



# **MEDICAL FORUM MONTHLY**

**APNS  
Member**

**CPNE  
Member**

**ABC  
Certified**

**RECOGNISED BY PMDC**

*Journal of all Specialties*

**“Medical Forum” Monthly Recognised and Indexed by**

- ☞ PMDC with Index Pakistan No. 48 Since 1998
- ☞ Pakmedinet Since 2011
- ☞ Medlip (CPSP) Since 2000
- ☞ PASTIC & PSA Since 2000
- ☞ NLP Since 2000
- ☞ WHO, Index Medicus (IMEMR) Since 1997
- ☞ EXCERPTA MEDICA, Netherlands Since 2000
- ☞ EMBASE SCOPUS Database Since 2008
- ☞ Registered with International Serials Data System of France bearing ISSN No. 1029-385X Since 1992
- ☞ Registered with Press Registrar Govt. of Pak bearing No. 1221-B Copr. Since 2009
- ☞ ABC Certification Since 1992
- ☞ On Central Media List Since 1995
- ☞ Med. Forum Published from Lahore Since 1989
- ☞ Peer Review & Online Journal
- ☞ Electronic Publication of Journal Now Available on website: [www.medforum.pk](http://www.medforum.pk)

# MEDICAL FORUM MONTHLY

ISSN 1029 - 385 X (Print)

ISSN 2519 - 7134 (Online)

APNS  
MemberCPNE  
MemberABC  
Certified

Peer Review Journal

Online Journal

Published Since 1989

e-journal available on: [www.medforum.pk](http://www.medforum.pk)

## Medical Forum Recognized and Indexed by

PMDC-IP-0048 (1998), Pastic and PSA, Isd (2000), Medlip, Karachi (2000), NLP, Isd (2000), Pakmedinet, Isd (2011), Excerpta Medica, Netherlands (2000), EMBASE Scopus Database (2008), Index Medicus (IMEMR) WHO (1997), ABC Certification, Govt. of Pak. (1992), Central Media list, Govt. of Pak (1995), Press Reg. No.1221-B Copr (2009)

## Editorial Executives

### Patron-in-Chief

**Dr. Mahmood Ali Malik**  
Prof. of Medicine

### Editor-in-Chief

**Dr. Azhar Masud Bhatti**  
Public Health Specialist & Nutritionist

### Managing Editor

**Dr. Nasreen Azhar**  
Consultant Gynaecologist

### Co-Editors

**Tahir Masud Jan** (Canada)  
**Dr. Meshaal Azhar** (Pak)  
**Dr. Faryal Azhar** (Pak)

### Editor

**Dr. Mohsin Masud Jan**

### Associate Editors

**Dr. Syed Mudassar Hussain** (Pak)  
**Dr. M. Mohsin Khan** (Pak)  
**Dr. Iftikhar A. Zahid** (Pak)

## National Editorial Advisory Board

Prof. Abdul Hamid	Forensic Medicine	Sialkot	03239824782	drabdulhamid12345@hotmail.com
Prof. Abdullah Jan Jaffar	Peads Medicine	Quetta	03008380708	ajanjaffar@yahoo.com
Prof. Abdul Khaliq Naveed	Biochemistry	Rawalpindi	03215051950	khalignaveed2001@yahoo.com
Prof. Aftab Mohsin	Medicine	Lahore	03314101516	aftabmohsin@yahoo.com
Prof. Anjum Habib Vohra	Neurosurgery	Lahore	03008443218	omer@brain.net.pk
Prof. Asad Aslam Khan	Ophthalmology	Lahore	03008456377	drasad@lhr.comsats.net.pk
Prof. Haroon Khurshid Pasha	Paed. Surgery	Multan	03008633433	haroonkpasha@hotmail.com
Prof. Kh. M. Azeem	Surgery	Lahore.	03334242122	khawaja.azeem@sihs.org.pk
Prof. Khalid Masood Gondal	Surgery	Lahore	03328483823	rc_lahore@csp.edu.pk
Prof. M. Amjad	ENT	Lahore	03334254695	professoramjad@yahoo.com
Prof. M. Amjad Amin	Surgery	Multan	03336103262	dramjadamin@gmail.com
Prof. M. Iqbal Mughal	Forensic Medicine	Lahore	03009448386	miqbalmughal@hotmail.com
Prof. M. Sabir	Anatomy	Lahore	03005183021	raosabirdr62@gmail.com
Prof. Mahmood Nasir Malik	Medicine	Lahore	03009487434	nasirphysician@yahoo.com
Prof. Majeed Ahmad Ch.	Surgery	Lahore	03008440415	prof_abdulmajeed@hotmail.com
Prof. Mian Rasheed	Forensic Medicine	AJK	03025033559	drmian1000@hotmail.com
Prof. Pervez Akhtar Rana	Forensic Medicine	Lahore	03009422511	pzrana@gmail.com
Prof. Rukhsana Majeed	Community Medicine	Quetta	03337808138	majidrukhsana@hotmail.com

Prof. Safdar Ali Shah	Urology	Lahore	03334391474	drsafdar-ali@hotmail.com
Prof. Sardar Fakhar Imam	Medicine	Lahore	03008451843	drfakhar@lhr.paknet.com.pk
Prof. Shahid Mehmood	Surgery	Rawalpindi	03215001120	shahid63@gmail.com
Prof. Syed M. Awais	Orthopaedics	Lahore	03334348716	awais@kemu.edu.pk
Prof. Syed Nazim Hussain Bukhari	Medical & Chest Diseases	Lahore	03009460515	nhbokhari@yahoo.com
Prof. Zafarullah Ch.	Surgery	Lahore	03072222533	administrator@csp.edu.pk

## International Editorial Advisory Board

Dr. Tahir Abbas	Medical Oncology	Canada	001306717852	drtgabbas@gmail.com
Dr. Amjad Shad	Neurosurgery	UK	447963442419	amjad.shad@uhcw.nhs.uk
Dr. Ghazanfar Ali	Gastroenterology	UK	447800760008	ghazanfarali@hotmail.com
Dr. Haider Abbas	Urology	UK	447816149374	haidersyed@hotmail.com
Dr. Khalid Rashid	Cardiology	UK	447740477756	khalid.rashid@cht.nhs.uk
Dr. Iqbal Adil	Surgery	UK	447872969928	drmiadil@hotmail.com
Dr. M. Shoaib Khan	Medicine	UAE	00971503111420	mkskd2000@yahoo.com
Dr. Shahid Ishaq Khan	Cardiology	USA	0019014855214	shahidishaqkhan@gmail.com
Dr. Shakeel Ahmad Awaisi	Orthopaedic	USA	0013134638676	msawaisi786@gmail.com
Dr. Basil Nouman Hashmi	Surgery	UK	00447806611517	basilhashmi@doctor.net.uk
Dr. Sohail Saied	Surgery	UK	00441923285114	sohailsaied@gmail.com
Dr. Safdar Ali	Cardiology	USA	0016307816668	safdarali@sbcglobal.net
Dr. Ejaz Butt	Pathology	KSA	00966551349289	drejazbutt@hotmail.com
Dr. Syed Taqadas Abbas	ENT	KSA	00966597052906	taqadasdr@yahoo.com
Dr. Shoab Tarin	Ophthalmology	UK	00447515370995	shoabtarin@gmail.com
Dr. Parashu Ram Mishra	Surgery & Gastroenterology	Nepal	+9779841233450	drparashuram.mishra@gmail.com
Dr. Mansoor M. Mian	Psychiatry	USA	+1 (972)375 7821	mmian2000@yahoo.com
Dr. Sohail Qureshi	Orthopaedic	UK	00447734329666	quraishisohail@yahoo.com
Dr. Mushtaq Ahmad Mughal	Orthopaedics	UK	00447971886006	mahmed01@blueyonder.co.uk
Dr. Mansoor Tahir	Radiology	UK	00447921838093	drmansooratahir@yahoo.com

**Business Manager: Nayyar Zia Ch.**

**Legal Advisors : Jan Muhammad Bhatti, Kh. Ejaz Feroz (Barrister),  
Kh. Mazhar Hassan & Firdos Ayub Ch. (Advocates)**

**Published By: Dr. Nasreen Azhar**, Gohawa Road, Link Defence / New Airport Road,  
Opposite Toyota Motors, Lahore Cantt. Lahore. **Mobile Nos.** 0331-6361436,  
0300-4879016, 0345-4221303, 0345-4221323. **E-mail:** med\_forum@hotmail.com,  
medicalforum@gmail.com **Website: www.medforum.pk**

**Printed By: Syed Ajmal Hussain**, Naqvi Brothers Printing Press, Darbar Market, Lahore

**Rate Per Copy: Rs.1500.00**

**Subscription Rates Annually:** Pakistan (Rs.15000.00), USA & Canada (US\$ 500.00), China, Japan,  
UK & Middle East (US\$ 450.00)

## CONTENTS

### **Editorial**

1. **Pertussis Vaccine: Whole Cell Vs Acellular** \_\_\_\_\_ 1  
Mohsin Masud Jan

