

Chronic heavy smoking is about 5 times more frequently associated with the positive TMT as compared to no smoking and incidence of positive TMT is directly proportional to years of smoking ($P < 0.001$). There is no significant difference between bidi and cigarette smoking and a positive TMT result ($P > 0.05$), but chronic smoking (either bidis or cigarettes) serves as an independent major risk factor for CAD.

Exercise electrocardiography is an important non-invasive test for detection of latent CAD. Hence, this study goes a long way in providing a useful non-invasive method to detect high-risk cases among chronic bidi and cigarette smokers and this is useful from both preventive and curative aspects.

REFERENCES

- Agarwal BL, Gupta OP, Gupta VK. Str testing in asymptomatic subjects with important coronary risk factors. *Md Heart J* 1981;3:6, 247.
- Kennel WB, Mc Gee D, Gordon T. A general cardiovascular risk profile. The framingham study. *Am Jor Cardiol* 1976;38:46.
- Bellet S, Roan LR. Comparison of the double two step test and the maximal exercise treadmill test. *Circulation* 1967;36:238
- Feil H, Seigal ML. Electrocardiographic changes during attacks of angina pectoris. *Am J Med Sci* 1928;175:355.
- Goldschlager N, Seizer A. Treadmill stress test as indicator of presence and severity of coronary artery disease. *Ann Int Med* 1976;85:277.
- Froelicher VF, Morrow K, Brown M, Atwood E. Prediction of atherosclerotic cardiovascular death in men using a prognostic score. *Am J Cardiol* 1994;73:133-8.
- Doan AE, Peterson DR, Biackmon JR, Bruce RA. Myocardial ischaemic after maximal exercise in healthy men. A method for detecting potential coronary heart disease. *Am Heart J* 1965;69:11.

How to cite this article: Siddiqui MS, Jain L, Shrivastav A, Thakur S. Incidence of Coronary Artery Disease in Asymptomatic Chronic Smokers Using Exercise Stress Test. *Int J Sci Stud* 2018;6(5):147-151.

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

A Clinical Study of the Different Types of Inguinoscrotal Swellings and Their Management in a Tertiary Care Referral Center

Radha Verma¹, Chirag Vaja², Swarup Anand³, Kiran Gaikwad⁴, Aditya Tripathi⁴, Rutuja Narvekar⁵

¹Professor and Head, Department of Surgery, K.J Somaiya Medical College and Research Centre, Mumbai, India, ²Senior Resident, Department of Surgery, K.J Somaiya Medical College and Research Centre, Mumbai, India, ³Junior Resident, Department of Surgery, K.J Somaiya Medical College and Research Centre, Mumbai, India, ⁴Professor, Department of Surgery, K.J Somaiya Medical College and Research Centre, Mumbai, India, ⁵Intern, Department of Surgery, K.J Somaiya Medical College and Research Centre, Mumbai, India

Abstract

Background: Inguinal hernias and hydrocele in children remain one of the most common congenital anomalies observed by pediatricians and surgeons requiring surgery.

Materials and Methods: 44 cases of inguinoscrotal swelling attending the pediatric surgery OPD or admitted in the wards of K. J. Somaiya Hospital and Research Center, Sion, Mumbai (tertiary care center), from October 2014 to April 2015 year were selected on the basis of the simple random sampling method. All patients below 12 years of age, both male and female attending surgery OPD with complaints of swelling in the inguinoscrotal region associated with symptoms as well as those found accidentally on examination were included. The age/sex distribution, birth history and side distribution, exact site of swelling, and operation performed were evaluated and compared with standard published literature. A predesigned pro forma was used to collect this information for individual cases.

Results: The incidence of inguinoscrotal swelling in pediatric patients was maximum in toddler age group (38.6 %), male (88.6%), term child (79.5%), and right side (59.1%) with a maximum number of swellings being in the inguinal region (77.3%). Of the 44 cases, 2 were diagnosed as inguinal hernia, 5 as congenital hydrocele, 3 as encysted hydrocele of the cord, and 4 as undescended testis.

Conclusion: Inguinal hernia and hydrocele along with associated conditions such as undescended testis and hypospadias are common congenital anomalies requiring surgical intervention. Inguinal herniotomy, whether open or laparoscopic, is considered safe and effective with less recurrences.

Key words: Inguinoscrotal swelling, Tertiary care centre, Pediatric hernia, Laproscopic hernia surgery

INTRODUCTION

The disease which makes the subject of the following tract, is one in which mankind are, on many accounts, much interested. No age, sex, rank, or condition of life, is exempted from it; the rich, the poor, the lazy, and the laborious, are equally liable to it; it produces certain

inconvenience to all who are afflicted by it. It sometimes puts the life of the patient in such hazard, as to require one of the most delicate operations in surgery; and it has in all times, from the most ancient down to the present, rendered those who labor under it subject to the most iniquitous frauds and imposition.^[1]

Inguino-scrotal swelling is one of most common surgical problems encountered in children.^[2] Of all the inguino-scrotal swellings, inguinal hernia and hydrocele top on the list in frequency. They represent the conditions most requiring surgical repair in the pediatric age group.

Hernia is Latin term meaning rupture of a portion of structure. It can be defined as an "abnormal protrusion of

Access this article online



www.ijss-sn.com

Month of Submission : 06-2018

Month of Peer Review : 07-2018

Month of Acceptance : 08-2018

Month of Publishing : 08-2018

Corresponding Author: Dr. Radha Verma, Department of Surgery, K.J Somaiya Medical College and Research Centre, Mumbai, India.
E-mail: drradha.verma@gmail.com

a viscus or part of a viscus through a normal or abnormal opening in the wall of its containing cavity.”^[3] As a result of improved neonatal intensive care, more and more premature babies are being delivered, and consequently, the incidence of neonatal inguinal hernia and hydrocele is increasing.

Pediatric hernias and hydrocele are fundamentally the results of incomplete or abnormal obliteration of the patient peritoneal diverticulum called processus vaginalis which accompanies that the test is on its journey into the scrotum.

A similar process occurs in a female but without the external phase of descent. In a female, a potential pocket associated with the round ligament, known as a diverticulum of Nuck corresponding to the processus vaginalis of males predisposes to formation of inguinal hernia in a female. Normally, the fusion of the processus continues after birth through infancy and childhood with some remaining patent even in adulthood but mostly occurs before 2 years of age. Studies suggest that 80–100% of infants are born with a patent processus, and additionally, a short inguinal canal that has not developed in an oblique direction along with direct superimposition of the external and internal rings favors the development of hernias and hydrocele. The incidence of inguinal hernias is 0.8–4.4% or 10–20/1000 live births. The risk factors include prematurity, low birth weight, family history, hydrops, meconium peritonitis, chylous ascites, liver disease with ascites, abdominal wall defects, ambiguous genitalia, hypospadias or epispadias, bladder extrophy, cryptorchidism, cystic fibrosis, and connective tissue disorders such as Ehlers–Danlos syndrome. The predisposing conditions include 4 prematurity, low birth weight, family history, hydrops, meconium peritonitis, chylous ascites, liver disease with ascites, abdominal wall defects, ambiguous genitalia, hypospadias or epispadias, bladder extrophy, cryptorchidism, cystic fibrosis, connective tissue disorders like Ehlers Danlos syndrome, Ventriculoperitoneal shunts, continues ambulatory peritoneal dialysis and mucopolysacchridosis. The indirect inguinal hernias occur as bubonocele (hernia limited to the inguinal canal), funicular (hernias extends into the scrotum and up to the upper pole of the testis), and complete (where hernia completely surrounds the testis) [Figures 1].

The presentation typically can be groin swellings which appear with increased intra-abdominal pressure such as crying or straining and may disappear spontaneously or with gentle manual pressure. The other features include groin pain during exercise which can be vague chronic sharp fleeting type. Abdominal distention, vomiting, and absence of stool/flatus would suggest intestinal obstruction, perforation, and peritonitis. With strangulation, occasional

bleeding per rectum may be seen. On the other hand, hydrocele presents as a translucent smooth non-tender swelling. The other differentials include inguinal lymph nodes, encysted hydrocele of cord, varicocele, lymph varix, funiculitis, ectopic or retractile testis, testicular malignancy, aneurysm of external iliac artery, cryptorchidism, abscess in inguinal region, and lipoma of the cord and femoral hernia.

The diagnosis is based on clinical history and examination and laparoscopic surgery with or without contralateral exploration. The complications include wound infection at 1–2% recurrences at 1% and uncommonly vas injury and testicular atrophy which commonly occurs after emergency surgery.

Aim

To study the different types of inguino-scrotal swellings and their management in the tertiary care referral centre.

Objectives

Primary objective

1. To study the differential diagnosis of inguino-scrotal swelling in children [Figures 2-7].

Secondary objectives

The secondary objectives are as follows:

1. To study the age, sex and sidewise distribution of inguinoscrotal swellings in children.
2. To study the various management options for various types of inguinoscrotal swelling open as well as minimal excessive surgery.
3. To study the associated anomalies like undescended testis, hypospadias and patency of processus vaginalis.
4. To study the postoperative complications such as wound infection, haematoma, recurrence etc.
5. To study complications like incarceration, strangulation and gonadal infarction.

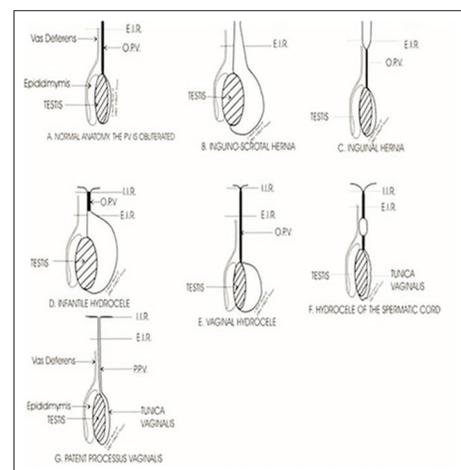


Figure 1: Diagrammatic representation of different types of inguinal hernias and hydrocele in boys[9]



Figure 2: Right inguinal swelling



Figure 5: Right congenital hydrocele



Figure 3: Left inguinal swelling



Figure 6: Right undescended testis



Figure 4: Left scrotal swelling

EMBRYOLOGY

Pediatric hernias and hydrocele are fundamentally the result of incomplete or abnormal obliteration of the patent processus vaginalis. During the fifth week of gestation, the gonadal ridge develop from an outgrowth of the coelomic epithelium overlying the medial aspect of the mesonephros. Primordial germ cells migrate from the endothelial lining of yolk sac to gonadal ridge during sixth week, forming



Figure 7: Open herniotomy position

the indifferent gonad. The gonad, is identifiably a testis by the eighth week. As testicular development proceeds, mullerian duct regression begins under the influence of

mullerian inhibiting substance, and wolffian duct begins under the influence of fetal testosterone.^[4]

The gubernaculum develops as a condensation of mesenchyme, extending from the caudal end of the testicle to the future site of inguinal canal and scrotum. The processus vaginalis, a diverticulum of the peritoneal cavity, can first be identified during the third month of fetal life. The round and ovarian ligaments in the female are analogous to the male gubernaculum and are distinguishable by the eleventh week, once mullerian duct fusion has occurred. The gubernaculum undergoes a period of rapid growth after week 15, filling and dilating inguinal canal. This development probably due to stimulation from testosterone but may also involve mullerian inhibiting substance. During week 27 to 28, the testicle, gubernaculum, and processus vaginalis descend through the inguinal canal in to scrotum. This transinguinal passage is probably a rapid process, because testicles are rarely found within the inguinal canal in fetal autopsy studies.

Prior to the descent of the testis and the ovary from their site of origin, a peritoneal diverticulum called the processus vaginalis is formed. The processus vaginalis passes through the layers of the lower part of the anterior abdominal wall. It traverses the fascia transversalis at the deep inguinal ring and acquires a tubular covering, the internal spermatic fascia, through the lower part of the internal oblique muscle, which form the cremasteric muscle. Muscle fibers are embedded in fascia and thus the second tubular sheath called cremasteric fascia. On reaching the aponeurosis of the external oblique it evaginates this to form the superficial inguinal ring and acquires a third tubular fascial coat, the external spermatic fascia. It is in this manner that the inguinal canal is formed.^[5]

The processus vaginalis accompanies the testicle on its journey in to the scrotum. Normal fusion of the processus occurs spontaneously after the testicle is in place. Precisely when, why, and how it occurs is not known. It is clear that the closure of the processus continues after birth through infancy and childhood with some remaining patent in to adulthood. Most closure of the processus appear to occur before the age of 2 years. Patency of the processus is necessary for the development of pediatric hernias and hydroceles. Why many patent processus remain asymptomatic can only be speculated.

Incomplete obliteration of the processus vaginalis results in the formation of various types of inguinal hernias and hydroceles in infancy and childhood, and accounts for the classification of these hernias and hydroceles as congenital anomalies, even though they may not be clinically present

at birth. Obliteration of the distal processus with proximal patency leads to the formation of a shorter inguinal hernia sac. Complete failure of obliteration of the processus leaves a sac extending all the way from the internal ring to the testicles, resulting in an inguino-scrotal hernia, the tunica vaginalis being contiguous with the hernia sac and the peritoneum. Narrowing of the processus vaginalis at the level of the internal ring results in the formation of a communication between the tunica vaginalis and the peritoneal cavity, leading to the establishment of a communicating hydrocele. Conversely, obliteration of the proximal portion of the processus with distal patency results in the formation of a non-communicating hydrocele or hydrocele of the tunica vaginalis. Finally, if complete obliteration of the processus occurs with patency of the mid portion, a hydrocele of the cord (or canal of nuck in the females) occurs. This presents as a mass in the inguinal canal, and frequently has a small connection to the peritoneal cavity at the inguinal ring. The exact timing of closure is uncertain. Studies have suggested that as many as 80% to 100% of infants are born with a patent processus vaginalis and the closure, if it occurs, is most likely within the first 6 months of life.^[6]

In the female, the descent of the gonads is similar to that in the male, except that there is no external phase of descent; the uterus is interposed between the ovarian ligament and the round ligament, which by the 3rd month of gestation appears as a thick mesenchymal band extending from the region of the uterus to the labia majora. A peritoneal pocket associated with the round ligament and known as the diverticulum of nuck correspond to the vaginal processus in the male and predisposes to the formation of inguinal hernias in the female.

ANATOMY

The foundation of the inguinal anatomy is the bony pelvis. The inguinal ligament a reflection of the aponeurosis of the external oblique muscle, rest on this foundation, stretching from the anterior superior iliac spine to the pubic tubercle. The inguinal canal allows passage of the spermatic cord from the abdomen into the scrotum. The spermatic cord contains the vas deferens; three arteries (testicular, cremasteric and deferential); three veins (pampiniform/testicular, cremasteric and deferential); and three nerves (ilioinguinal, genital branch of the genitofemoral, and sympathetic nerves). The spermatic cord passes through the deep inguinal ring or arch, which is composed of the transverse abdominis and internal oblique muscles. The cord structures then continue through the inguinal canal. Anteriorly the canal is formed by aponeurosis of the external oblique muscle. The posterior wall or floor of the canal is formed by the transverses abdominis muscles

and the transversalis fascia. Roof is formed by conjoint tendon and the floor by the reflected part of inguinal ligament. Hesselbach's triangle is a region of the posterior wall at risk for direct herniation. Its boundaries consist of inferior epigastric artery on lateral, rectus muscle on medial and base formed by inguinal ligament. The cord then exist the external inguinal ring, which is formed by external oblique muscle just superior and lateral to pubic tubercle. The spermatic cord passes down to scrotum and covered with external spermatic fascia, which are derived from the fascia of external oblique muscle and transversalis fascia respectively.

The basic anatomy of inguinal canal is same as in the adult. However, it is important to emphasize that in infancy till 2 years of age, the inguinal canal is extremely short and has not developed an oblique direction, the external ring being situated almost directly over the internal ring. Scarpa's fascia is more prominent in children can be easily mistaken for external oblique aponeurosis. The internal ring is superior and lateral to the external ring, providing a protective mechanism so that when there is an increase in intra-abdominal pressure, the posterior wall of the canal is forced against the anterior wall, thus obliterating the space.

EPIDEMIOLOGY AND RISK FACTORS

The origin of inguinal hernia is unclear, although it is a common condition of infancy and childhood. Inguinal hernia occurs in 0.8–4.4% of children, and are unilateral in 75–90%.^[7,8] Incidence is higher in premature infants (13% of those <32wks gestation) and low birth weight infants (30% in infants <1000g). The inguinal hernia occurs in 0.8% - 4.4% of children, which roughly translates as 10 to 20 per 1000 live births.^[7,8] The incidence rises in premature infants (13% of those <32 weeks gestation) and low birth weight infants (30% in infants <1000g).^[8] The incidence is highest during the first year of life with peak during the first month. It has been documented that approximately one third of children with inguinal hernias are less than 6 months of age. Boys are affected approximately 6 times more often than girls. The higher incidence of inguinal hernia on the right side is related to the fact that the right testis descends at a later than the left and, therefore the right processus vaginalis obliterates later than the on the left processus. Consequently, patients who present with left sided inguinal hernia have a higher incidence of occult right sided inguinal hernia. The association of undescended testis and inguinal hernia is common. It has been reported that in both boys and girls, approximately 60%-70% of inguinal hernias occur on the right, 25%-30% on the left, and 5%-10% occur bilaterally.^[9]

Extrophy of the bladder, Ehlers-Danlos syndrome and

Prune belly syndrome are associated with an increased incidence of inguinal hernia and patients who have ventriculo-peritoneal shunts are prone to the development of inguinal hernia, secondary to the increase in intra-abdominal pressure.

Conditions that predispose to hernia development include^[4] Prematurity, Low birth weight, Family history, Hydrops, Meconium peritonitis, Chylous ascites, Liver disease with ascites, Abdominal wall defects, Ambiguous genitalia, Hypospadias, Epispadias and Extrophy of the bladder, Cryptorchid testis, Cystic fibrosis, Connective tissue disease, Ventriculoperitoneal shunts, Continuous ambulatory peritoneal dialysis & Mucopolysaccharidosis

PRESENTATION AND EVALUATION

Most inguinal hernias are accidental findings, either by parents or during a well-baby or preschool check. There is usually a history of an intermittent bulge appearing in the groin, scrotum, or labia, especially noted at times of increased intra-abdominal pressure, such as crying or straining. Its presentation may be present at birth or may not appear until weeks, months, or even years later. Nevertheless, they are thought to be present at birth, and not related to crying or straining with bowel movements, or other activities of daily living. Hernias are usually asymptomatic. Parents are frequently concerned that hernia may cause the infant to be irritable or have a loss of appetite. In most cases the only complaint is the appearance of groin swelling, which disappear when the patient relaxes, either spontaneously or with gentle manual pressure. Older children may complain of groin or inguinal pain during exercise. This pain may be vague or chronic, sharp and fleeting.^[3]

If a loop of bowel becomes entrapped in a hernia, the patient becomes extremely irritable and develops intense pain, followed by signs of intestinal obstruction (abdominal distention, vomiting, absence of flatus/stool). Vomiting is common in incarceration, and is usually secondary to visceral distention. If bile-stained vomitus is seen, then intestinal obstruction must be suspected. If the hernia is not reduced, the blood supply may be compromised leading to perforation and peritonitis. This process can occur within 2 hours, so the urgency to reduce a suspected incarcerated hernia is of the highest priority. If strangulation occurs, blood may occasionally be seen per rectum. Incarceration occurs more frequently with in the first 6 months of life. It becomes less common after 2nd year, and after 5 years of age is relatively rare. Occasionally patient presents with symptoms of intestinal obstruction without a history of an inguinal hernia. Infancy is the most common time for this to occur. All pediatric patients with intestinal obstruction, regardless of age, should be examined for an incarcerated

hernia. A small groin hernia in an overweight baby may be overlooked easily.

With the child in supine position and undressed, the examiner observes for inguinal asymmetry or an obvious mass. If no visible mass is seen, the older child should be allowed to cry or strain, frequently despite increasing intra-abdominal pressure, a mass may not be demonstrated. In this situation, the cord is palpated to determine the thickening – the silk glove sign. This sign, although suggestive of a hernia, is unreliable. An exaggerated cremasteric reflex will produce a groin swelling that may be mistaken for a hernia. It is, therefore important that both testicles are examined and are demonstrated to be within the scrotum when the groin swelling is demonstrated.

In females, the incidence of incarceration is higher, but the incidence of strangulation is lower. This is owing to the fact that in females it is the ovary, not the intestine that incarcerates most frequently. The ovary, unlike the air filled intestines, is a solid organ that swells when it becomes incarcerated. Although this swelling of a solid organ makes the ovary more difficult to reduce, the blood supply to the ovary is not usually compromised. An incarcerated ovary which is not tender or mobile is an urgent but not emergent problem.

If incarceration has occurred, the child may be dehydrated if repeated vomiting has occurred, and an elongated mass can be felt along the inguinal canal. This mass is exquisitely tender and may be associated with edema of the surrounding tissue. If intestinal obstruction has occurred, although rare, abdominal distension/hyperactive bowel sounds may be noticed. If bowel strangulation has occurred the child will become toxic; if peritonitis is present, there will be abdominal tenderness with involuntary guarding.

Different types of indirect inguinal hernias are:

- a) Bubonocoele - Where hernia is limited to the inguinal canal.
- b) Funicular - hernia extends into the scrotum and upto the upper pole of the testis.
- c) Complete - where hernia completely surrounds the testis.

DIFFERENTIAL DIAGNOSIS

A hydrocele is differentiated from a hernia by the ability to palpate above the mass and not feel continuity between the scrotal hydrocele and the inguinal canal at the level of the internal ring. An incarcerated hernia may be mistaken for a tense hydrocele especially in the neonate. However, if the diagnosis is that of a hydrocele, there will be no history of reducibility and no associated symptoms. The swelling is translucent, smooth and usually non-tender. Occasionally

an acute hydrocele of the cord cannot be differentiated clinically from an incarcerated inguinal hernia, and surgery is required. A transilluminated mass does not rule out an incarcerated hernia.^[3]

Torsion of the testis may also be misdiagnosed as an inguinal hernia. This may occur without any previous history of groin swelling, or may associate with a history of undescended testis. In case of torsion of testis, there is acute, severe pain with vomiting and the tender mass in the inguinoscrotal region does not extend through the internal ring in to the inguinal canal. Torsion of appendix testis usually present with acute scrotal pain. On examination, there will be no evidence of an inguinal hernia in the inguinal canal or scrotum, and the testis itself may not be tender; a tender, blue nodule will be present at the upper pole of the testis.