### **Original Articles**

2. **Clinicians Diagnostic Accuracy and Management Practices for Benign Anorectal Disorders** \_\_\_\_ 2-6  
1. Muhammad Taha Junaid 2. Atif Mahmood 3. Faria Khan 4. Ali Akbar 5. Hamza Akhtar  
6. Safdar Ali
3. **Pneumococcal Meningitis Burden in Children Admitted Under 5 Years at Saidu Teaching Hospital Swat** \_\_\_\_\_ 7-11  
1. Ihsan ul Haq 2. Sajjad Hussain 3. Salman Mustaan Khan 4. Sardar Khan 5. Zahir Syed  
6. Samreen Khan
4. **Comparison of Efficacy and Tolerability of Melatonin and Amitriptyline in Children Suffering with Migraine** \_\_\_\_\_ 12-15  
1. Khurram Shah Nawaz 2. Beenish Bashir Mughal 3. Bushra Madni 4. Kaleem Akhtar Malhi  
5. Muhammad Asif Siddiqui
5. **Comparison of Periumbilical versus Intraumbilical incision in laparoscopic appendectomy** \_\_\_\_ 16-19  
1. Muhammad Amjad Khan 2. Humara Gul 3. Shahid Mansoor Nizami
6. **Frequency of Response with Eltrombopag in Patients with Persistent Immune Thrombocytopenia** \_\_\_\_ 20-22  
1. Amna Arooj 2. Madiha Islam 3. Mona Aziz 4. Sadia Taj
7. **Etiology and Presentation of Stroke in Hospitalized Children** \_\_\_\_\_ 23-26  
1. Farrukh Saeed 2. Amna Iqtidar 3. Farhan Zahoor 4. Muhammad Asif Siddiqui
8. **Sickle Cell Trait and Disease in Anaemic Patients, Visiting Health Care Centre, KFU, Al Hasa** . 27-30  
1. Hussain Mohammed Alhiwaishil 2. Ashok Kumar 3. Ali Hussain Alrufayi 4. Ali Abdulkarim Alsuliman 5. Chetan Lal
9. **Prevalence of Anxiety and Depression Among the Patients Attending Surgical Ward at Public Sector Tertiary Care Hospitals in Karachi** \_\_\_\_\_ 31-35  
1. Atif Mahmood 2. Atif Jawad 3. Ali Maqbool 4. Hamza Akhtar 5. Safdar Ali 6. Faria Khan
10. **Pattern of Medico-Legal Deaths at Abbasi Shaheed Hospital Autopsy Based 6 Years Study** \_\_\_\_ 36-39  
1. Roohi Ehsan 2. M. Faiz 3. M. Irfan 4. Wasiq Ahmed 5. Raffat Rasool 6. Summaiya Tariq
11. **New Onset Post-Operative Seizures Associated with Ventriculoperitoneal Shunts; A Retrospective Study** \_\_\_\_\_ 40-43  
1. Muhammad Aamir Saghir 2. Muhammad Samir Irfan Wasi 3. Syed Sheeraz ur Rehman
12. **Response of Add-On Oral Levetiracetam in Neonates Having Refractory Seizure** \_\_\_\_\_ 44-47  
1. Farhan Zahoor 2. Beenish Bashir Mughal 3. Bushra Madni 4. Kaleem Akhtar Malhi  
5. Farrukh Saeed
13. **Efficacy and Safety of Ferric Carboxymaltose for Iron-Deficiency Anemia (IDA) in Postpartum Women: An Observational Study** \_\_\_\_\_ 48-51  
1. Shahina Ishtiaq 2. Urooj Malik 3. Minahil Majid 4. Muhammad Athar Khan 5. Mehreen Yousaf Rana 6. Rozina Khaskheli
14. **Study of Biochemical, Hematological & Clinical Profile of Dengue Fever patients in a Tertiary Care Hospital in Northern Pakistan** \_\_\_\_\_ 52-55  
1. Mohsin Shafi 2. Syed Shahmeer Raza 3. Zarmina Hussain 4. Fatima 5. Syed Muhammad Owais
15. **Compliance in Type 2 Diabetic Patients Treated with SGLT2 Inhibitors in a Tertiary Care Hospital Peshawar Pakistan** \_\_\_\_\_ 56-58  
1. Jamaluddin 2. Nizamuddin 3. Manzoor Khan 4. Shafaq Naz 5. Amjad Mustafa 6. Waheed Iqbal



16. **Comparison of Ischemic and Hemorrhagic Strokes in Hypertensive Patients at Tertiary Care Hospital** \_\_\_\_\_ 59-62  
1. Shahzad Memon 2. Hamid Ali Shaikh 3. Kamal Ahmed 4. Mujahid Ali Chandio 5. Muhammad Zarar 6. Arslan Badar Shaikh
17. **Comparison of Postoperative Outcomes of Open Versus Closed Hemorrhoidectomy at Tertiary Care Hospital** \_\_\_\_\_ 63-65  
1. Abdul Hakeem Jamali 2. Mashooq Ali Khowaja 3. Inayat Ali Zardari 4. Zulfqar Ali Imtiaz Memon 5. Altaf Hussain Ghumro 6. Imtiaz Ali Soomro
18. **Frequency of Pre Diabetes in Patients With Positive Family History at Tertiary Care Hospital** \_\_\_\_\_ 66-68  
1. Muhammad Zarar 2. Shahzad Memon 3. Arslan Badar Shaikh 4. Mujahid Ali Chandio 5. Anwar Ali Jamali 6. Ruqayya Farhad
19. **Effect of Cause of Death on Postmortem Cerebrospinal Fluid Electrolytes (K<sup>+</sup>, Na<sup>+</sup> and Cl<sup>-</sup>) Concentration** \_\_\_\_\_ 69-72  
1. Riasat Ali 2. Nasreen Akhtar 3. Mansoor Mirza 4. Syed Mudassir Hussain 5. Saman Ambreen 6. Syeda Maira Hussain
20. **Laparoscopic Cholecystectomy with or without Drain** \_\_\_\_\_ 73-76  
1. Abdul Manan 2. Ashar Ahmad Khan 3. Irfan Ahmad 4. Muhammad Usman 5. Tania Mahar 6. Muhammad Afzal Sajid
21. **Prevalence of Anemia Among Women of Reproductive Age Presenting at Teaching Hospital Gujrat** \_\_\_\_\_ 77-80  
1. Zahid Azam Chaudry 2. Ammara Khan 3. Nawal Moeen
22. **Prognosis of Childhood Tetanus (Age Group 1-12 Years) in Cases Presented in DHQ Teaching Hospital DGK** \_\_\_\_\_ 81-83  
1. Mukhtar Ahmad 2. Asma Akbar 3. Ayaz Ali 4. Sara Ilyas Khan 5. Sidra Choudhary
23. **Analysis of Liver Histology and Severity of Metabolic Syndrome in Patients Suffering from Non-alcoholic Fatty Liver Disease** \_\_\_\_\_ 84-87  
1. Kashif Aziz Ahmad 2. Akmal Khurshid Bhatti 3. Zara Tahir 4. Tahir Mahmood Butt 5. Imran Idris Butt
24. **The Impact on Teaching Strategies on BDS Students Learning and Academic Improvement at Faryal Dental College** \_\_\_\_\_ 88-91  
1. Maryam Masood 2. Sana Akram 3. Hira Asghar 4. Rumana Aqeel 5. Ayesha Riaz 6. Muhammad Omer Aslam
25. **Frequency of Cerebrospinal Fluid Leakage in Patients with Caries Spine Treated with Cage Fixation Procedure with Anterior Approach** \_\_\_\_\_ 92-95  
1. Mumtaz Ahmed 2. Muhammad Feroz Nawaz 3. Habib Ullah 4. Faisal Ali
26. **Prevalence of Pathologic Tooth Migration in Patients with Periodontitis** \_\_\_\_\_ 96-99  
1. Fareedullah Shan 2. Muhammad Naeem 3. Raham Zaman
27. **Comparison of Surgical Options in Typhoid Ileal Perforation at Tertiary Care Hospital** \_\_\_\_\_ 100-103  
1. Inayat Ali Zardari 2. Abdul Hakeem Jamali 3. Mashooq Ali Khowaja 4. Farkhanda Jabeen Dahri 5. Zulfqar Ali Imtiaz Memon 6. Altaf Hussain Ghumro
28. **Placebo-Controlled Trial of Pharmaceutical Optimized Hydralazine 25mg (F-6) in Patients with Essential Hypertension** \_\_\_\_\_ 104-107  
1. Sohail Iqbal 2. Khurram Shahzad Khan 3. Farooq Munfaet Ali Khan 4. Asnad
29. **Different Causes of Anaemia in Elderly Patients** \_\_\_\_\_ 108-112  
1. Madiha Islam 2. Amna Arooj 3. Mona Aziz 4. Sadia Taj
30. **Clinical Presentation of Hepatitis C Virus in Urban and Rural Patients** \_\_\_\_\_ 113-116  
Marifat Shah

## Editorial

# Pertussis Vaccine: Whole Cell Vs Acellular

Mohsin Masud Jan

Editor

The older vaccine for whooping cough that was phased out in the late 1990s is more effective than the current version of the vaccine, a new study contends.

Teenagers who received four shots with the older vaccine, called whole cell vaccine, before they were 2 years old were significantly less likely to become infected with whooping cough during a recent outbreak in California, compared to children who received all of their immunizations with the new vaccines, called the acellular vaccine. Teens who were vaccinated with the acellular vaccine appear to have a six times higher risk of (whooping cough) than teens who received four doses of the whole cell vaccine. And, the teens who received some whole cell vaccine and some acellular had about a four times higher risk than teens who received all whole cell vaccines, said the study's lead author, Dr. Nicola Klein, co-director of the Northern California Kaiser Permanente Vaccine Study Center, in Oakland.

Whooping cough, which is also known as pertussis, is a highly contagious respiratory infection. In 2012, the United States had the highest number of whooping cough cases since 1959 with more than 41000 infections and 18 deaths. Most of the deaths occurred among infants, according to the U.S. Centers for Disease Control and Prevention. The whole cell vaccine was used from the 1940s to 1990s, but was phased out due to potential side effects. The reason we switched away from the whole cell vaccine was that there were some safety concerns, such as high fevers, Klein explained.

The acellular vaccine was introduced in the 1990s, and has few side effects. However, in recent years, a number of studies have found that the newer vaccine doesn't seem to work for as long as the older vaccine. California experienced an outbreak of whooping cough in 2010 and 2011. This gave researchers the chance to see how effective the acellular vaccine was compared to the whole cell vaccine in teens who may have received all of their shots with one or the other vaccine, or possibly with both.

The study included teens born from 1994 to 1999 who got their initial four shots of whooping cough

vaccine before they were 2 years old at Kaiser Permanente Northern California. Of the study participants, 138 teens had confirmed whooping cough. They were compared to 899 teens who'd had a lab test that confirmed they didn't have whooping cough, and to 54339 matched control teens. The researchers found that the fewer number of whole cell vaccines a teen had received, the greater the risk of whooping cough.

Teens who had received all acellular vaccines had a 5.63 times greater risk of whooping cough than teens who'd gotten all whole cell vaccines. Teens who received both acellular and whole cell vaccines had a 3.77 times higher risk of whooping cough compared to those who had all whole cell vaccines. The whole cell vaccine may stimulate the immune response more, but there were a lot of safety concerns with that vaccine.

Dr. Kenneth Bromberg, director of the Vaccine Research Center and chairman of pediatrics at The Brooklyn Hospital Center in New York City, agreed that there's no going back to the whole cell vaccine because of its side effects. It is a moot point. We don't have whole cell vaccine anymore, he said. The acellular vaccine doesn't last as long as the whole cell vaccine, but it's not like it doesn't work. It does, he said. And it's a vaccine that's had almost all of the side effects removed. Bromberg said it's important to make sure that those who are most vulnerable are protected, and in the case of whooping cough that's usually infants. Newborns and babies in the first few months of life are the most likely to die from pertussis, he said. That's why the CDC recommends that pregnant women get the acellular vaccine in the last trimester of pregnancy.