Inguinal lymph nodes, although lateral and inferior to the inguinal canal, may often be mistaken for an incarcerated hernia. This is especially true in the female, since a lymph node's size and consistency are similar to that of an ovary. There is usually evidence of recent infection in the area of lymphatic drainage, and the nodes are tender and fixed.

In children, femoral hernia, although rare, and direct inguinal hernias, even rarer, must also be looked for. These hernias tend to be large and do not descend in to the scrotum. Although very infrequently demonstrated, direct hernias are associated with Extrophy of the bladder and other anomalies. They tend not to incarcerate.

RADIOLOGICAL INVESTIGATION

The diagnosis of an inguinal hernia can be usually be made on the basis of the clinical history and examination. However, there are a few patients who have histories suggestive of a hernia, but do not have a convincing physical examinations. In these situations, several surgeons have recommended herniography, although this remains controversial. Water soluble radiopaque contrast media is injected in to the peritoneal cavity via an infraumbilical injection. Radiographs of the inguinal regions, taken at 5, 10 and 45 minutes apart will demonstrate contrast in the hernia sac or hydrocele if present. However, it is of no value for detecting an incarcerated hernia, since the neck of the sac is plugged with a loop of bowel, preventing contrast from entering the sac. Complications include intramural intestinal hematoma, intestinal perforation, and adverse reaction to the contrast media. It should not be used routinely to simply rule out the presence of a hernia or determine the presence of contralateral hernia. As such, the decision to order a herniogram should be left to the pediatric surgeon.^[5]

HYDROCELE

Hydrocele is an abnormal collection of serous fluid in the layers of the tunica vaginalis, the persistently patent processus vaginalis surrounding the testis.^[10] About 5 percent of inguinal hernias are associated with a vaginal hydrocele on the same side.

Hydrocele are common in infants. Most infant hydroceles (perhaps 90%) will spontaneously subside owing to ongoing changes in the processus. Although hernias and hydroceles co-exist, only a confident diagnosis of hernia requires early surgical intervention. Some hydroceles persist beyond infancy and some occur for the first time later in childhood, these hydroceles do requires an operative procedure.

Different types of hydrocele are:

- a) Communicating (congenital)
 - A patent processus vaginalis flow of peritoneal fluid in to the scrotum.
 - Indirect inguinal hernias are associated with this type.
- b) Non communicating
 - There is a patent processus vaginalis but no peritoneal cavity communication.
- c) Hydrocele of the cord
 - The closure of tunica vaginalis is defective. Distal end of the processus vaginalis closes correctly, but the mid portion remains patent. Proximal end may be open or closed.

On examination, a nontender, cystic swelling of the scrotum, which surrounds the testicle and is able to be transilluminated, is evident. A word of caution: simple Transillumination does not exclude the diagnosis of an incarcerated hernia. It is usually possible to palpate the spermatic cord above the hydrocele. However, this may be difficult in the case of a hydrocele of the cord, which may extend from the scrotum or in the inguinal canal.

In the majority of infants, there is no indication for surgery within the first 12 to 24 months of age, as hydroceles not associated with inguinal hernias tend to resolve spontaneously during this time; the parents should be reassured and advised to observe the child over the ensuing months. A hydrocele that persist beyond 2 years of age, those that do not become apparent until the child is several years old, or those associated with an inguinal hernia require operations. The operation performed is high ligation of the patent processus vaginalis, the same procedure as that performed for inguinal hernia repair. Under no circumstances should a hydrocele be aspirated.

OTHER CAUSES OF INGUINO-SCROTAL SWELLINGS

Encysted hydrocele of the cord, Varicocele, Lymph varix, Funiculitis, Diffuse lipoma of the cord, Inflammatory thickening of the cord extending upwards from the testis and epididymis, Testicular malignancy, Ectopic testis, Undescended testis, Torsion of the testis, Retractable testis, Enlarged lymph nodes, Abscess in inguinal region, Aneurysm of external iliac artery

MANAGEMENT

Inguinal hernia are not known to resolve spontaneously and must therefore is repaired surgically shortly after diagnosis on an elective basis; the definitive treatment for inguinal hernia is early operation, a herniotomy. That can be open or laparoscopic. This will reduce the risk of incarceration with its attendant complication, such as obstruction and strangulation. While congenital hydrocele is known to resolve spontaneously, one can wait till one year of age. If hydrocele persist beyond 1 year or if it is very large and rapidly increasing in size then herniotomy is done.

OPERATIVE TECHNIQUE

The patient is placed in the supine position, and the skin is prepared with an iodophor solution from umbilicus to mid-thigh. Care is taken not to soak the underlying sheet, because thermoregulation is of special importance in small infants and children, who are placed on warming blanket.

OPEN HERNIOTOMY

The procedure involves a herniotomy through a transverse or oblique incision made in the lowest inguinal skin crease.

1. The incision is deepened through the camper's fascia, subcutaneous fat, and scarpa's fascia (in the process, one will encounter the superficial epigastric and the external pudendal vessels, which may be retracted aside, coagulated, or tied with suture) until the aponeurosis of the external oblique abdominal muscle is reached. After cleaning it of overlying fat, the external inguinal ring is identified.

In neonates and infants, the external inguinal ring almost overlies the internal inguinal ring, so there may not be the need to open the aponeurosis of the external oblique muscle to get to the hernia. In large hernias, it is advisable to incise the aponeurosis of the external oblique to open in to the inguinal canal before looking for the hernia sac. Here, too, one may decide to open the external oblique aponeurosis to include the external inguinal ring or not to include it in the incision.

2. The sac is normally found on the anteromedial aspect of the elements of the spermatic cord after bluntly

spreading the fibres of the cremasteric muscle; it is picked up with hemostats and dissected free of the cord, using both blunt and sharp dissection.

3. Once the sac is dissected up to the internal inguinal ring, it is opened and its content(s) replaced into the peritoneal cavity to make sure it is empty.

Where the sac is big and extends into the scrotum, no attempt should be made to dissect it completely into the scrotum. This will lead to unnecessary bleeding and hematoma formation postoperatively. Using sharp dissection and several hemostats (a minimum of 6), a large hernia sac can be circumferentially dissected, clamped, and amputated distally without having to follow it into scrotum.

4. The dissection is then continued proximally towards the internal inguinal ring until the pre peritoneal fat is visualized.
5. The sac is then twisted several times on itself to make sure the reduced content(s) stay in the peritoneal cavity out of harm's way and neck is then transfixated and ligated high up in the internal ring with Vicryl 3/0 and excess sac excised.

High ligation of the hernia sac is all that required. Sometimes, an enlarged internal inguinal ring is narrowed at the medial margin by placing one or two sutures through the transversalis fascia.

6. Hemostasis is secured and, where the aponeurosis was opened, it is approximated with Vicryl and the skin is closed with a suitable suture material. Usually one Vicryl 2/0 or 3/0 suture of 90cm in length is adequate enough to suture- ligate the sac, and close the aponeurosis and the skin. Especially if one uses the subcuticular method of closure.^[9]

LAPAROSCOPIC HERNIA SURGERY

Laparoscopic hernia surgery is performed with the patient under general anesthesia in supine position and a nasogastric tube and Foley or straight catheter in place.

A 5mm trocar is placed infraumbilical, and a pneumoperitoneum is established. A laparoscopic inspection is then performed. Bilateral or unusual hernias, such as femoral or direct hernias, are easily identified. Two 3-mm stab incision are made in the right and left lower quadrant s, respectively, allowing the trocarless introduction of 3-mm instruments. Placing the ports in this way allows both side to be addressed easily. A purse-string stitch is placed at the neck of the sac using a laparoscopic 3-mm needle driver. The cord structures are readily identified and excluded from the purse-string stitch. Once the stitch is placed, it is tied intracorporeally. The 3-mm ports do not require suture closure, and the umbilical port is closed with absorbable suture.

CONTRALATERAL EXPLORATION

Controversy continues among surgeons over the treatment of the contralateral processus vaginalis in the infant and child with a unilateral hernia. In an attempt to address this controversy, both the risk of contralateral inguinal exploration versus no exploration must be examined. The advantages of contralateral exploration include the avoidance of second anesthetic, early repair of an asymptomatic hernia, and avoidance of later incarceration or strangulation with risk to testis or intestine. The disadvantage of exploration include unnecessary surgery when negative and the potential risk of infection and injury to the testis and vas deferens. To minimize these risks a selective approach to contralateral inguinal exploration based on age, sex, sided presentation, incidence of patent processus vaginalis, the risk of incarceration is needed.

COMPLICATIONS

The complication rate for repair of inguinal hernias and hydrocele in children ranges from 1.7 to 8%. The wound infection rate is 1% to 2% and recurrence rate is less than 1%. Most recurrences are associated with comorbid condition and occur within 2 years of the original operation. Other factors predisposing to inguinal hernia recurrence include failure to ligate the sac high enough at the internal ring, Failure to repair the internal ring or canal floor injured at initial surgery, infection, incarceration requiring emergency surgery, and deferred Orchidopexy in infants with a concomitantly undescended testis.

Testicular complications associated with hernia and hydrocele repair may be more common than previously expected. Vas injury is recognized as a cause of subsequent infertility in the adult who underwent inguinal surgery as an infant or child. Testicular atrophy following hernia repair ranges from 0% to 19% and is much more common after emergency surgery for incarcerated hernia repair.^[4]

Inguinal hernia and hydrocele in pediatric age group has been studied worldwide. The present study has been contemplated to find out the age, sex, side wise distribution of inguinal hernia and hydrocele in children and also to document the patency of processus vaginalis, associated congenital anomalies and postoperative complications.

MATERIALS AND METHODS

Study Site

The patient was selected from those attending the Pediatric Surgery O.P.D. or admitted in the wards of K. J. Somaiya Hospital and Research Center, Sion, Mumbai (tertiary

care center).

Study Population

All consecutive male and female below 12 years of age with inguinoscrotal swellings satisfying the pro forma were selected.

Study Design

This study would be the prospective observational study.

Sample Size

The patient for the study was selected by simple random sampling with computer-generated random number in the below mentioned time period, including both males and females below the age of 12 years.

Using open EPI software with following information, the estimated sample size is 597 at 95% confidence level and 1.5% absolute precision 1%.

1. Population size - Number of children in the age group of 0–12 years eligible for the enrolment in study attending pediatric surgery O.P.D. during study duration approximately 1000.
2. Proportion of children having inguinoscrotal swelling attending O.P.D = 4%.^[3]
3. Absolute precision = 1%.

Study Period

This study was carried out from October 2014 to April 2016.

Inclusion criteria

Patients below 12 years of age including both males and females attending surgery O.P.D with swelling in inguinoscrotal region associated with symptoms as well as found accidentally on examination were included in the study.

Exclusion criteria

Patients with multiple congenital anomalies were excluded from the study.

Methodology

The study was conducted in the Department of Surgery, K.J. Somaiya Hospital and Research Center. The patients for the study were selected by simple random sampling with computer-generated random number from October 2014 to April 2016. All the selected patients were below 12 years including both males and females. It includes patients who attended pediatric surgery O.P.D and fitted in pro forma. All the registered patients were examined clinically thoroughly after taking a detailed history. Routine investigations such as CBC, PT, aPTT, routine urine examination, and chest X-ray were carried out for the fitness for operation. All the operations were carried out under general anesthesia.

Injection Amoxicillin + clavulanate (30–40 mg/kg) was given just before the incision. The operating field, i.e. from the level of umbilicus to mid-thigh was painted with 10% povidone-iodine solution. This was followed by sterile skin draping. Incision was made in the lowest skin crease in the groin approximately one finger above pubic tubercle on the same side of a hernia. The subcutaneous tissues were bluntly separated to expose the Scarpa's fascia, which was grasped and incised with scissors exposing oblique aponeurosis. After safeguarding the ilioinguinal nerve, the cremasteric muscle was separated on the anteromedial surface, thereby exposing the hernia sac, which was usually presented as a white and glistening membrane. The spermatic vessels and vas deference were bluntly teased off from the hernias sac. Hernial sac cut opened between two hemostats. The distal portion of hernia sac dissected up to the deep inguinal ring and completed when the neck of the sac was reached as indicated by the presence of pre-peritoneal fat. High ligation of the sac was done by twisting and transfixing the sac at the level of internal ring with 3–0 vicryl. The rest of the distal portion of the sac is excised. The proximal portion of the sac is cut open on the anterior aspect by safeguarding vas and vessels. Hemostasis checked. The testis was always replaced in the normal location.

In female patient, the hernia sac separated from the round ligament, cut open between two hemostats, dissected and transfixed at its neck. The hernia sac was always widely opened and inspected before twisting and ligating as the fimbriated end of fallopian tube was apt to be adherent to the neck of the sac.

In cases where the internal ring was wide enough, repair of the fascia transversalis was done with non-absorbable suture to narrow the deep ring.

In case of undescended testis, testis was brought down and placed in the scrotum by making a sub dartos pouch after separating the hernia sac, dissecting and lengthening vas and vessels.

In case of encysted hydrocele of the cord, above-mentioned herniotomy was done with excision of the cyst.

For congenital hydrocele, high ligation of patent processus vaginalis (PPV) at the deep ring was done, and the distal portion was kept slit open to prevent the collection of fluid.

The external oblique aponeurosis was sutured with 3–0 Vicryl and skin closed subcuticularly with 3–0 vicryl.

In case of laparoscopic herniotomy, a 5-mm trocar was placed infraumbilically, and a pneumoperitoneum was established. After then, laparoscopic inspection was

performed both deep inguinal rings, and the patency of processus vaginalis was identified. Two 3-mm stab incision was made in the right and left lower quadrants, respectively, allowing the trocarless introduction of 3-mm instruments. A purse-string stitch was placed at the neck of the sac using a laparoscopic 3-mm needle driver. The cord structures and testicular vessels were readily identified and excluded from the purse-string stitch. Once the stitch was placed, it was tied intracorporeally [Figure 12]. The 3-mm ports did not require suture closure, and the umbilical port was closed with port closure vicryl.

The patient was usually discharged from the hospital from the same day or 2nd day.

Post-operative follow-up of the cases was done after 1 week, 1 month, and 6 months from the date of operation.

Management

Inguinal hernia is not known to resolve spontaneously and must, therefore, be repaired surgically shortly after the diagnosis on an elective basis; the definitive treatment for inguinal hernia is early operation, a herniotomy, that can be open or laparoscopic. This will reduce the risk of incarceration with its attendant complication, such as obstruction and strangulation. While congenital hydrocele is known to resolve spontaneously, one can wait until 1 year of age. If hydrocele persists beyond 1 year or if it is very large and rapidly increasing in size, then herniotomy is done.

Operative Technique

The patient is placed in the supine position [Figure 8], and the skin is prepared with an iodophor solution from umbilicus to mid-thigh. Care is taken not to soak the underlying sheet because thermoregulation is of special importance in small infants and children, who are placed on warming blanket.

Open Herniotomy

The procedure involves a herniotomy through a transverse or oblique incision made in the lowest inguinal skin crease [Figure 9].

1. The incision is deepened through the Camper's fascia, subcutaneous fat, and Scarpa's fascia (in the process, one will encounter the superficial epigastric and the external pudendal vessels, which may be retracted aside, coagulated, or tied with suture) until the aponeurosis of the external oblique abdominal muscle is reached. After cleaning it of overlying fat, the external inguinal ring (EIR) is identified.

In neonates and infants, the EIR almost overlies the internal inguinal ring (IIR), so there may not be the need to open the aponeurosis of the external oblique muscle to

get to the hernia. In large hernias, it is advisable to incise the aponeurosis of the external oblique to open into the inguinal canal before looking for the hernia sac. Here, too, one may decide to open the external oblique aponeurosis to include the EIR or not to include it in the incision.

2. The sac is normally found on the anteromedial aspect of the elements of the spermatic cord after bluntly spreading the fibers of the cremasteric muscle; it is picked up with hemostats and dissected free of the cord, using both blunt and sharp dissection [Figure 10].
3. Once the sac is dissected up to the IIR, it is opened and its content(s) replaced into the peritoneal cavity to make sure it is empty.

Where the sac is big and extends into the scrotum, no attempt should be made to dissect completely into the scrotum. This will lead to unnecessary bleeding and hematoma formation postoperatively. Using sharp dissection and several hemostats (a minimum of 6), a large hernia sac can be circumferentially dissected, clamped, and amputated distally without having to follow it into the scrotum.

4. The dissection is then continued proximally toward the IIR until the preperitoneal fat is visualized.
5. The sac is then twisted several times on itself to make sure the reduced content(s) stay in the peritoneal cavity out of harm's way, and neck is then transfixed and ligated high up in the internal ring with vicryl 3/0 and excess sac excised.

High ligation of the hernia sac is all that required. Sometimes, an enlarged IIR is narrowed at the medial margin by placing one or two sutures through the transversalis fascia.

6. Hemostasis is secured and, where the aponeurosis was opened, it is approximated with Vicryl and the skin is closed with a suitable suture material. Usually one Vicryl 2/0 or 3/0 suture of 90cm in length is adequate enough to suture- ligate the sac, and close the aponeurosis and the skin. Especially if one uses the subcuticular method of closure.^[9]

Laparoscopic Hernia Surgery

Laparoscopic hernia surgery is performed with the patient under general anesthesia in the supine position and a nasogastric tube and Foley or straight catheter in place [Figure 9].

A 5-mm trocar is placed infraumbilical, and a pneumoperitoneum is established. A laparoscopic inspection is then performed [Figure 11]. Bilateral or unusual hernias, such as femoral or

direct hernias, are easily identified. Two 3-mm stab incision is made in the right and left lower quadrants, respectively, allowing the trocarless introduction of 3-mm instruments. Placing the ports in this way allows both sides to be addressed easily. A purse-string stitch is placed at the neck of the sac using a laparoscopic 3-mm needle driver. The cord structures are

readily identified and excluded from the purse-string stitch. Once the stitch is placed, it is tied intracorporeally [Figure 12]. The 3-mm ports do not require suture closure, and the umbilical port is closed with absorbable suture.

Contralateral Exploration

Controversy continues among surgeons over the treatment of the contralateral processus vaginalis in the infant and child with a unilateral hernia. In an attempt to address this controversy, both the risk of contralateral inguinal exploration and no exploration must be examined. The advantages of contralateral exploration include the avoidance of second anesthetic, early repair of an asymptomatic hernia, and avoidance of later incarceration or strangulation with risk to the testis or intestine. The disadvantage of exploration includes unnecessary surgery when negative and the potential risk of infection and injury to the testis and vas deferens. To minimize these risks of a selective approach to contralateral inguinal exploration based on age, sex, sided presentation, and incidence of PPV, the risk of incarceration is needed.

Complications

The complication rate for the repair of inguinal hernias and hydrocele in children ranges from 1.7% to 8%. The wound infection rate is 1–2% and the recurrence rate is <1%. Most recurrences are associated with comorbid condition



Figure 8: Skin crease incision



Figure 9: Dissection of sac



Figure 11: Intracorporeal sac ligation

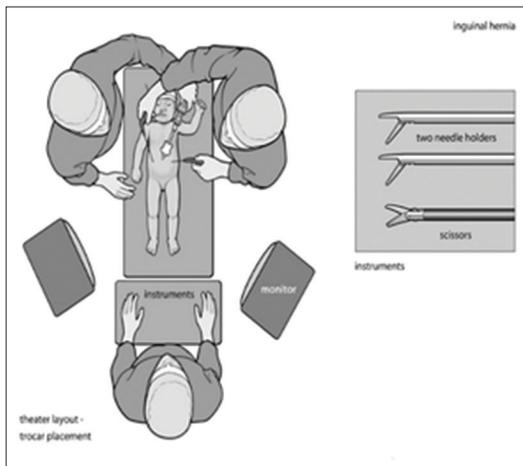


Figure 10: Laparoscopic herniotomy repair

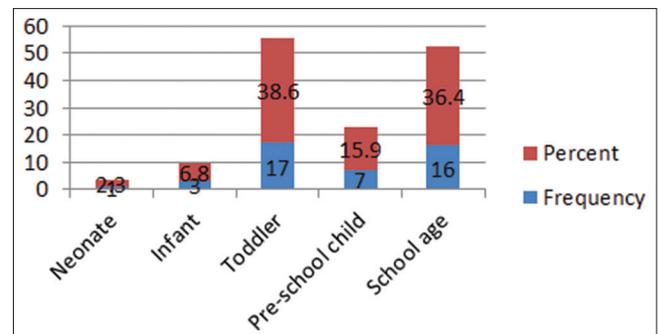


Figure 12: Age

and occur within 2 years of the original operation. Other factors predisposing to inguinal hernia recurrence include failure to ligate the sac high enough at the internal ring. Failure to repair the internal ring or canal floor injured at initial surgery, infection, incarceration requiring emergency surgery, and deferred orchidopexy in infants with a concomitantly undescended testis.

Testicular complications associated with a hernia and hydrocele repair may be more common than previously expected. Vas injury is recognized as a cause of subsequent infertility in the adult who underwent inguinal surgery as an infant or child. Testicular atrophy following hernia repair ranges from 0% to 19% and is much more common after emergency surgery for incarcerated hernia repair.^[4]

Inguinal hernia and hydrocele in the pediatric age group have been studied worldwide. The present study has been contemplated to find the age, sex, and sidewise distribution of inguinal hernia and hydrocele in children and also to document the patency of processus vaginalis, associated congenital anomalies, and post-operative complications.

RESULTS AND OBSERVATION

The present study was carried out in 44 children who were operated for an inguinal hernia and hydrocele at the Department of Surgery, K. J. Somaiya Hospital and Research Center, Mumbai, from October 2014 to April 2016. The initial diagnosis was made from history and clinical examination. The cases were followed up for a period of 12–52 weeks. All the operations were performed under general anesthesia. The operating time ranged from 25 min to 35 min for unilateral hernia, 40–45 min for bilateral hernia, and 45–50 min for laparoscopic herniotomy. The post-operative stay was 1–2 days.

Age Distribution

The age of the patient ranges from 0 to 12 years. They were divided into five groups. The maximum number of cases was in the toddler age group (38.6%) and the minimum number was in the age group of neonate (2.3%) [Figure 13 and Table 1].

Sex Distribution

In this study, 39 (88.6%) were males and 5 (11.4) were females, the ratio being 7.8:1 [Figure 14 and Table 2].

Birth History

In this study, 35 were term children and 9 were pre-term children [Figure 15 and Table 3].

Side Distribution

Among these cases, 26 cases were on the right side, 13 cases

were on the left side, and 5 cases were bilateral [Figure 16,17 and Table 4].