According to the researchers, the way forward would be to develop a new vaccine. But, until then, right now, make sure your children receive all their vaccines and boosters on schedule. The acellular vaccine does work, just not for as long as we would've hoped. So, until a newer longer lasting vaccine is developed, the acellular vaccine available right now is our best shot at preventing Whooping Cough in our children.

# Clinicians Diagnostic Accuracy and Management Practices for Benign Anorectal Disorders

Muhammad Taha Junaid<sup>1</sup>, Atif Mahmood<sup>2</sup>, Faria Khan<sup>3</sup>, Ali Akbar<sup>2</sup>, Hamza Akhtar<sup>4</sup> and Safdar Ali<sup>4</sup>

## ABSTRACT

**Objective:** Hemorrhoid is the most popular diagnosis for patients coming to the doctors with anorectal complaints, especially with bleeding from the anal region. This has caused many serious anorectal problems to be ignored resulting in increased morbidity and mortality. This raised the need to determine the diagnostic accuracy of surgeons, physicians, general practitioners and medical students for common benign anorectal pathologies and measuring the impact of years of experience on the diagnostic accuracy as well.

**Study Design:** Cross sectional study

**Place and Duration of Study:** This study was conducted at the Department of Surgery, Abbasi Shaheed Hospital and JPMC, Karachi from October 2017 to May 2018.

**Materials and Methods:** Seven common anorectal disorders were selected, including, prolapsed internal hemorrhoid, thrombosed external hemorrhoid, anal abscess, anal fissure, anal fistula, condyloma acuminata, and full thickness rectal prolapse. Non-probability purposive sampling included medical students, general physicians, postgraduates of Medicine / Surgery, registrar or senior registrar, residents of Medicine / Surgery, and fellows of Medicine / Surgery. Subjects were given a self-administered questionnaire which included several questions, including demographic questions, image identification and management related questions. Evaluation was then done to compare diagnostic accuracy for different specialties and to see the correlation between diagnostic accuracy and years of experience.

**Results:** The overall diagnostic accuracy of surgeons was the best among all specialties at 72%. Medical students had overall better diagnostic accuracy than Physicians and GPs at 57%. The overall diagnostic accuracy of Physicians and general practitioners were almost the same, at 49% and 48% respectively. Doctors with less than 5 years' experience show an overall diagnostic accuracy of 66%. Years of experience had no correlation in the improvement of diagnostic accuracy for all specialties.

**Conclusion:** The diagnostic accuracy for common benign anorectal pathologies for all types of specialties was suboptimal and Multidimensional continued medical education programs are needed to update the knowledge of clinicians in this regard.

**Key Words:** Internal & External hemorrhoids, anal abscess, anal fissure, anal fistula, condyloma acuminata, full thickness rectal prolapse

**Citation of articles:** Junaid MT, Mahmood A, Khan F, Akbar A, Akhtar H, Ali S. Clinicians Diagnostic Accuracy and Management Practices for Benign Anorectal Disorders. Med Forum 2019;30(5):2-6.

## INTRODUCTION

Constipation and anorectal disorders are those disorders which have not being considerable importance on a global level<sup>1</sup>. The fact that anorectal disorders are highly prevalent in many populations increases their significance and demand adequate consideration by the worldwide health care systems<sup>2,3</sup>.

Anorectal disorders include a variety of pathological diseases, which cause substantial pain and disability for the patients, however, usually the treatment measures are focused only on short-term relief<sup>4</sup>. Majority of such patients with are not seen by consultant surgeon instead by quacks or family physicians.<sup>5</sup>

The area of concern here is that physical examination of the anorectal area is either not done or inadequately done by the doctors of initial contact, i.e. GPs. This problem is further aggravated with it being a social taboo and thus most of the patients never seek medical advice<sup>4</sup>. Majority of the anorectal pathologies are, therefore, misdiagnosed largely because of lack of proper training and experience among the first line doctors for the management of anorectal disorders<sup>7,8</sup>. The common anorectal diseases are not fatal but have full potential to negatively impact patient's quality of life<sup>9</sup>. Some of the most common benign anorectal pathologies include prolapsed internal hemorrhoid, thrombosed external hemorrhoid, anal abscess, anal

<sup>1</sup>. Department of Surgery, JM&DC, Karachi.

<sup>2</sup>. Department of Physiology / Anatomy<sup>3</sup>, Bhitai Dental and Medical College, Mirpurkhas

<sup>4</sup>. Department of Surgery, DUHS, Karachi.

Correspondence: Dr. Atif Mahmood, Associate Professor of Physiology, Bhitai Dental and Medical College, Mirpurkhas.  
Contact No: 0345-2073773  
Email: atif\_mahmood20@yahoo.com

Received: March, 2019

Accepted: April, 2019

Printed: May, 2019

fissure, anal fistula, condyloma acuminata, and full thickness rectal prolapse<sup>6</sup>.

A thorough physical examination is of utmost importance for detection and evaluation of all anorectal disorders and must include examination of abdomen, inspection of anal and perineal areas, digital rectal examination (DRE) and anoscopy<sup>10,11</sup>. Other tests like sigmoidoscopy or colonoscopy are recommended for selected patients only<sup>12</sup>. Fortunately, once the malignancy is ruled out, more than 90% of anorectal complaints can be easily managed in the clinics using simple techniques<sup>13</sup>.

Hemorrhoids are among the commonest anorectal diseases which affect millions of people around the globe<sup>4,14,15</sup>. Majority of the patients with other anorectal diseases have been reportedly misdiagnosed with hemorrhoids by general physicians (6). The objective of this study is to evaluate the diagnostic accuracy of clinicians in identification of benign anal pathologies.

## MATERIALS AND METHODS

A cross sectional study was conducted on the doctors doing general practice in Karachi and consultants, residents, and students from the Tertiary Care Hospitals of Karachi operating in Public Sector. The questionnaire was distributed to 430 subjects of whom only 400 questionnaires were returned and complete. Of these 400 subjects, 211 were general practitioners, 64 were consultant physicians, 62 were consultant surgeons and 63 were medical students. Final year students who were attending different clinical rotations in the same hospitals were also selected. General practitioners with at least five years of practicing experience were included in the study. Five years of experience was taken as cut off as it is assumed that the doctors with such experience must have seen a few patients with anorectal diseases during this time period. However, a doctor with lesser experience may or may not have encountered such patients in his general practice as it also considered as a social taboo and the fact that people are more aware of the scope of general physicians and specialists these days.

Images of seven common benign anorectal pathologies were selected including prolapsed internal hemorrhoid, thrombosed external hemorrhoid, anal abscess, anal fissure, anal fistula, condyloma acuminata, and full thickness rectal prolapse<sup>6,16</sup>. These images were shown to general practitioners, physicians (belonging to medicine wards only), surgeons (including fellows, residents, and postgraduates) and medical students (mainly final year students) and they were asked to diagnose these seven common anorectal conditions in written for which they were provided 5 minutes. The selection of the doctors was done by non-probability purposive sampling. Demographic questionnaire and the questionnaire analyzing the effectiveness of

conservative management of hemorrhoids were also filled by all subjects.

Anonymity of the subjects was ensured and written informed consent was taken from all the patients. The project was approved from the ERC of Bhitai Dental and Medical College, Mirpurkhas.

All the data was analyzed with SPSS Version 20. Chi-square statistical analysis was done to provide statistical association between years of experience and diagnostic accuracy of anorectal diseases.

## RESULTS

The overall diagnostic accuracy of seven common benign anorectal pathologies across all surveyed specialties was suboptimal at 53.5%. Surgeons had overall better knowledge of the anorectal pathologies and their diagnosis was the best among all other groups at 72%. Surprisingly, diagnostic accuracy of medical students was better (57%) than physicians (49%) and general practitioners (48%). This maybe in part due to the updated knowledge and recently studied topic or clinical rotation thus, have a much better academic profile and knowledge of the anorectal diseases.

**Table No.1: Demographic characteristics of the subjects (N=400)**

Association of the Doctors	Frequency	Percent
Private clinic	229	57.25
Teaching Hospital	54	13.5
Non-teaching Hospital	54	13.5
Medical school	63	15.75
Specialty of the subjects	Frequency	Percent
General practitioner	211	52.75
General Physician	64	16.0
Medical student	63	15.75
General Surgeon	62	15.5
Age Groups of the subjects	Frequency	Percent
21-30 years	101	25.25
31-40 years	71	17.75
41-50 years	161	40.25
51-60 years	64	16.0
60 years plus	3	0.75
Years of Clinical Experience	Frequency	Percent
No Experience except clinical rotations	63	15.75
Less than 5 years	38	9.5
5 to 10 years	84	21.0
10 to 15 years	120	30.0
15 to 20 years	52	13.0
More than 20 years	43	10.75
<b>Total</b>	<b>400</b>	<b>100.0</b>



**Table No.2: Association of the differential Diagnosis with the specialty of the subjects**

	Prolapsed internal hemorrhoid				Total	p value*
	Yes (n)	Yes (%)	No (n)	No (%)		
General Practitioner	191	91	20	9	211	0.003*
General Physician	54	84	10	16	64	
Medical Students	47	75	16	25	63	
General Surgeon	58	94	4	6	62	
Total	350	87.5	50	12.5	400	
	Thrombosed external hemorrhoid				Total	
	Yes (n)	Yes (%)	No (n)	No (%)		
General Practitioner	12	6	199	94	211	0.000*
General Physician	16	25	48	75	64	
Medical Students	27	43	36	57	63	
General Surgeon	29	47	33	53	62	
Total	84	21	316	79	400	
	Anal Abscess				Total	
	Yes (n)	Yes (%)	No (n)	No (%)		
General Practitioner	67	32	144	68	211	0.000*
General Physician	18	28	46	72	64	
Medical Students	30	48	33	52	63	
General Surgeon	43	69	19	31	62	
Total	158	39.5	242	60.5	400	
	Anal Fissure				Total	
	Yes (n)	Yes (%)	No (n)	No (%)		
General Practitioner	82	39	129	61	211	0.000*
General Physician	25	39	39	61	64	
Medical Students	39	62	24	38	63	
General Surgeon	39	63	23	37	62	
Total	185	46	215	54	400	
	Anal Fistula				Total	
	Yes (n)	Yes (%)	No (n)	No (%)		
General Practitioner	90	43	121	57	211	0.010*
General Physician	24	38	40	62	64	
Medical Students	29	46	34	54	63	
General Surgeon	40	65	22	35	62	
Total	183	46	217	54	400	
	Condyloma Acuminata				Total	
	Yes (n)	Yes (%)	No (n)	No (%)		
General Practitioner	110	52	101	48	211	0.001*
General Physician	38	59	26	41	64	
Medical Students	42	67	21	33	63	
General Surgeon	49	79	13	21	62	
Total	239	60	161	40	400	
	Full thickness rectal prolapse				Total	
	Yes (n)	Yes (%)	No (n)	No (%)		
General Practitioner	162	77	49	23	211	0.000*
General Physician	44	69	20	31	64	
Medical Students	36	57	27	43	63	
General Surgeon	56	90	6	10	62	
Total	298	74.5	102	25.5	400	

\*p value <0.05 is significant, < 0.01 is very significant, <0.001 is highly significant  
Chi square is used to determine the association among these factors

## DISCUSSION

Cases of anorectal complaints being misdiagnosed have been reported in other studies as well. A study was done on 100 patients with anorectal problems who were seen by a newly hired colorectal surgeon. The surgeon misdiagnosed 49 cases and thus the correct diagnosis was delayed. There were also reports of unnecessary referrals for colonoscopy in this study<sup>7</sup>.