Swelling

Of all these cases, 34 cases presented with inguinal swelling, 6 were presented with scrotal swelling, and 4 were presented with inguinoscrotal swelling [Figure 18 and Table 5].

Diagnosis

In this study, 32 children diagnosed as inguinal hernia, 5 children as congenital hydrocele, 3 children as encysted hydrocele of cord, and 4 children as undescended testis [Figure 19 and Table 6].

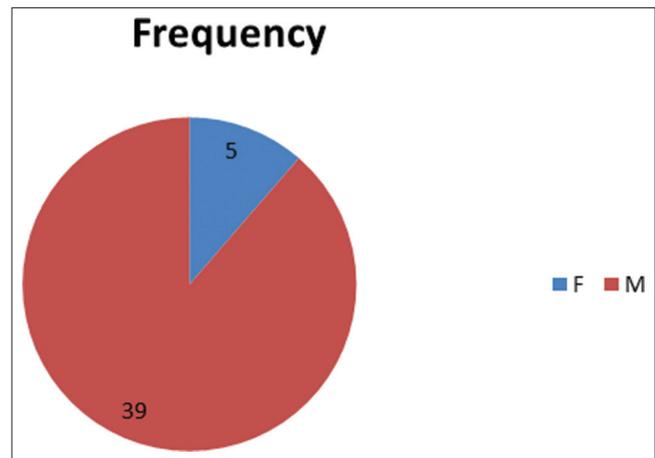


Figure 13: Sex distribution

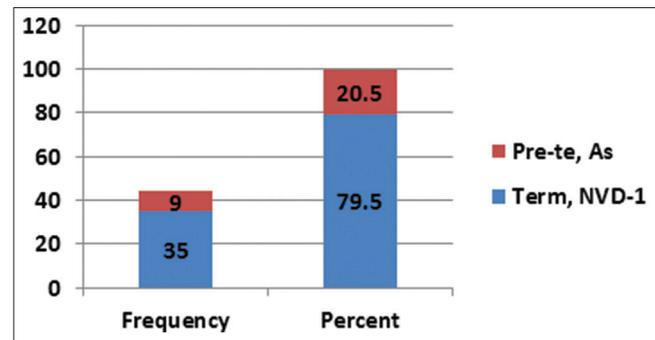


Figure 14: Birth history

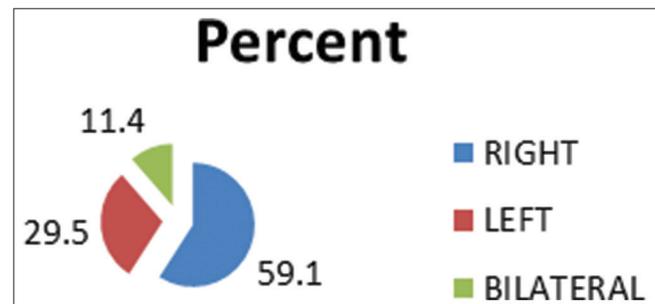


Figure 15: Side (%)

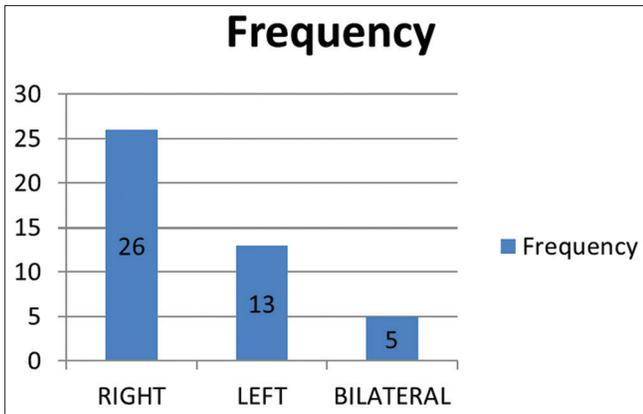


Figure 16: Side (frequency)

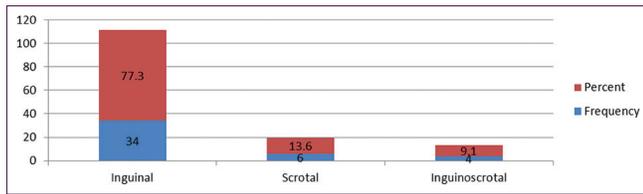


Figure 17: Swelling

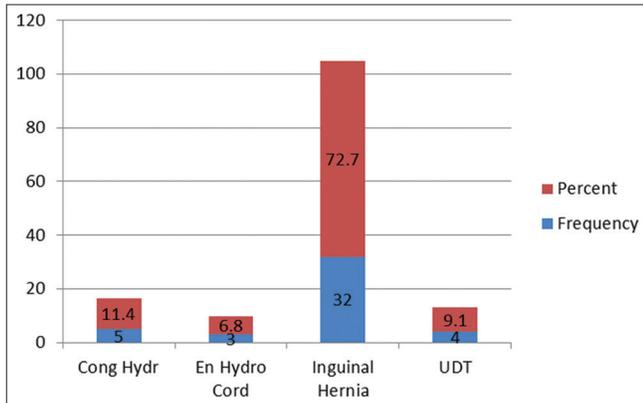


Figure 18: Diagnosis

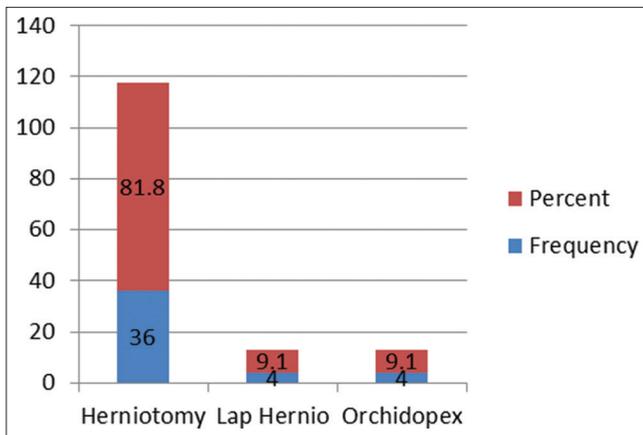


Figure 19: Procedure

Table 1: Age

Age	Frequency (%)
Neonate	1 (2.3)
Infant	3 (6.8)
Toddler	17 (38.6)
Pre-school child	7 (15.9)
School age	16 (36.4)
Total	44 (100.0)

Table 2: Sex

Sex	Frequency (%)
Female	5 (11.4)
Male	39 (88.6)
Total	44 (100.0)

Table 3: Birth history

Birth history	Frequency (%)
Term, NVD-1	35 (79.5)
Pre-test	9 (20.5)
Total	44 (100.0)

Table 4: Side

Side	Frequency (%)
Right	26 (59.1)
Left	13 (29.5)
Bilateral	5 (11.4)
Total	44 (100.0)

Table 5: Swelling

Swelling	Frequency (%)
Inguinal	34 (77.3)
Scrotal	6 (13.6)
Inguinoscrotal	4 (9.1)
Total	44 (100.0)

Table 6: Diagnosis

Diagnosis	Frequency (%)
Congenital hydrocoele	5 (11.4)
Encysted hydrocoele of the cord	3 (6.8)
Inguinal hernia	32 (72.7)
UDT	4 (9.1)
Total	44 (100.0)

UDT: Undescended testis

Operation Performed

Among these patients with inguinoscrotal swellings, 36 were undergone herniotomy, 4 were undergone laparoscopic herniotomy, and 4 were undergone orchiopexy [Table 7].

Table 7: Procedure

Procedure	Frequency (%)
Herniotomy	36 (81.8)
Lap hernio	4 (9.1)
Orchidopexy	4 (9.1)
Total	44 (100.0)

DISCUSSION

Today, inguinal hernia and hydrocele in children remain one of the most common congenital anomalies observed by pediatricians and surgeons requiring surgical intervention. In the general population, the incidence of inguinal hernia is not precisely known; however, in controlled population based studies, there are between 10 and 20 inguinal hernias per 1000 live births.^[5]

Age Distribution

Adesunkanmi AR^[35] *et al.* reported 71% of the inguinal hernia in a study of 208 children in the age group of 5 years and below and Charles M.R. *et al.*^[37] reported 71.6% of the inguinal hernia in a study of 133 children in the age group of below 6 years. Jadhav *et al.*^[64] found in their study of 50 children that 46% of cases were between 2 and 7 years. In the present study, the youngest patient was 20 days and oldest was 12 years old. The maximum number of patients was in the age group of between 0 and 5 years comprising >50% of the cases, and these findings show similar trend in the incidence of inguinal hernia when compared to the above-mentioned studies. Peak incidence of hernia in this study was in toddlers with 38.6%. Chang S.J. *et al.*^[63] reported that the peak incidence of inguinal hernia was at 0 years of age for males and 5 years of age for females. Jadhav *et al.*^[64] found in their study of 50 children that the maximum number of cases was in the age group of 2–3 years. On comparison of the findings of the foreign authors (Chang) with the present study, it was observed that >1/3rd of the cases were diagnosed to have inguinal hernia in the age of 1–3 years, but this age is slightly more with respect to the age of the patients in the above studies by a year. The reason for this could be better health care facilities, awareness among the parents to seek opinion early, and better reporting and documentation of the data. However, when these findings were compared to a study done in our country, it shows almost the same findings suggesting some geographical, above-mentioned factors, or yet unidentified factor contributing to this delay in the diagnosis probably increasing the risk of complications.

Sex Distribution

In all the studies of inguinal hernia in children, there is male preponderance. Rowe and Clatworthy^[19] reviewed 2764 children treated for inguinal hernia and found 87%

of the children to be boys, giving male-to-female ratio of 7:1. Powell T.G.^[25] in our study of 44 children with inguinal hernia and hydrocele, there were 39 males and 5 female female in the ratio of 9.2:1. Dinesh L. Jadhav *et al.*^[64], in a study of 50 children found male to female ratio of 11.5:1. In our study of 44 children with inguinal hernia and hydrocele, there were 39 males and 5 female.. The ratio being 7.8:1, William B Kiesewetter and Kook Sand^[21] studied 400 paediatric patient for inguinal hernia and hydrocele over a period of 2 years. In their study, 85% were male and 15% female. Adesunkanmi A.R.^[35] *et al.*, in a study of 208 children for inguinal hernia and hydrocele found that 197 (19.7%) of the cases to be male and only 11 (5.3%) to be female. In present study 88.6% were males and 11.8% were females. The findings of the above mentioned studies that inguino-scrotal swellings are found more commonly in male then female but the percentage varies according to study duration and geographical areas.

Side Distribution

Childhood inguinal hernias are generally more predominant on the right side, and this has been attributed to the delay in descent of the right testis. Hernias occurred bilaterally in 10–15% of the cases and in as many as 40–45% affect premature infants compared to 8–10% of the full term infants. Larsen and Tenn^[13] in a study of 111 cases of inguinal hernia in children found 60 cases on the right side, 39 cases on the left and 12 cases as bilateral. Muhammad T. Salaymeh^[17] studied 240 inguinal hernia in infants and children. He encountered 60% of the cases to be on the right side, 30% on the left and 10% bilateral. Rowe M. I. *et al.*^[18] documented the higher incidence of inguinal hernia on the right side. In their study of 2764 cases, 60% of the cases were on the right, 30% on the left and 10% were bilateral. William B. Kiesewetter and Kook Sang^[21] in a study of 400 paediatric patient for inguinal hernia over a period of 2 year found 64% to be on the right side, 26% on the left and 10% bilateral. Charles M.R. *et al.*^[37] found 61.6% on right side, 36.8% on left side and 1.5% bilateral. Dinesh L.J. *et al.*^[64] documented in a study of 50 children with inguinal hernia, 64% on right side, 28% on left side and 8% bilateral. In this study of 1 inguinal hernia in children up to 12 years of age, 26 cases were on right side, 13 cases were on the left and 5 cases were bilateral. On the basis of collected data the figure in the present study correlates well with other studies mentioned.