Years of experience across all specialties did not have any impact on the diagnostic accuracy. The results show that the fresh medical graduates tend to have more knowledge and thus better understanding of the anorectal diseases which is similar to other studies as well<sup>17</sup>. With additional experience, these doctors are no longer updating their academics because of their increased engagement in clinics and lack of continuing medical education<sup>18</sup>. Grucela et al. also concluded that the diagnostic accuracy was not affected by the years of experience<sup>6</sup>. Surgeons and emergency medicine doctors did better by virtue of ample experience of managing such patients. Psychiatrists and pediatricians do not get such patients, so the resultant poor diagnosis is self-explanatory.

The diagnostic accuracy of physicians in this study was 49% which is really worrisome and draws attention towards lack of their exposure to the anorectal patients and thus the required training is of pivotal importance. A study found out changing trend of sub-specialization in General Surgery as increasing number of General Surgery graduates are going for fellowship training. Literature search on this topic indicates that a positive relationship exists between specialty training and better surgery outcomes. Large number of studies has validated the benefits of pursuing sub-specialization, as it is related to a wide range of colorectal care, which includes management of benign anorectal diseases as well as complex neoplastic diseases<sup>19</sup>.

The poor diagnostic accuracy is also attributed to the fact that the number of colorectal surgeons is extremely limited. A study was done to highlight the importance of Colon and Rectal Surgery. Data from American Board of Colon and Rectal Surgery was used to compare one-year experience of colorectal residency with five-year residency (1989-1996) in General Surgery. It was found out that in one year, a colorectal resident performed much greater number of anorectal operations than a general surgeon performed in five years of experience<sup>19</sup>. There are many similar studies which have concluded that specialized training in colorectal surgery is of pivotal importance for the general surgeons, which equips them with all necessary expertise in the management of disorders of colon, rectum and anus and produces a true subspecialist. Such data should be collected on a continued basis to critically evaluate the nature of expertise of the colorectal residents, as there is evolving pattern of

referrals with an environment of improved management and overall care of the patients. University and hospital deans can utilize the data to revamp rotations of the residents to improve the technical aspect of different residency programs<sup>15</sup>.

The significance of the presence of a colorectal surgeon in a surgical ward is undeniable and this has amazing impact not only on the result of surgeries but also on the junior surgeons. A study was conducted to determine if the addition of a colon and rectal surgeon to the General Surgery faculty could have qualitative and quantitative improvement in anorectal surgeries for the residents of the department. For this the surgical experience of the graduating residents for a total of ten-year period was taken into account. All cases related to colon, rectum and small intestine were analyzed for five-year period before the joining of the colorectal surgeon and compared with the five-year period post the surgeon's joining. Hyman found out that quantitatively anorectal and small intestine cases increased to a significant extent. The most notable finding was more than fourfold increase in number of anorectal cases performed during the main resident year, which clearly depicts the impact of inclusion of a colorectal surgeon in the form of augmented interest in anorectal cases for the General Surgery residents (20).

Lastly, there is lack of emphasis on anorectal diseases in teaching curricula as well as limited information in majority of medical textbooks<sup>20</sup>. Our study also provides strong evidence that both trainees and surgeons need better academic curricula and training for improved identification of the anorectal conditions.

## CONCLUSION

The diagnostic accuracy for common benign anorectal pathologies for all types of specialties was suboptimal. Years of experience had no correlation in the improvement of diagnostic accuracy for all specialties. The poor diagnostic accuracy of physicians should be seriously taken into account and prompt measures need to be taken, as this is the specialty, which is more likely to get a large number of anorectal patients.

### Author's Contribution:

Concept & Design of Study:	Muhammad Taha Junaid
Drafting:	Atif Mahmood, Faria Khan
Data Analysis:	Ali Akbar, Hamza Akhtar, Safdar Ali
Revisiting Critically:	Muhammad Taha Junaid, Atif Mahmood
Final Approval of version:	Muhammad Taha Junaid

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. Lankarani KB. Why colorectal diseases are important. *Ann Colorectal Res* 2013;1(1):1-2.
2. Zanutti C, Martinez-Puente C, Pascual I, Pascual M, Herreros D, García-Olmo D. An assessment of the incidence of fistula-in-ano in four countries of the European Union. *Int J Colorectal Dis* 2007;22(12):1459-62.
3. Nelson RL, Abcarian H, Davis FG, Persky V. Prevalence of benign anorectal disease in a randomly selected population. *Dis Colon Rectum* 1995;38(4):341-4.
4. Gupta PJ. Common anorectal conditions. *Turkish J Med Sci* 2004;34(5):285-94.
5. Helton WS. 2001 consensus statement on benign anorectal disease. *J Gastrointestinal Surg* 2002; 6(3):302-3.
6. Grucela A, Salinas H, Khaitov S, Steinhagen RM, Gorfine SR, Chessin DB. Prospective analysis of clinician accuracy in the diagnosis of benign anal pathology: comparison across specialties and years of experience. *Dis Colon Rectum* 2010;53(1):47-52.
7. Goldstein ET. Outcomes of anorectal disease in a health maintenance organization setting. *Dis Colon Rectum* 1996;39(11):1193-8.
8. Lamah M, Ahmad S, Charalampopoulos A, Ho J, Leicester R. Three-year evaluation of a rapid-access coloproctology clinic. *Digestive Surgery* 2000;17(2):150-3.
9. Henderson PK, Cash BD. Common anorectal conditions: evaluation and treatment. *Current gastroenterology reports* 2014;16(10):408.
10. Mapel DW, Schum M, Von Worley A. The epidemiology and treatment of anal fissures in a population-based cohort. *BMC Gastroenterol* 2014;14(1):129.
11. Spanos CP, Tsapas A, Abatzis-Papadopoulos M, Theodorakou E, Marakis GN. Medical student recognition of benign anorectal conditions: the effect of attending the outpatient colorectal clinic. *BMC Surg* 2014;14(1):95.
12. Fargo MV, Latimer KM. Evaluation and management of common anorectal conditions. *Am Family Phys* 2012;85(6).
13. Pfenninger JL, Zainea GG. Common anorectal conditions. *Obstet Gynecol* 2001;98(6):1130-9.
14. Lohsiriwat V. Hemorrhoids: from basic pathophysiology to clinical management. *World J Gastroenterol: WJG* 2012;18(17):2009.
15. Wald A, Bharucha AE, Cosman BC, Whitehead WE. ACG clinical guideline: management of benign anorectal disorders. *Am J Gastroenterol* 2014;109(8):1141.
16. Jimeno J, Vallverdú H, Tubella J, Sánchez-Pradell C, Comajuncosas J, Orbeal R, et al. Prospective analysis of clinician accuracy in the diagnosis of benign anorectal pathology: the value of clinical information. *Revista Espanola de Enfermedades Digestivas* 2012;104(3):122.
17. Schubert MC, Sridhar S, Schade RR, Wexner SD. What every gastroenterologist needs to know about common anorectal disorders. *World J Gastroenterol: WJG* 2009;15(26):3201.
18. Ommer A, Herold A, Berg E, Fürst A, Sailer M, Schiedeck T. German S3 guideline: anal abscess. *Int J Colorectal Dis* 2012;27(6):831-7.
19. Patel SS, Senagore AJ, editors. General surgeons vs. colorectal surgeons: Who should be doing what to whom? *Seminars in Colon and Rectal Surgery*; 2013: Elsevier.
20. Hyman NH. Impact of a colon and rectal surgeon on a general surgery residency training program. *Dis Colon Rectum* 1999;42(2):249-51.

# Pneumococcal Meningitis Burden in Children Admitted Under 5 Years at Saidu Teaching Hospital Swat

Pneumococcal  
Meningitis  
Burden in  
Children

Ihsan ul Haq, Sajjad Hussain, Salman Mustaan Khan, Sardar Khan, Zahir Syed and Samreen Khan

## ABSTRACT

**Objective:** To estimate the burden of pneumococcal meningitis in hospital admitted children under 5 years.

**Study Design:** Descriptive / cross sectional study

**Place and Duration of Study:** This study was conducted at the Department of Pediatrics, Saidu Group of Teaching Hospital Swat over a period of 2 years (from September 2016 to August 2018).

**Materials and Methods:** A total of 246 patients with the clinical suspicion of meningitis were selected for the study. The parents were explained the need for doing lumbar puncture to rule out or confirm the disease. Minimum 3ml of CSF was collected and was sent immediately to the laboratory Saidu Group of Teaching Hospital Swat along with the CSF examination request form.

**Results:** The mean age of the patients was  $11.6 \pm 4.1$  months. There were 189(77%) patients in the age range of 1-12 months, 30(12%) in the age range of 13-24 months, 10(4%) in the age range of 25-36 months and 17(7%) in the age range of 49-60 months. There were 154(62.6%) male and 92 (37.4%) female patients. Pneumococcal meningitis was found in 7 patients. Neisseria meningitidis were isolated in 5 patients and H influenza in 3 patients.

**Conclusion:** Seven cases of pneumococcal meningitis were found in this study, making streptococcus pneumoniae as the commonest bacteria isolated followed by meningococcus on second number necessitating the need for meningococcal vaccination.

**Key Words:** Streptococcus Pneumoniae, Meningitis, Serotypes, Pneumococcal isolates, Meningococcus, Sensitivity pattern.

**Citation of articles:** Haq I, Hussain S, Khan SM, Khan S, Syed Z, Khan S. Pneumococcal Meningitis Burden in Children Admitted Under 5 Years at Saidu Teaching Hospital Swat. Med Forum 2019;30(5):7-11.

## INTRODUCTION

Streptococcus Pneumoniae is a major cause of human disease, ranging from upper respiratory tract infections to severe invasive diseases such as bacteremia, pneumonia, and meningitis. In 2005, the pneumococcus was estimated to be responsible for approximately 1 million deaths worldwide in children younger than 5 years of age. Most of these deaths occurred in developing countries. Following widespread use of the Haemophilus influenzae type B (Hib) conjugate vaccine in infants, S pneumoniae emerged as the leading cause of bacterial meningitis in children younger than 2 years of age.<sup>1</sup> Invasive infections caused by streptococcus pneumoniae in infants and children result in significant morbidity and mortality worldwide.<sup>2</sup>

Department of Pediatrics, Saidu Group of Teaching Hospital Swat.

Correspondence: Dr. Ihsan ul Haq, Professor of Pediatrics, Saidu Group of Teaching Hospital Swat.

Contact No: 0301-8423222

Email: ihsanulhaqdr@gmail.com

Received: January, 2019

Accepted: March, 2019

Printed: May, 2019

The development of effective pneumococcal conjugate vaccine has focused considerable attention on the epidemiology of invasive pneumococcal disease (IPD) in children and more than 90 immunologically distinct serotypes have been found.<sup>3</sup> Although 90 pneumococcal serotypes are known, 7 serotypes (14, 6B, 19F, 18C, 23F, 4, and 9V) have been noted to account for 78% of invasive strains.<sup>4</sup>

In 2000, a 7-valent polysaccharide protein conjugate vaccine (Pneumovax) was incorporated into the universal childhood vaccination schedule. Since implementation, the number of invasive pneumococcal infections caused by vaccine Serogroups isolates declined.<sup>5</sup> In 2005, the coverage reached over 80% in children aged 19-35 months. The total incidence of IPD declined by 75%.<sup>6</sup> The diagnosis of central nervous system (CNS) infection is made on examination of cerebrospinal fluid (CSF).<sup>7</sup> The exact etiological diagnosis is often not possible, because prior antibiotic therapy, low bacterial load and delay in plating for culture. In children the pathogen responsible for most cases of meningitis in developing countries are streptococcus pneumoniae and Haemophilus influenzae.<sup>8</sup>

Deaths resulting from pneumococcus pneumonia are more than pneumococcus meningitis, but surveillance for pneumonia is difficult and complex to be done on



routine basis. Therefore, surveillance for meningitis is the best method for the measurement of disease burden among young children.<sup>9</sup>

Acute bacterial meningitis (ABM) is an important cause of childhood mortality and those survive are at higher risk of developing permanent neurological disability.<sup>10</sup> ABM is among the top 10 causes of infection related deaths worldwide. Meningitis is a major cause of child mortality in Pakistan. The fatality rate in India and other developing countries has been reported as 3-5% in children. Data from Pakistan had also shown complication rate of 57% in children with ABM.<sup>11</sup> Half of the children who survive ABM develop neurological sequelae, which include intellectual deficits, behavioral problems and hearing loss.<sup>12</sup> The burden of pneumococcal disease is largely under investigated in developing countries. However, quantification of the burden of pneumococcal disease through surveillance remains a challenge because the organism is difficult to grow, and adequate laboratory facilities are limited. This has resulted in the problem being largely invisible to health care policy planners, although efficacious vaccines are available. Information about the burden of *Streptococcus pneumoniae* disease among children in Pakistan, is extremely limited, although acute respiratory infection is known to be a major cause of childhood deaths.<sup>13</sup>

## MATERIALS AND METHODS

This was a descriptive, cross-sectional study, conducted at Pediatric Unit of Saidu Group of Teaching Hospital Swat over a period of 2 years (from September 2016 to August 2018). Children from 1 month to 5 years with clinical suspicion meningitis were enrolled.

Sample technique was non-probability purposive sampling.

**Inclusion Criteria:** 1. Age 1 month to 5 years.

2. Clinical suspicion of meningitis.

**Exclusion Criteria:** 1. If patient's clinical condition did not permit the collection of CSF, e.g. patient is comatose or having repeated seizures.

2. Patients who did not give consent to participate.

3. Patients who did not undergo LP.

**Data Collection Procedure:** A detailed history was taken from the parents/attendants of all the selected patients and a thorough clinical examination including detailed neurological examination was performed. The parents were explained the need for doing lumbar puncture in suspected meningitis to rule out or confirm the disease and an informed consent was taken before doing the procedure. Lumbar puncture was performed under aseptic condition before the administration of antibiotics. It was made sure that therapy is not delayed unnecessarily. Other laboratory investigations like FBC, ESR, Blood Glucose and serum electrolytes were also performed.

**CSF Sample:** Minimum 3ml of CSF was collected and sent immediately to the laboratory along with CSF examination request form, for Cytology, Biochemistry, Gram staining, Culture and sensitivity. In case patient had taken antibiotic prior to CSF collection, name and dose of antibiotic was mentioned in the form. All the laboratory investigations were done in the Microbiology laboratory of Saidu Group of Teaching Hospital, Swat.

Upon receiving of specimen macroscopic findings (color, consistency) of the CSF were recorded and the specimen was subjected to the cytology and bacterial culture.

**CSF Cytology and Culture Protocol:** CSF specimen was centrifuged for 15min at 200RPM and sediment was used for cytology and culture, in case quantity of CSF was less than 1ml, specimen was used directly (without centrifugation) for cytology and culture.

**Cytology:** CSF sediment was used for cytology. CSF cytology was done for the presence of leukocytes, RBCs and bacteria. Results were reported as positive if a CSF WBC were more than 5 per mm<sup>3</sup>

**Culture and Sensitivity:** Culture of CSF was performed on chocolate agar plate containing 5% sheep blood agar and vitoX supplement. This was used to promote the growth of all the three organisms of interest i.e. *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Neisseria meningitidis*. One drop of centrifuged CSF deposit was placed and streaked to get isolated colonies. The plate was incubated at 37°C in CO<sub>2</sub> atmosphere for 24 hours.

In case of positive culture, identification of the organism was performed on the basis of colonial morphology, gram stain of colony (if required) and biochemical tests.

Identification of primary organisms of interest was based on following tests:

**S. pneumoniae:** Optochin susceptibility and bile solubility.

**H. influenzae:** Oxidase test and X and V factor test.

**N. meningitidis:** Oxidase test

Sensitivity testing of the isolated organisms was also performed by disk diffusion method against recommended antibiotics for that particular organism. CLSI guidelines were followed in this context.

**Statistical Analysis:** The collected data was entered into statistical computer software SPSS version 22 and analyzed accordingly. Numerical variable like age was presented by calculating mean and standard deviation.

## RESULTS

The mean age of the patients was 11.6±4.1 months. There were 189 (77%) patients in the age range of 1-12 months, 30 (12%) in the age range of 13-24 months, 10 (4%) in the age range of 25-36 months and 17 (7%) in the age range of 49-60 months (Table 1).

In the distribution of patients by sex, there were 154 (62.6%) male and 92 (37.4%) female patients (figure. 1).

In the distribution of patients by clinical examination, fever was found in 202 (82%), neck stiffness in 56 (23%), poor sucking found in 175 (71%), irritability in 224 (91%), bulging fontanelle in 59 (24%), altered level of consciousness in 125 (51%), seizures in 170 (69%), and vomiting in 39 (16%) patients (Table 2).

**Table No.1: Distribution of patients by age (n=246)**

Age (Months)	No. of patients	Percentage
1-12	189	77.0
13-24	30	12.0
25-36	10	4.0
37-48	0	0
49-60	17	7.0
Mean	11.6 $\pm$ 4.1	

Key: n: Number of patients

**Table No.2: Distribution of patients by clinical examination (n=246)**

Clinical examination	Yes		No	
	No.	%tage	No.	%tage
Fever	202	82.0	44	18.0
Neck stiffness	56	23.0	190	77.0
Poor sucking	175	71.0	71	29.0
Irritability	224	91.0	22	9.0
Bulging fontanelle	59	24.0	187	76.0
Altered level of consciousness	125	51.0	121	49.0
Seizures	170	69.0	76	31.0
Vomiting	39	16.0	207	84.0

Key: n: Number of patients

**Table No. 3: Sensitivity patterns of the organism isolated (n=246)**

Antibiotics	Sensitive	Resistance
Ampicillin	Yes	No
Ceftriaxone	Yes	No
Cefotaxime	Yes	No
Vancomycin	Yes	No
Piperacillin/ Tazobactam	Yes	No
Meropenem	Yes	No
Trimethoprim/ sulfamethoxazole	No	Yes
Tetracycline	No	Yes

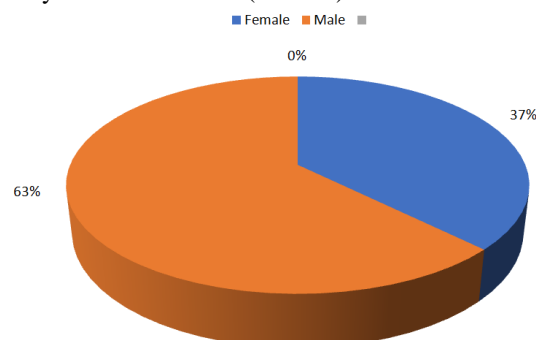
Key:n Number of patients

On CSF cytology meningitis was positive in 30 cases and out of 30, 18 patients were male and 12 were female. On CSF culture, S.pneumoniae was isolated in 7 patients out of 246 suspected cases. In all these 7 cases meningitis was also proven on CSF cytology.

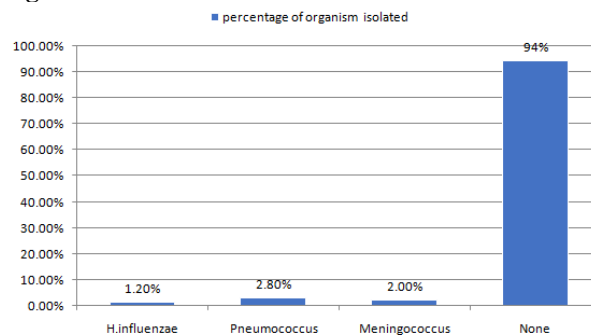
In the distribution of patients by organism isolated, there were 7(2.8%) patients of streptococcus

pneumonia, 5(2%)patients of Neisseria meningitidis and 3 (1.2 %) patient of H.influenzae (figure.2).

On CSF culture and sensitivity of S. Pneumonia was sensitive to, Ampicillin, Ceftriaxone, Cefotaxime, Vancomycin, Piperacillin/Tazobactam, Meropenem and resistant to Trimethoprim / Sulphamethoxazole and Tetracycline as shown in (Table 3).