Associated Congenital Anomalies Included

Undescended testis

During the course of this study, four cases of undescended testis were detected. Two were on the right side and two were bilateral. All of them were situated in the superficial inguinal pouch. These patients underwent herniotomy at the time of orchidopexy, and the testis was placed in the subdartos pouch.

Encysted hydrocele of cord

There were three cases of encysted hydrocele of the cord, 1 on the right side and 2 were on the left side. All patient had undergone herniotomy.

Congenital hydrocele

There were five cases of congenital hydrocele, of which all were on the right side. All of them had high ligation at the deep ring while the distal portions were kept slit open. Willis J. Potts^[14] in a study of inguinal hernia in 600 children found hydrocele to be associated in 9% of the cases. Venugopal S.^[31] while treating 271 cases of inguinoscrotal hernias and hydrocele at the university hospital of West Indies found that 12.5% of the cases were hydroceles. Unlike the hernias, 20 of the 34 cases of hydrocele were on the left side..

Hypospadias

In this study, association of hypospadias was not observed.

In this study, 9 cases of inguinal hernia were found to be associated with prematurity and all of them were males. Boocock G.R.^[23] found 23 boys and 3 girls were below 36 weeks of gestation among 61 children who were operated for hernia at Liverpool Hospital in 1981. Davis N. *et al.*^[27] reviewed 85 cases of irreducible inguinal hernia in children below 2 years of age and found that 30 children had preterm delivery.

First Person to Notice the Swelling

In the present study of 44 cases, 36 swellings were noticed by parents, 5 by grandmother, and 3 by doctor. Parents are usually the first person to notice the swelling. Usually parents and grandmother notice the swelling while bathing the child or changing clothes. This could be because of the closeness of parents and grandmother to the child. In this series, three cases were detected while checking for immunization.

In this series, infants and children required general anesthesia for operative repair of inguinoscrotal swellings. Open herniotomy was done for 36 cases and laparoscopic herniotomy done was done for 4 cases.

Laparoscopic techniques

To improve the results and outcome of treatment, there have been a various modifications in the technique of laparoscopic inguinal hernia repair in children. This modification has done in the methods of ligation of the PPV at the IIR.

Various techniques

Extracorporeal suturing and knotting technique

This technique employs two-port and non-absorbable suture material. The trend is shifting toward this technique

because it is simple, safe, feasible, and reproducible. This method has low recurrence rates (0–2.0%), and more importantly, knotting does not require any special skill because it is done externally in the subcutaneous tissue in the conventional manner. The limitation of this technique is that special needles and introducers are required.

Intracorporeal suturing and knotting technique

The technique employs three ports and uses non-absorbable suture materials. Intraperitoneal knotting is performed to close the IIR in this technique. The closure is achieved by applying a suturing in purse-string fashion and knotting tight the IIR.

Inversion and ligation technique

This method of laparoscopic inguinal repair is widely used in female children. This is a modification of the intracorporeal technique, using three ports and non-absorbable sutures. In the inversion and ligation technique, the sac is isolated, inverted, and ligated laparoscopically.

Resection and ligation technique

This is another modification of the intracorporeal technique, with three ports and non-absorbable sutures employed. In this technique, the hernia sac is resected and closed with a purse-string suture at the level of the IIR.

Resection and no ligation technique

Here, the hernia sac is resected at the level of the internal inguinal and allowed to close spontaneously.

Flip-flap technique

In this procedure, a flip-flap is raised in the IIR and used to close the defect. This is a three-port technique that uses absorbable sutures.

Three-port or single-port technique

The pioneer procedures for inguinal hernia repair in children by laparoscopy used the three-port method. Recently, with refinements in technology, the single procedure is currently attracting attention.

Use of tissue adhesives

Today, tissue adhesive is being employed in a host of pediatric endoscopic surgeries, including inguinal hernia repair

In the present study, as per hospital setup, open herniotomy was most convenient. Yang *et al.*^[65] observed in his study that there was no significant difference between LH and OH in patients' age, sex, affected side, operative time for unilateral hernias, duration of hospital stay, time to resume full activity, recurrence, and complication. LH is superior to OH in the repair of bilateral inguinal hernia and low rate of metachronous contralateral hernia. The current trend

shows the preference for extracorporeal technique because it is simple, safe, reproducible and has low recurrent rates.^[47] The other trend is toward the single-port technique because it results in virtually scarless abdomen as the surgical incision is hidden within the umbilicus.^[66,67]

For congenital hydrocele, the procedure followed was high ligation of the PPV at the deep ring and keeping the distal portion slit open.

After unilateral herniotomy, the appearance of a hernia on the opposite side (metachronous presentation) occurred in two cases, and both were males and both were presented with left inguinal hernia. The time interval between initial herniotomy and appearance of the opposite hernia was 3 months in one case and 7 months in the other. Routine exploration of contralateral hernia is not preferred these days because the literature suggests that laparoscopically identified CPP is a poor indicator of future contralateral hernia. Almost a third of patients will have a CPP, while less than one in 10 will develop MCH when managed expectantly. Performing contralateral hernia repair in patients with CPP results in overtreatment in roughly 2 of 3 patients.^[64]

Zamakhshary M *et al.*^[48] found in his study of 1065 infants and children that a wait time for surgery of more than 14 days was associated with a doubling of the risk of hernia incarceration among infants and young children with inguinal hernia. But Chang S.J. *et al.*^[63] found in his study that incarceration was not associated with prematurity or waiting time for surgery. In this present study there was not even single case of incarceration or strangulation.

The postoperative complications comprised 1 case of wound haematoma, 1 case of wound infection. All of them responded to conservative treatment. Dinesh L. Jadhav *et al.*^[64] found 2 cases of wound infection and 2 cases of hypoglycemia in his study of 50 children. Lawrence R. Moss and Edwin I. Hatch^[28] in a study of 384 patients who underwent inguinal hernia repair during a 5 years period found 9 minor postoperative complications

Recurrent inguinal hernias are relatively uncommon. In general, the reported recurrence rate for uncomplicated hernia repair is 0–0.8%; this rises to about 15% for premature infants and about 20% after operation for incarcerated hernias.^[6] Factors associated with the recurrence are increased abdominal pressure, prematurity, malnutrition, anemia, and connective tissue disorder. Other causes of recurrence include a missed sac and injury to the floor of the inguinal canal resulting in a direct hernia. There was no recurrence during the period of one and half year study and follow-up for 12 weeks. Mestel *et al.*^[16]

stated that the repair of child's hernia is not a parlor piece, but a master's work should be performed or supervised by a skilled surgeon. Certainly, if recurrence is >1%, the surgeon should perhaps give up children's surgery or at the very least review.

Summary

This study was carried out in 44 children with inguinoscrotal swellings who were operated at the K. J. Somaiya Hospital And Research Center from October 2014 to April 2016. All the patients in the study were subjected to minimum investigation such as CBC, PT, aPTT, urine routine, and chest X-ray. The age of the patients varied from 0 to 12 years. The maximum number of cases was in toddler group (38.6%) and the minimum number of case was in the age group of neonate (2.3%). There were 39 males and 5 females, thereby giving ratio of 7.8:1. Of the 44 cases, 26 cases were on the right side, 13 cases were on the left side, and 5 cases were bilateral; prematurity was associated in 9 cases who were all males. 36 swellings were first noticed by parents, 5 were noticed by grandmother, and 3 cases were detected by doctors at routine checkup during immunization. Congenital anomalies such as undescended testis were associated with inguinal hernias in four cases. The two undescended testes were on the right side and two were bilateral. Orchidopexy done and the testis was kept in the subdartos pouch. Of 3 encysted hydrocele of the cord, two on the left side and one was on the right side. In the case of 5 hydroceles, all were on the right side. High ligation at the level of deep ring was done in all the cases. In this study, no case of associated hypospadias was encountered. Open herniotomy done for 36 cases and laparoscopic herniotomy done for 4 cases. For female patients, the hernia sac was always widely opened and inspected for the entrapment of ovary or other structures before twisting and ligating at its neck. The distal portion of the sac was cut open after incising the wall to prevent the collection of fluid. All 44 cases were operated as elective. None had incarceration, obstruction, or strangulation. The operating time ranged from 25 min to 35 min for unilateral hernia, 40 to 45 min for bilateral hernia, and 45 to 50 min for laparoscopic herniotomy. The period of post-operative stay ranged from 1 day to 2 days. The cases were followed up to 12–52 weeks. There were two minor post-operative complications which include one case of wound hematoma and one case of wound infection, all of them responded to conservative treatment. In this study of 44 cases during the period of 1½ years with follow-up of 12–52 weeks, there was no case of recurrence.

CONCLUSION

Inguinal hernia and hydrocele in children remain one

of the most common congenital anomalies observed by surgeons. The threat to loss of testis, ovary or a portion of bowel due to incarceration or strangulation remains. Prompt diagnosis and early treatment of the inguinal hernia continue to be the mainstay if these complications are to be avoided. As many hydrocele of the tunica vaginalis may involute spontaneously, hydroceles that do not change over time should be observed at least up to 1 year of age before considering repair. The childhood inguinal hernias are generally more predominant on the right side, and this has been attributed to the delay in descent of the right testis. Regarding the sex prevalence, males are more commonly affected. Congenital anomalies such as undescended testis and hypospadias can be associated with inguinal hernia and hydrocele. In the case of undescended testis, herniotomy is done at the time of orchidopexy. Parents are usually the first person to notice the swelling or bulge in the inguinal region when changing a diaper or bathing or while the child is crying or straining. An inguinal hernia will not resolve spontaneously and should be repaired as soon as possible after the diagnosis because of the risk of incarceration, obstruction, or strangulation. In general, infants and children require general anesthesia for the operative repair of inguinal hernia and hydrocele. Post-operative complications are usually rare following elective operation, whereas minor complication does occur after emergency operation. Recurrence is usually rare if operated by experienced surgeon. Inguinal herniotomy in children is safe and effective operation whether open or laparoscopic.