**Figure No. 1 Gender Distribution of Patients.**



**Figure No..2: Percentage of organism isolated.**

## DISCUSSION

Worldwide ABM remains a devastating disease and cause fatal outcome and neurological sequelae, particularly in the developing countries. Most of the deaths occur during first 48 hours<sup>14, 15</sup>. In the developing countries, where an attempt has been made to measure the burden of Pneumococcal meningitis, Its incidence has been found to be higher than Europe and USA, before the implementation of conjugated vaccine.<sup>16</sup>

In this study majority of the patients (77%) presented below one year of age with mean age of 11.6 $\pm$ 4 months, confirming that meningitis is more common in younger age group. These findings are comparable with the research work done by Zaidi et al<sup>17</sup>, Iregbu K C et al<sup>18</sup> and Naz S et al<sup>19</sup>, however Dhurbajooti. J et al<sup>20</sup> has reported only 46.8% cases under one year.

This study shows a male to female ratio 1.67 to 1. Similar male preponderance was observed in the studies conducted by Bari A et al<sup>24</sup> and Dhurbajooti. J et al<sup>20</sup> showing the male to female ratio of 1.6 to 1 and 1.8 to 1 respectively. The relative frequency of different signs and symptoms in this study are much similar to those observed by Marji S<sup>22</sup>, Bari A et al<sup>21</sup>, Zaidi et al<sup>17</sup> and Fayyaz J et al<sup>23</sup>.

CSF culture was positive only in 15 patients (6%) in our study. Bari A et al<sup>21</sup> in their comparative study has shown 7% CSF culture positivity in 2013 while they have reported 12% positivity in 2012. Similarly, Afridi J M et al<sup>24</sup> has reported 7.9% CSF culture positivity in their study. However CSF culture positivity was relatively higher (13.9%) in a study conducted by Gaurav B M et al<sup>25</sup> at Ahmedabad India. These high incidences of sterile CSF may be due to empirical antibiotic use prior referral to a tertiary care hospital or improper laboratory handling of specimen

In our study *Pneumococcus* was the predominating organism, 7(2.8%), followed by *Meningococcus* 5(2%) and *H. influenzae* 3(1.2%). The results are comparable with the research papers by Bari A et al<sup>14,21</sup>. The sensitivity pattern of common organisms found in our study is also comparable with the studies of Afridi J M et al<sup>24</sup> conducted in Peshawar and Sharma B et al<sup>26</sup> conducted at New Dehli India

Based on the above discussion, it is suggested that a nationwide multicenter study should be conducted to properly assess the burden of pneumococcal meningitis in our country. Like our research work other studies have also reported a low frequency of 2 to 3% positivity.<sup>7, 27</sup>

## CONCLUSION

Seven cases of pneumococcal meningitis were found in this study, making *Streptococcus pneumoniae* as commonest bacteria isolated followed by *Meningococcus* on second number necessitating the need for Meningococcal vaccination.

**Suggestion:** It is suggested that to further assess the invasive pneumococcal disease (IPD) burden in the form pneumococcal meningitis a nationwide multicenter study should be conducted.

### Author's Contribution:

Concept & Design of Study:	Ihsan ul Haq
Drafting:	Sajjad Hussain, Salman Mustaan Khan
Data Analysis:	Sardar Khan, Zahir Syed, Samreen Khan
Revisiting Critically:	Ihsan ul Haq, Sajjad Hussain
Final Approval of version:	Ihsan ul Haq

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

- Alter SJ. Pneumococcal infections. *Pediatr Rev* 2009;30:155-64.
- Lin PL, Marian G. Incidence of invasive pneumococcal disease in children 3 to 36 months of age at the tertiary care pediatric center 2 years after licensure of the pneumococcal conjugate vaccine. *Pediatr* 2003;111:896-9.
- Hausdorff WP. Invasive pneumococcal disease in children: geographic and temporal variations in incidence and serotype distribution. *Pediatr* 2002; 161:S135-39.
- Mann K, Jackson MA. Pneumococcal serotypes. *Pediatr Rev* 2008; 29: 417-30.6.
- Catherine A, Lynfield R. Epidemiology of invasive pneumococcal disease among older adults in the era of pediatric pneumococcal conjugate vaccine. *JAMA* 2005; 294: 2043-51.
- Lopalco PL. Use of 7-valent pneumococcal conjugate vaccine Europe 2006;11:3092.
- Sadek AA, Mohamad MA, Ali SH, Hassan IAA-A, Hussein MF. Diagnostic value of lumbar puncture among infants and children presenting with fever and convulsions. *Electron Physician*. 2016;8(4): 2255-2262.
- Nhantumbo AA, Gudo ES, Caierao, Munguambe AM, Come CE, Zimba TF, et al. Serotype distribution and antimicrobial resistance of *Streptococcus pneumoniae* in children with acute bacterial meningitis in Mozambique: implication of for a national immunization strategy. *BMC Microbiol* 2016;16(1):134.
- WHO. Hib-pediatric bacterial meningitis (Hib-PBM) surveillance network, surveillance manual. Field test version 2001.
- Jarousha AMA, Affi AA. Epidemiology and risk factors associated with developing bacterial meningitis among children in Gaza strip. *Iran J Public* 2014;43:1176-1183.
- De Gans, Jan-Van De Beek, Diederik V. Dexamethasone in adults with bacterial meningitis. *N Engl J Med* 2002;347: 1549-1556.
- Chandaran A, Herbet H, Misurski D, Santosham M. Long-term sequelae of childhood bacterial meningitis: an underappreciated problem. *Pediatr Infect Dis J* 2011;30:3-6.
- Zaidi AK, Awasthi S, deSilva HJ. Burden of infectious diseases in South Asia. *Br Med J* 2004; 328:811-5.
14. Bari A, Zeeshan F, Zafar A, Ejaz H, Jabeen U, Rathore AW. Acute bacterial meningitis in children presenting to The Children Hospital's Lahore before after pneumococcal vaccine in Pakistan National Immunization program; A comparison. *Pak J Med Sci* 2017;33(2):447-51.
15. Erum A, Zafar MZ, Rasool S, Ali Z, Yousaf K, et al. Different incidences of Acute Bacterial Meningitis of Central Punjab In Pakistan. *J Neurol Neuro Sci* 2017;8(S4):231.
- Campbell JD, Kotloff KL, Sow SO. Invasive pneumococcal infections among hospitalized children in Bamako, Mali. *Pediatr Infect Dis J* 2004;23: 642-49.

17. Zaidi AKM, Khan H, Lasi R, Mahesar W. Surveillance of Pneumococcal Meningitis among Children in Sindh, Southern Pakistan. Clin Infect Dis 2009;48:S129-35.
18. Iregbu KC, Abullahi N. Profiles of acute bacterial meningitis isolates in children In National Hospital, Abuja. Niger Med J 2015;56(\$): 297-300.
19. Naz S, Mushtaq A, Khan MZ, Bari A, Ahmad TM, Spectrum of acute complications and mortality in bacterial meningitis. Pak Med J 2012; 36:132-6
20. Dhurbajaooti J, Debnath, Wanjpe A, Kakrani V, Singru S. Epidemiological of acute bacterial meningitis in admitted children below twelve years of age in a tertiary care teaching hospital in Pune. India. Ind Med J DY Patil Univ 2012; 5:28-30.
21. Bari A, Zeeshan F, Zafar F, Ejaz H et al. Child Acute Bacterial Meningitis: Clinical Spectrum Bacteriological Profile and Outcome. J Coll Physi Surgeons Pak 2016;26(10):822-26.
22. Marji S, Bacterial Meningitis in Children. Rawal Med J 2007;32:102-11.
23. Fayaz J, Rehman A, Hamid A et al, Age related clinical manifestation of acute bacterial meningitis in children. J Pak Med Assoc 2014;64(3):296-99.
24. Muhammad J, Rehman Y, Amir S, Rahim F. Etiological spectrum and antibiotic sensitivity in children with acute pyogenic meningitis. J Med Sci 2018;26(3):234-36.
25. Gaurav B M, Komal D P, Sumeeta T S, et al. Bacteriological profile of pyogenic meningitis in tertiary care hospital. National J Med Res 2012;2(3):3133-17.
26. Sharma B, Kasana D, Sen P: Emerging pathogen bacterial profile sensitivity pattern of acute bacterial meningitis in a tertiary care centre, Delhi India. Int J Current Res 2016;8(03)-27656-61.
27. Roca A, Sigauque B, Quinto LI, Mandomando I, Valle X, Espasa M, et al. Invasive pneumococcal disease in children <5 years of age in rural Mozambique. Trop Med Int Health 2006;11: 1422-31.



# Comparison of Efficacy and Tolerability of Melatonin and Amitriptyline in Children Suffering with Migraine

Tolerability of  
Melatonin and  
Amitriptyline in  
Children with  
Migraine

Khurram Shah Nawaz<sup>1</sup>, Beenish Bashir Mughal<sup>2</sup>, Bushra Madni<sup>3</sup>, Kaleem Akhtar Malhi<sup>4</sup>  
and Muhammad Asif Siddiqui<sup>2</sup>

## ABSTRACT

**Objective:** To compare the efficacy along with tolerability of melatonin and amitriptyline in children suffering with migraine.

**Study Design:** Randomized clinical, parallel group trial study.

**Place and Duration of the Study:** This study was conducted at the Department of Pediatrics, Sahara Medical College, Narowal from July 2018 to December 2018.

**Materials and Methods:** A total of 90 children (45 in each group), with age 5 to 15 years, having migraine were enrolled. Frequency of headache along with its severity and the duration and pedMIDAS were noted on monthly bases, and compared after 3 months of treatment with studied drugs. A good response was labeled if reduction of 50% in headache frequency on a monthly basis was recorded.

**Results:** Out of a total of 90 children, 47 (52.2%) were male and 43 (47.8%) female. Mean age of the study participants was 9.28 years. At the end of the treatment period when both groups were compared, good response, monthly frequency of headache, severity and duration, and headache disability pedMIDAS, all turned out to be significantly better in amitriptyline group (P value < 0.05). A total of 32 (35.6%) children experienced some kind of side effects. No children experienced any serious adverse event during the study period.

**Conclusion:** Melatonin and amitriptyline have both been found to produce good response in children for prophylaxis of migraine. Both drugs have nominal and manageable side effects. In comparison to melatonin, amitriptyline significantly better good response for migraine prophylaxis.

**Key Words:** Melatonin, amitriptyline, migraine, good response.

**Citation of articles:** Shah Nawaz K, Mughal BB, Madni B, Malhi KK, Siddiqui MA. Comparison of Efficacy and Tolerability of Melatonin and Amitriptyline in Children Suffering with Migraine. Med Forum 2019;30(5):12-15.

## INTRODUCTION

In children, migraine is known to be a common problem. It is estimated that around 28% of teenagers are affected with migraine.<sup>1</sup> About 30% of children are said to meet criteria regarding drug prophylaxis. Experts are advocating advise prevention therapies for migraine if children are experiencing 3 to 4 episodes of headache monthly with an aim to reduce this frequency

frequency to 2 or less attacks in a month. Pediatric migraine Disability Assessment Score (pedMIDAS) is the focus while looking at the control of migraine in children, therapies achieving a score of less than 10 are rated good in children.<sup>2</sup>

Wide variety of drugs including antihistamines, antidepressants as well as antiepileptics have been in practice for migraine prophylaxis in children while no generalized guidelines exist.<sup>3</sup> Recently, topiramate got FDA approval for use in children but data is scarce regarding its use.<sup>4</sup> Amitriptyline is a tricyclic antidepressant, known to have minimum side effects and considered very common for managing migraine in children.<sup>5</sup> However, amitriptyline is not recommended for children who have irregular heartbeat and/or prolonged QT syndrome.<sup>6</sup> Melatonin is known to be an indole compound, produced in the pineal gland. Its major function is adjustment of the circadian rhythm related to sleep while during migraine, its levels might be reduced that is supposed to play an important role in the pathophysiology of migraine.<sup>7</sup> Melatonin is said to exhibit anti-inflammatory, hypnotic, analgesic as well as antioxidative properties while it is also hypothesized

<sup>1</sup>. Department of Paediatrics, Sahara Medical College, Narowal.

<sup>2</sup>. Department of Paediatrics, Services Hospital, Lahore.

<sup>3</sup>. Department of Paediatrics, Shalamar medical and Dental College, Lahore.

<sup>4</sup>. Department of Paediatrics, The Children's Hospital and The Institute of Child Health, Lahore.

Correspondence: Dr. Khurram Shah Nawaz, Assistant Professor of Paediatrics, Sahara Medical College, Narowal.  
Contact No: 0314-4904442  
Email: drksn1@hotmail.com

Received: January, 2019

Accepted: March, 2019

Printed: May, 2019

to inhibit the release of dopamine along with neurovascular modulation.<sup>8</sup>

Efficacy of melatonin as 3 mg daily at bedtime has been studied in children from 6 to 16 years of age<sup>8</sup> but not data is available in Pakistan comparing the use of melatonin with amitriptyline regarding migraine prophylaxis that could give us a better insight in to both these drugs for our use in the local population. The aim of current study was to compare the efficacy along with tolerability of metatonin and amitriptyline in children suffering with migraine.

## MATERIALS AND METHODS

This was a randomized clinical trial, conducted at The Department of Pediatrics, Sahara Medical College, Narowal, from July 2018 to December 2018. A total of 90 children (45 in each group), with age 5 to 15 years, having migraines with or without aura, who had fulfilled the criteria for migraine prevention therapy as described by 2<sup>nd</sup> edition of the International Classification of Headache Disorders criteria<sup>9</sup> as per clinical evaluation, exhibiting > 1 headache attack weekly, stating moderate or severe headache disability pedMIDA > 20, and no history of using migraine prevention therapies, were enrolled in this study.

Informed consent was sought from parents/guardians of all the study participants before starting them drugs, assessed in the study. The study was approved by institute's ethics and research committee while no funding was asked from pharmaceutical companies.

Those children who had secondary headaches or who accompanied any systemic illness (renal or hepatic impairment, heart disease, hematological disorders or any other endocrine disorder) were not enrolled in this study. As per physical, clinical and laboratory evaluation, children with raised intracranial pressure or those who were not able to complete 3 months period of treatment, were also excluded from the study.

Randomization was done through lottery method as slips containing 90 numbers were mixed while 1<sup>st</sup> forty five slip drawn containing numbers were considered as children to be given oral melatonin (0.3mg/kg, maximum 6mg) whereas remaining were given oral amitriptyline as 1mg/kg/day (maximum 50mg) for 3 months at bedtime.<sup>10</sup>

Follow up visits were planned at an interval of 2 weeks up till a period of 3 months. Parents were enquired regarding frequency of headaches, its severity along with the duration and the disability score.<sup>11</sup> Adverse events regarding both treatment groups were also noted along with physical examination and assessment of vital signs. In the form any serious adverse event, parents or guardians of the children were asked to reach nearest emergency healthcare facility for the appropriate management. Routine laboratory studies were done during follow up visits in children who

experienced any adverse effects during the study period. All children were allowed to use acetaminophen or ibuprofen (if needed) for the relief of moderate to severe headache episodes during the study period. Visual analog scale (VAS) was used to assess the intensity of headache. Children were asked to rate most of headache pain on VAS on a 10 point scale as zero indicated no pain whereas a score of 10 on VAS highlighted most severe pain.<sup>12</sup>

Frequency of headache along with its severity and the duration and pedMIDAS were noted on monthly bases, and compared after 3 months of treatment with studied drugs. A good response was labeled when reduction of 50% in headache frequency on a monthly basis was recorded.

A predesigned proforma was made to record all the study information while SPSS version 21 was used for data entry and analysis. Chi square test was used for comparing qualitative variables between the groups while independent sample t test was applied for comparing means between the two study groups. P value < 0.05 was taken as of statistical significance.

## RESULTS

Out of a total of 90 children, 47 (52.2%) were male and 43 (47.8%) female. Mean age of the study participants was 9.28 years with a standard deviation of 2.92.

In terms of baseline characteristics between the both groups, gender, age, recent monthly frequency of headache, severity and duration, types of migraine or family history of migraine had no statistical difference between the two groups (p value > 0.05).

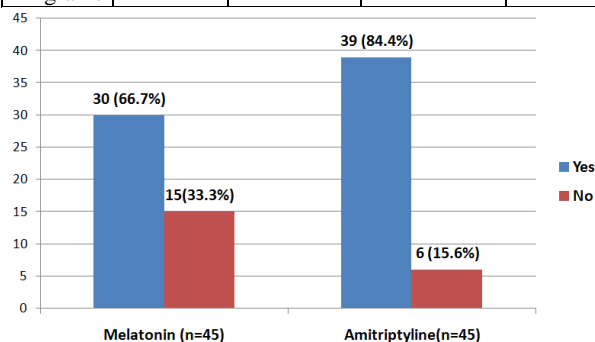
At the end of the treatment period when both groups were compared, monthly frequency of headache, severity and duration, and headache disability pedMIDAS, all turned out to significant better in amitriptyline group.

After three months of treatment, good response (more than 50% reduction in monthly headache frequency) was noted in 30 (66.7%) children using melatonin whereas 39 (84.4%) showed good response in amitriptyline group. Although both groups showed good response but the statistical comparison between two groups was significantly better in amitriptyline in its comparison to melatonin with a significant p value of 0.04.

In terms of side effect, a total of 32 (35.6%) children experienced some kind of side effects. Daily sleepiness was noted as the commonest side effect in both the (n=17, 17.9%), while other frequent side effects were as 6 (6.7%) had constipation, body aches and pain in 4 (4.3%) and weakness in 3 (3.3%). When both groups were compared for side effects, no statistical difference was found amongst the both study groups (p value > 0.05). No children experienced any serious adverse event during the study period.

**Table No.1: Baseline Characteristics of Children Between Both the Study Groups**

Study Characteristics		Groups		P Value
		Melatonin (n=45)	Amitriptyline (n=45)	
Gender	Male	25	22	0.67
	Female	20	23	
Age in years (Mean+SD)		9.78 + 2.3	9.48 + 2.7	0.55
Onset Age of Migraine (Mean+SD)		7.46 + 2.5	7.83 + 2.9	0.50
Recent Monthly Frequency of Headache (Mean+SD)		18.47 + 5.8	17.24 + 6.4	0.31
Severity of Headache (Mean+SD)		7.12 + 1.9	7.65 + 1.5	0.13
Recent Duration of Headache in hours (Mean+SD)		2.34 + 1.3	2.49 + 1.5	0.59
pedMIDAS: Headache Disability		38.47 + 11.9	41.68 + 13.4	0.21
Migraine Type	With Aura	19	15	0.51
	Without Aura	26	30	
Family History of Migraine	Yes	36	32	0.46
	No	9	13	

**Figure No.1: Good Response between the Study Groups**  
P Value = 0.04**Table No.2: Comparison of Study Parameters At The End of Treatment Between Both The Study Groups**

Parameter	Groups		P Value
	Melatonin (n=45)	Amitriptyline (n=45)	
Monthly Frequency of Headache (Mean+SD)	8.03. + 3.7	4.7 + 3.9	0.0001
Severity of Headache (Mean+SD)	3.71 + 1.7	2.37 + 1.3	0.0001
Duration of Headache in hours (Mean+SD)	1.27 + 0.9	0.74 + 0.65	0.59
pedMIDAS: Headache Disability	38.47 + 11.9	41.68 + 13.4	0.0019

## DISCUSSION

In children, headache is commonly reported in pediatric clinics. Migraine is known to be the commonest form of headaches in children while migraine with aura can sometimes accompany neurological symptoms (e.g. hemiparesis, visual disturbances or difficulty in speaking).<sup>13</sup>

Number of medicines are proposed for prophylaxis of migraine in children, and all have their own advantages and disadvantages. In the present study, we noted number of children reporting good response at the end of treatment period in both study groups but the difference between the study groups was turned out to be significant in favor of amitriptyline group in comparison to melatonin. Our results are aligned with another study conducted in Iran<sup>10</sup> where they found that 63% of children using melatonin and 83% in amitriptyline group presented with good response at the end of the treatment period of 3 months with a significant difference (p value = 0.04) favoring amitriptyline group. On the other hand, in adult population in Brazil, less frequency of migraine headache along with improved tolerability in melatonin group was reported in comparison to amitriptyline.<sup>14</sup>

In the present study, we noted 66.7% children in melatonin group with good response (more than 50% reduction in monthly headache frequency) which is better than what was found from Italy<sup>8</sup> where they noted it to be 58%. Another study from Brazil<sup>14</sup> report good response of melatonin in children with migraine as 75% that could be due to different sample size, age group and dose of the drug.