REFERENCES

- Leo N. Zimmarson: The History of Hernia Lloyd. 2nd ed. Philadelphia, PA: NYHUS Hernia; 2001. p. 1-13.
- Vidhyarthi K. Advances in Pediatrics. 2nd ed. New Delhi: Jaypee Brothers; 2012.
- Townsend CM Jr., Beauchamp RD, Evers MB, Mattox KL. Sabiston Textbook of Surgery: Expert Consult Premium Edition: Enhanced Online Features. 18th ed. New York: Elsevier Health Science; 2007.
- Skoog SJ, Conlin MJ. Pediatric hernias and hydroceles. The urologist's perspective. Urol Clin North Am 1995;22:119-30.
- Kapur P, Caty MG, Glick PL. Pediatric hernias and hydroceles. Pediatr Clin North Am 1998;45:773-89.
- Grosfeld JL, O'Neill JA, Fonkalsrud EW, Coran AG. Pediatric Surgery. 6th ed. Philadelphia, PA: Mosby Elsevier; 2006.
- Brandt ML. Pediatric hernias. Surg Clin North Am 2008;88:27-43.
- Ron O, Eaton S, Pierro A. Systematic review of the risk of developing a metachronous contralateral inguinal hernia in children. Br J Surg 2007;94:804-11.
- Ameh E, Bickler S, Lakhoo K, Nwomeh B, Poenaru D. Paediatric Surgery: A Comprehensive Text For Africa. Seattle: Global Health; 2010.
- Scherer 3rd LR, Grosfeld JL. Inguinal hernia and umbilical anomalies. Pediatr Clin North Am 1993;40:1121-31.
- Lennon TM, Russel LH. The radical cure of inguinal hernia in children. Br J Surg 1922;9:445-8.
- Herzfeld G. The radical cure of hernia in infants and young children. Edinburgh Med J 1925;32:281-90.
- Larsen RM. Inguinal hernia in infancy and early childhood. Surgery 1949;25:307-28.
- Potts WJ, Riker WL, Lewis JE. The treatment of inguinal hernia in infants and children. Ann Surg 1950;132:566.
- McLaughlin CW, Coe JD. Inguinal hernia in pediatric patients. Am J Surg 1960;99:45-7.
- Mestel AL, Turner HA. Recurrent inguinal hernia in infants and children. Int Surg 1966;45:575-8.
- Salaymeh MT. Complications of inguinal hernia in infants and children. Int Surg 1969;51:95-9.
- Rowe MI, Copelson LW, Clatworthy HW. The patent processus vaginalis and the inguinal hernia. J Pediatr Surg 1969;4:102-7.
- Rowe MI, Clatworthy HW. Incarcerated and strangulated hernias in children: A statistical study of high-risk factors. Arch Surg 1970;101:136-9.
- Palmer BV. Incarcerated inguinal hernia in children. Ann R Coll Surg Engl 1978;60:121.
- Kiesewetter WB, Oh KS. Unilateral inguinal hernias in children: What about the opposite side? Arch Surg 1980;115:1443.
- Viidik T, Marshall DG. Direct inguinal hernias in infancy and early childhood. J Pediatr Surg 1980;15:646-7.
- Boocock GR, Todd PJ. Inguinal hernias are common in preterm infants. Arch Disease Childhood 1985;60:669-70.
- Harvey MH, Johnstone MJ, Fossard DP. Inguinal herniotomy in children: A five year survey. Br J Surg 1985;72:485-7.
- Powell TG, Hallows JA, Cooke RW, Pharoah PO. Why do so many small infants develop an inguinal hernia? Arch Disease Childhood 1986;61:991-5.
- Campbell JR. Inguinal and scrotal problems in infants and children. Pediatr Ann 1989;18:189-91.
- Davies N, Najmaldin A, Burge DM. Irreducible inguinal hernia in children below two years of age. Br J Surg 1990;77:1291-2.
- Moss RL, Hatch EI. Inguinal hernia repair in early infancy. Am J Surg 1991;161:596-9.
- Grosfeld JL, Minnick K, Shedd F, West KW, Rescorla FJ, Vane DW. Inguinal hernia in children: factors affecting recurrence in 62 cases. J Pediatr Surg 1991;26:283-7.
- Gazayerli MM. Anatomical laparoscopic hernia repair of direct or indirect inguinal hernias using the transversalis fascia and iliopubic tract. Surg Laparosc Endosc Percutan Tech 1992;2:49-52.
- Venugopal S. Inguinal hernia in children. West Indian Med J 1993;42:24-6.
- Surana R, Puri P. Is contralateral exploration necessary in infants with unilateral inguinal hernia? J Pediatr Surg 1993;28:1026-7.
- Sarin YK, Wakhlu A, Agarwal LD, Sharma AK. Inguinal herniotomy in children: A decade's experience. Indian Pediatr 1993;30:1363-6.
- Misra D, Hewitt G, Potts SR, Brown S, Boston VE. Inguinal herniotomy in young infants, with emphasis on premature neonates. J Pediatr Surg 1994;29:1496-8.
- Adesunkanmi AR, Adejuyigbe O, Agbakwuru EA. Prognostic factors in childhood inguinal hernia at Wesley Guild Hospital, Ilesa, Nigeria. East Afr Med J 1999;76:144-7.
- Ameh EA. Incarcerated and strangulated inguinal hernias in children in Zaria, Nigeria. East Afr Med J 1999;76:499-501.
- Charles MR, Christian LB, Sen T, Mahapatra S, Joshi BR. A two year retrospective study of congenital inguinal hernia at western regional hospital. J Nepal Med Assoc 2000;39:172-5.
- Schier F, Danzer E, Bondartschuk M. Incidence of contralateral patent processus vaginalis in children with inguinal hernia. J Pediatr Surg 2001;36:1561-3.
- Bonnard A, Aigrain Y. Inguinal hernias in children. Rev Prat 2003;53:1667-70.
- Nyhus LM. The posterior (preperitoneal) approach and iliopubic tract repair of inguinal and femoral hernias—an update. Hernia 2003;7:63-7.
- Abantanga FA. Groin and scrotal swellings in children aged 5 years and below: A review of 535 cases. Pediatr Surg Int 2003;19:446-50.
- Toki A, Watanabe Y, Sasaki K, Tani M, Ogura K, Wang ZQ. Adopt a wait-and-see attitude for patent processus vaginalis in neonates. J Pediatr Surg 2003;38:1371-3.
- Oak S, Parelkar S, Agarwal P, Sailukar M, Gera P, Pathak R, *et al.* Laparoscopic surgery of inguinal hernia in children—experience with 110 repairs. Indian J Surg 2004;66:70.
- Hata S, Takahashi Y, Nakamura T, Suzuki R, Kitada M, Shimano T. Preoperative sonographic evaluation is a useful method of detecting

- contralateral patent processus vaginalis in pediatric patients with unilateral inguinal hernia. *J Pediatr Surg* 2004;39:1396-9.
45. Ozgediz D, Roayaie K, Lee H, Nobuhara KK, Farmer DL, Bratton B, *et al.* Subcutaneous endoscopically assisted ligation (SEAL) of the internal ring for repair of inguinal hernias in children: Report of a new technique and early results. *Surg Endoscopy* 2007;21:1327-31.
 46. Han YJ, Nam SH, Kim DY, Kim SC, Kim IK. Contralateral incidence of pediatric inguinal hernia and hydrocele after unilateral operation. *J Korean Assoc Pediatr Surg* 2008;14:48-57.
 47. Bharathi RS, Arora M, Baskaran V. Pediatric inguinal hernia: Laparoscopic versus open surgery. *JSLs* 2008;12:277-81.
 48. Zamakhshary M, To T, Guan J, Langer JC. Risk of incarceration of inguinal hernia among infants and young children awaiting elective surgery. *Canadian Med Assoc J* 2008;179:1001-5.
 49. Vogels HD, Bruijnen CJ, Beasley SW. Predictors of recurrence after inguinal herniotomy in boys. *Pediatr Surg Int* 2009;25:235-8.
 50. Vaos G, Gardikis S, Kambouri K, Sigalas I, Kourakis G, Petoussis G. Optimal timing for repair of an inguinal hernia in premature infants. *Pediatr Surg Int* 2010;26:379-85.
 51. Gholoum S, Baird R, Laberge JM, Puligandla PS. Incarceration rates in pediatric inguinal hernia: Do not trust the coding. *J Pediatr Surg* 2010;45:1007-11.
 52. Mirilas P, Mentessidou A, Kontis E, Argyris I, Tsitouridis I, Petropoulos A. Sonographic evidence for patency of the processus vaginalis in children with acquired undescended testis. *Int J Androl* 2011;34:49-54.
 53. Lautz TB, Raval MV, Reynolds M. Does timing matter? A national perspective on the risk of incarceration in premature neonates with inguinal hernia. *J Pediatr* 2011;158:573-7.
 54. Karabulut B. One surgeon experiences in childhood inguinal hernias. *J Korean Surg Soc* 2011;81:50-3.
 55. Choi YM, Lee GM, Yi JB, Yoon KL, Shim KS, Bae CW, *et al.* Two cases of female hydrocele of the canal of Nuck. *Korean J Pediatr* 2012;55:143-6.
 56. Kumar A, Ramakrishnan TS. Single port laparoscopic repair of paediatric inguinal hernias: Our experience at a secondary care centre. *J Minim Access Surg* 2013;9:7.
 57. Pant N, Aggarwal SK, Ratan SK. Laparoscopic repair of hernia in children: Comparison between ligation and nonligation of sac. *J Indian Assoc Pediatr Surg* 2014;19:76.
 58. Kokorowski PJ, Wang HH, Routh JC, Hubert KC, Nelson CP. Evaluation of the contralateral inguinal ring in clinically unilateral inguinal hernia: A systematic review and meta-analysis. *Hernia* 2014;18:311-24.
 59. Ibrahim MM. Two ports laparoscopic inguinal hernia repair in children. *Minim Invasive Surg* 2015;2015:1-5.
 60. Rafiei MH, Jazini A. Is the ligation of hernial sac necessary in herniotomy for children? A randomized controlled trial of evaluating surgical complications and duration. *Adv Biomed Res* 2015;4:97.
 61. Ibrahim M, Abdussalam US, Getso KI, Mohammad MA, Chukwuemeka AL, Owolabi FL, *et al.* Open inguinal herniotomy: Analysis of variations. *Afr J Paediatr Surg* 2015;12:131.
 62. Feng S, Zhao L, Liao Z, Chen X. Open versus laparoscopic inguinal herniotomy in children: A systematic review and meta-analysis focusing on postoperative complications. *Surg Laparosc Endosc Percutan Tech* 2015;25:275-80.
 63. Chang SJ, Chen JC, Hsu CK, Chuang FC, Yang SD. The incidence of inguinal hernia and associated risk factors of incarceration in pediatric inguinal hernia: a nation-wide longitudinal population-based study. *Hernia* 2015;2015:1-5.
 64. Jadhav DL, Manjunath L, Vikas G, Krnishnamurthy, *et al.* A study of inguinal hernia in children. *Int J Sci Res* 2014;12:2149-55.
 65. Yang C, Zhang H, Pu J, Mei H, Zheng L, Tong Q. Laparoscopic vs open herniorrhaphy in the management of pediatric inguinal hernia: A systemic review and meta-analysis. *J Pediatr Surg* 2011;46:1824-34.
 66. Rothenberg SS, Shipman K, Yoder S. Experience with modified single-port laparoscopic procedures in children. *J Laparoendosc Adv Surg Tech* 2009;19:695-8.
 67. Chang YT. Technical refinements in single-port laparoscopic surgery of inguinal hernia in infants and children. *Diagn Ther Endosc* 2010;2010:392847.

How to cite this article: Verma R, Vaja C, Anand S, Gaikwad K, Tripathi A, Narvekar R. A Clinical Study of the Different Types of Inguinoscrotal Swellings and Their Management in a Tertiary Care Referral Center. *Int J Sci Stud* 2018;6(5):1-5.

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

A Rare Case of Leiomyosarcoma with Hemoperitoneum in Pregnancy

Ragini Agrawal¹, Pallavi Vasal², Bijal Bhati³, Charu Dutt Arora⁴

¹Head of Department, ²Consultant, ³Senior Resident, Department of Obstetrics and Gynecology, W Pratiksha Hospital, Gurgaon, Haryana, India, ⁴Clinical Associate, Department of Critical Care Medicine, W Pratiksha Hospital, Gurgaon, Haryana, India

Abstract

Uterine leiomyosarcoma during pregnancy is an extremely rare event. We report a retrospectively diagnosed case of a ruptured primary uterine leiomyosarcoma with hemoperitoneum diagnosed during pregnancy. The patient came to the emergency room (unbooked with us, taking treatment at the other hospital) with G4P1A2L0 with GDM + pregnancy-induced hypertension (PIH) and ultrasonography (USG) diagnosed large fibroid with degeneration (19 cm × 13.2 cm × 13.2 cm) at 30.5 weeks of gestation, breech presentation with complaints of pain in abdomen and vomiting. An initial conservative treatment was started considering prematurity with fibroid degeneration. Due to severe pain in abdomen and history of PIH, USG was repeated after 2 days of admission which showed hemoperitoneum, so the decision for emergency preterm LSCS was taken. During cesarean section, a ruptured sessile uterine fibroid was removed and hemoperitoneum was drained. Histopathological diagnosis of the tumor revealed a poorly differentiated uterine leiomyosarcoma. The patient underwent laparotomy after weeks with radical hysterectomy and received adjuvant chemotherapy. The diagnosis and suspicion for leiomyosarcoma during pregnancy at young age stand difficult, and the treatment options seem to be reduced in pregnant women and are mainly dependent on the patient's condition as well as the gestational age at the time of presentation.

Key words: Degenerated fibroid, Hemoperitoneum, Leiomyosarcoma, Pregnancy, Radical hysterectomy

INTRODUCTION

Uterine leiomyosarcomas (LMS) are rare, highly malignant neoplasms that make up about 1% of all uterine malignancies.^[1] The risk of local recurrence and metastasis is high, with reported 5-year survival rates ranging between 12% and 25%. The median age for women with LMS is after childbearing age (between 43 and 53 years). Total abdominal hysterectomy and bilateral salpingo-oophorectomy are considered the standard therapy for LMS of the uterus.^[2,3] The role of conservative fertility-sparing surgery in young women remains controversial.^[4] Uterine LMS associated with pregnancy is even rarer and only a few cases are reported in the literature.^[4-6] Here, we report a case of a patient with retrospectively diagnosed uterine LMS during the third trimester of pregnancy.

CASE REPORT

The patient came to the ER with G4P1A2L0 with GDM and ultrasonography (USG) diagnosed large degenerated fibroid at 30.5 weeks of gestation with breech presentation with pain in abdomen and vomiting associated with pregnancy-induced hypertension (PIH). The patient came to us for the first visit, previously taking treatment at other hospitals. On taking detailed history, the patient was G4P1A2L0 at 30.5 weeks:

LMP: 16/12/16, EDD: 23/9/17.

Obstetric history was as follows:

- G1: Missed abortion at 10 weeks followed by D and C 10 years back.
- G2: Preterm vaginal delivery at 6 months, 7 years back and the baby died after 4 days.
- G3: Missed abortion at 10 weeks f/b D and C, 6 years back.
- G4: Present pregnancy, spontaneous conception.

Medical history: The patient was diagnosed with GDM in the second trimester on tablet metformin 500 mg thrice daily

Access this article online



www.ijss-sn.com

Month of Submission : 06-0000
Month of Peer Review : 07-0000
Month of Acceptance : 08-0000
Month of Publishing : 08-0000

Corresponding Author: Dr Charu Dutt Arora, Department of Critical Care Medicine, 2nd floor, C block, W Pratiksha Hospital, Gurugram, India. E-mail: charu.dutt@w-hospital.in

(controlled blood sugar levels). Diagnosed with PIH 2 days back was on tablet labetalol 200 mg thrice daily for 2 days. The patient was given antenatal steroid coverage 2 days back.

There was no significant family history.

On admission, the patient was conscious and oriented, afebrile, pulse rate was 84/min, blood pressure (BP) 160/80 mmHg; on P/A examination, uterus size was 34 weeks, relaxed, fibroid was palpable separately and slightly tender. Gentle P/S showed os closed, no discharge.

Initially, conservative management was planned in view of PIH + GDM and prematurity. The patient was given injectable labetalol for uncontrolled PIH, injection PCM, and injection Rantac/Emset. USG was done on admission which showed: Single live intrauterine pregnancy of 31.2 weeks maturity, breech presentation, EBW: Approximately 1.79 kg, anterior placenta, normal Doppler findings, and a large subserosal/intramural fibroid of 19 cm × 13.2 cm × 13.2 cm. Laboratory investigation showed - serum glutamic oxaloacetic transaminase: 18, lactate dehydrogenase: 196, serum glutamate-pyruvate transaminase: 15, CREAT: 0.4, uric acid: 6.1, HB: 10.1 g%, and blood group: O positive. Blood sugar charting was done and was managed along with the physician; insulin was started.

Pain and vomiting were controlled for 1 day, but dull aching pain was still persistent. After 2 days of admission, the pain aggravated and not relieving with IV painkillers and repeat PIH profile showed deranged coagulation profile, altered liver function tests, raised urine ketone bodies, and unstable blood sugar and BP. USG was done which showed live intrauterine fetus with hemoperitoneum. The patient was reviewed by physician and anesthetist and was taken for emergency LSCS under general anesthesia. She delivered male baby weighing 1.6 kg breech footling presentation with meconium stained liquor. Baby admitted in NICU for 3 weeks and discharged in healthy condition.

The intraoperative findings are as follows:

1. After opening abdomen in layers, parietal peritoneum was visualized and blood shown in the peritoneal cavity. Dark red blood presents in the cavity on opening the peritoneum suggestive of hemoperitoneum. Approximately: 2500 mL of blood was suctioned out.
2. Baby was delivered and uterus sutured. Uterus was bulky and exteriorized. Small 3 cm × 2 cm sessile subserosal fibroid shown on posterolateral side of uterus. A tear was visualized just below the right tuboovarian ligament and extending laterally toward the broad ligament. Large uterine fibroid with degenerative material and clots was coming out. Around 1 L/1 kg of fleshy pieces removed.

3. All the degenerative tissue manually removed by finger manipulation into the tear which was going deep posteriorly to the uterus. Clots of dark blood and degenerative fibroid found lying in the peritoneum, which were removed manually. Degenerated tissue removed to a great extent.
4. Right tube and ovary were very edematous. Tear in the right mesosalpinx and near ampulla of the right fallopian tube shown which was sutured. The left tube and ovary, omentum appeared normal. Hemostasis was achieved and specimen was sent for HPE. The patient was transfused 3 units PRBC and 2 units FFP and was closely monitored in ICU for 24 h with iv fluids, higher antibiotics and hemostatics with DVT pump.

The only positive finding in the USG performed on day 4 post operatively was borderline hepatosplenomegaly. Postpartum bulky uterus with subserosal fibroid with 8.4 cm × 8.4 cm × 8.4 cm visualized. The patient was discharged on 4th post-operative day in stable condition.

Histopathological diagnosis of the tumor revealed undifferentiated malignant neoplasm. Microscopic findings showed: Grayish-brown soft to firm tissue shows highly cellular neoplasm arranged in sheets comprising moderately pleomorphic round-to-oval cells, coarse chromatin, moderate amount of cytoplasm, and indistinct nucleoli. Fair number of mitosis and necrosis is also shown. Perivascular arrangement of tumor cells is also shown.

After the HPE report, the patient and attendant were thoroughly explained and counseled about the condition and were referred to oncology center, where the patient was investigated thoroughly and underwent laparotomy with radical hysterectomy and received adjuvant chemotherapy.

DISCUSSION

All reported cases of uterine LMS associated with pregnancy were found incidentally in pregnancy. Kyodo *et al.* reported the only case in which they had observed the progress of the tumor during pregnancy.^[5] Similarly, the diagnosis of our patient was made histopathologically after operation. The fibroid was detected at the beginning of pregnancy and follow-ups with ultrasound examinations were performed. Neither any progress nor any clinically suspicious indications could be detected during pregnancy, and therefore, the tumor was mistakenly diagnosed as degenerating leiomyoma. As the fibroid was ruptured, with hemoperitoneum and tissues spread in the peritoneal cavity, attempt to remove maximum tissue with homeostasis, and drainage of hemoperitoneum during C/S was done. The indication for elective C/S at 31 weeks of pregnancy was

uncontrolled pain in abdomen and USG showing significant hemoperitoneum, which was alarming. Tumor growth during pregnancy is not unusual and has been demonstrated for uterine leiomyoma as a result of high estrogen and progesterone levels. In our patient, progression in size was documented during serial antenatal scans. The appropriate management of uterine LMS in pregnancy remains unclear. Since the patients are of a childbearing age, there is a desire to conserve fertility if possible. Uterine LMS is generally considered to be more aggressive than other types of uterine tumor and is well known for its frequent recurrence and resistance to chemotherapy. Therefore, an aggressive surgical procedure is usually considered to be the treatment of choice at the time of diagnosis.^[1] Our patient underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy, omentectomy, and paraaortal lymphadenectomy 6 weeks after CS. A total of 6 adjuvant chemotherapy cycles were given at an outside tertiary care center. The diagnosis of uterine LMS was made in the end third trimester and the pregnancy was not influenced by the disease. A case-control study in Iowa, USA, examined the effect of parity and age at first birth on the risk for various types of carcinomas treatment generally consists of surgical resection. In our patient, conservative management was possible for 3 days to allow fetal lung maturation, and

at the end of 31.3 weeks of gestation, an emergency C/S was performed.

In conclusion, we describe an extremely rare case of uterine leiomyosarcoma with rupture and hemoperitoneum in pregnancy. Treatment options seem to be reduced in pregnant women and mainly depend on the patient's condition as well as on the gestational age at presentation. In a multidisciplinary approach, an optimal therapy schedule should be assessed depending on the conditions.

REFERENCES

1. Zaloudek CJ, Norris HJ. Mesenchymal tumors of the uterus. In: Kurman RJ, editor. *Blaustein's Pathology of the Female Genital Tract*. New York: Springer-Verlag; 1994. p. 849-914.
2. Bell SW, Kempson RL, Hendrickson MR. Problematic uterine smooth muscle neoplasms. A clinicopathologic study of 213 cases. *Am J Surg Pathol* 1994;18:535-58.
3. Barter JF, Smith EB, Szpak CA, Hinshaw W, Clarke-Pearson DL, Creasman WT, *et al.* Leiomyosarcoma of the uterus: Clinicopathologic study of 21 cases. *Gynecol Oncol* 1985;21:220-7.
4. Lau TK, Wong WS. Uterine leiomyosarcoma associated with pregnancy: Report of two cases. *Gynecol Oncol* 1994;53:245-7.
5. Kyodo Y, Inatomi K, Abe T. Sarcoma associated with pregnancy. *Am J Obstet Gynecol* 1989;161:94-6.
6. Schiavone MB, Smok D, Wright TC, Wright JD. High-grade uterine sarcoma during pregnancy. *Gynecol Oncol* 2011;123:424-5.

How to cite this article: Agrawal R, Vasal P, Bhati B, Arora CD. A Rare Case of Leiomyosarcoma with Hemoperitoneum in Pregnancy. *J Sci Stud* 2018;6(5):1-3.

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