Disturbance in sleep pattern have been noted to be linked with migraine while impaired production of melatonin has been connected with sleep disorders and headache episodes. Melatonin for the control of migraine can ultimately contribute to normal sleep patterns which has been also been documented.<sup>15</sup>

In the present work, amitriptyline group was recorded to have a good response rate of 84.4% which quite similar to what Hershey and colleagues<sup>16</sup> found (84%) while Lewis and coworkers<sup>17</sup> had also noted a good response rate of 83% in their research. A study from Bangladesh<sup>18</sup> report that amitriptyline was associated with very few side effects while common side effects with its use have been noted as daily sleepiness, constipation, malaise which are quite similar to what we found in the current study. Some previous researchers<sup>19,20</sup> also report side effects like dry mouth, dryness of eyes and cardiac arrhythmia but we did not observe anything similar in our study. In current study, no major adverse events related to any of the study drugs were noted while noted adverse events were pretty much similar to what has been found in earlier researches.<sup>14-18</sup>

The current study shows an overall good response rate of prophylactic migraine treatment that encourages all the clinicians considering these options more often when treating children with migraine. Efforts are

needed to be put to create more awareness and management options for migraine in children so that most children bearing this disease gather the benefits. In the current study benefits of amitriptyline were pronounced in for prophylaxis of migraine in children as compared to melatonin which again highlights the benefits of this tricyclic antidepressant that has been in the market since 1970s.

There were few limitations of this current study like the duration of treatment was comparatively shorter while we could not follow the patients once treatment was completed. We did not have any data about the previous use of any herbal or homemade remedies commonly used for the treatment of migraine. Studies with bigger sample size having longer follow up details will further guide us about the benefits of both studied drugs.<sup>19-20</sup>

## CONCLUSION

Melatonin and amitriptyline have both been found to produce good response in children for prophylaxis of migraine. Both drugs have nominal and manageable side effects. In comparison to melatonin, amitriptyline significantly better good response for migraine prophylaxis.

### Author's Contribution:

Concept & Design of Study:	Khurram Shah Nawaz
Drafting:	Beenish Bashir Mughal, Bushra Madni,
Data Analysis:	Kaleem Akhtar Malhi, Muhammad Asif Siddiqui
Revisiting Critically:	Khurram Shah Nawaz, Beenish Bashir Mughal
Final Approval of version:	Khurram Shah Nawaz

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. Antonaci F, Voiticovschi-Iosob C, Di Stefano AL, Galli F, Ozge A, Balottin U. The evolution of headache from childhood to adulthood: a review of the literature. *J Headache Pain* 2014;18:15.
2. Kacperski J, Hershey AD. Newly Approved Agents for the Treatment and Prevention of Pediatric Migraine. *CNS Drugs* 2016;30(9):837-44.
3. Victor S, Ryan S. Withdrawn: Drugs for preventing migraine headaches in children. *Cochrane Database Syst Rev* 2014;7:CD002761.
4. Sakulchit T, Meckler GD, Goldman RD. Topiramate for pediatric migraine prevention. *Can Fam Phys* 2017;63(7): 529–531.
5. Powers SW, Kashikar-Zuck SM, Allen JR, LeCates SL, Slater SK, Zafar M, et al. Cognitive behavioral therapy plus amitriptyline for chronic migraine in

- children and adolescents: a randomized clinical trial. *JAMA* 2013;310:2622.
6. Bonfert M, Straube A, Schroeder S, Reilich P, Ebinger F, Heinen F. Primary headache in children and adolescents: update on pharmacotherapy of migraine and tension type headache. *Neuro Pediatr* 2013;44(1):3-19.
7. Fallah R, Shoroki FF, Ferdosian F. Safety and efficacy of melatonin in pediatric migraine prophylaxis. *Curr Drug Saf* 2015;10(2):132-5.
8. Miano S, Parisi P, Pelliccia A, Luchetti A, Paolino MC, Villa MP. Melatonin to prevent migraine or tension-type headache in children. *Neurol Sci* 2008;29:285-7.
9. Oleson J. The International Classification of Headache Disorders: 2nd edition. Headache Classification Subcommittee of the International Headache Society. *Cephalalgia* 2004;24(Suppl 1): 9-160.
10. Fallah R, Fazelishoroki F, Sekhavat L. A Randomized Clinical Trial of Efficacy of Melatonin and Amitriptyline in Migraine Prophylaxis of Children. *Iran J Child Neurol*. Winter 2018;12(1):47-54.
11. Hershey AD, Powers SW, Vockell ALB, LeCates SL, Kabbouche MA, Maynard MK. PedMIDAS: Development of a questionnaire to assess disability of migraines in children. *Neurol* 2001;57:2034-9.
12. Wewers ME, Lowe NK. A critical review of visual analogue scales in the measurement of clinical phenomena. *Res Nurs Health* 1990;13:227-36.
13. Lewis DW. Pediatric Migraine. *Pediatrics in Review* 2007;28(2):43-53.
14. Peres M, Gonçalves A. Double-blind, placebo controlled, randomized clinical trial comparing melatonin 3 mg, amitriptyline 25 mg and placebo for migraine prevention. *Neurology* 2013;80.
15. Alstadhaug KB, Odeh F, Salvesen R, Bekkelund SI. Prophylaxis of migraine with melatonin: a randomized controlled trial. *Neurol* 2010;75:1527-32.
16. Hershey AD, Powers SW, Benti AL, Degrauw TJ. Effectiveness of amitriptyline in the prophylactic management of childhood headaches. *Headache* 2000;40(7):539-49.
17. Lewis DW, Diamond S, Scott D, Jones V. Prophylactic treatment of pediatric migraine. *Headache* 2004;44(3):230-7.
18. Israil A, Ahmed S, Rahman KM, Uddin MJ, Dey SK, et al. Efficacy of amitriptyline, pizotifen and propranolol in the prevention of migraine. *Mymensingh Med J* 2013;22(1):93-100.
19. Hershey AD, Winner PK. Pediatric migraine: recognition and treatment. *J Am Osteopath Assoc* 2005;105(4 Suppl 2):2S-8S.
20. Lewis DW, Yonker M, Winner P, Sowell M. The treatment of pediatric migraine. *Pediatr Ann* 2005;34:448–460.



# Comparison of Periumbilical versus Intraumbilical Incision in Laparoscopic Appendectomy

Muhammad Amjad Khan<sup>1</sup>, Humara Gul<sup>2</sup> and Shahid Mansoor Nizami<sup>3</sup>

## ABSTRACT

**Objective:** To compare the rate of wound complication of perforated appendicitis in intraumbilical versus periumbilical incision for laparoscopic appendectomy.

**Study Design:** Randomized Control Trail study.

**Place and Duration of Study:** This study was conducted at the General Surgery Department Bakhtawar Amin Hospital Multan, and Nishtar Hospital, Multan from 20 February 2018 to January 2019.

**Materials and Methods:** This randomized control has been performed upon 200 patients. They have been further categorized into intraumbilical (IU) and periumbilical (PU) group. Then the perioperative and post-operative outcomes of each group was determined and compared.

**Results:** The mean operative time, post-operative hospital stay, morphine equivalent, and visual analogous scale of IU group was  $75.93 \pm 2.87$  minutes,  $8.09 \pm 3.06$  days,  $4.75 \pm 1.37$  mg and  $4.94 \pm 1.38$  respectively. Wound infection, incisional hernia and internal organ injury was observed in  $n=9$  (9.0%),  $n=3$  (3.0%) and  $n=5$  (5.0%) respectively. While, the mean operative time, post-operative hospital stay, morphine equivalent, and visual analogous scale of PU group was  $81.20 \pm 1.92$  minutes,  $6.54 \pm 3.11$  days,  $4.09 \pm 1.45$  mg and  $4.59 \pm 1.80$  respectively. Wound infection, incisional hernia and internal organ injury was observed in  $n=5$  (5.0%),  $n=6$  (6.0%) and  $n=10$  (10.0%) respectively.

**Conclusion:** There is no difference in the rate of wound complication of intraumbilical or periumbilical incision. Nevertheless, the intraumbilical incision appears to be safer and expedient substitute for periumbilical incision which can be performed with more ease and yields better cosmetic results.

**Key Words:** Intraumbilical, Periumbilical, Laparoscopic Appendectomy, Wound Infection, Appendicitis.

**Citation of articles:** Khan MA, Gul H, Nizami SM. Comparison of Periumbilical versus Intraumbilical Incision in Laparoscopic Appendectomy. Med Forum 2019;30(5):16-19.

## INTRODUCTION

One of the extensively adopted and largely accepted methods in the field of general surgery is the technique of general surgery<sup>1</sup>. Creating pneumoperitoneum and placing the initial trocar safely are believed to be salient feature in the laparoscopic surgery. For the purpose of approaching laparoscope inside the abdominal cavity, a paraumbilical incision is usually in practice<sup>2</sup>. The incision is commonly U-shaped into the skin with the facial incision being linear. The site of incision is above or below the umbilicus. It pierces skin, subcutaneous fat and fascia.

Whereas in case of para umbilical incision, a linear vertical incision is made that extends from skin to fascia only up till the length of umbilical ring<sup>3</sup>. As there is only division of skin and fascia, the intraumbilical incision requires lesser time, lesser trauma and more ease in performing. The intraumbilical incision is in more frequent use being widely adapted for "single incision laparoscopic surgery" (SILS)<sup>4</sup>. This surgery is believed to be practical substitute of customary laparoscopic surgery providing more desirable cosmetic outcomes<sup>5</sup>.

As the umbilicus is placed at a deeper level than neighbouring abdominal wall it contains a greater number of bacteria<sup>6</sup>. Recently it has been found that there are about 1400 types of bacteria residing in umbilical bacterial culture. Previously, no study was done to compare the efficacy and rate of complications of intraumbilical and per-umbilical incision<sup>7</sup>. It has been hypothesized that after preparation for surgery, the inner part of umbilical ring as aseptic as the outer skin of umbilicus and rate of wound infection does not differ<sup>8</sup>. Also, the hypothesis was made regarding adequate closure of wound will lead to no aberration in the occurrence rate of incisional hernia<sup>9,10</sup>.

It is seen that complication of wound of perforated appendicitis are greater than that of other simple

<sup>1</sup>. Department of General Surgery / Anatomy<sup>2</sup>, Bakhtawar Amin Medical and Dental College, Multan.

<sup>3</sup>. Department of General Surgery, Nishtar Medical University, Multan.

Correspondence: Dr. Muhammad Amjad Khan, Associate Professor of General Surgery, Bakhtawar Amin Medical and Dental College, Multan.

Contact No: 0333 6142878

Email: amjad36@gmail.com

Received: February, 2019

Accepted: April, 2019

Printed: May, 2019

laparoscopic procedures inclusive of non-perforated cases.

## MATERIALS AND METHODS

The nature of study was Randomized Control Trial done on 200 patients of perforated appendicitis. The duration of study was from February 2018 to January 2019 in General surgery department of Bakhtawar Amin Hospital and Nishtar Hospital, Multan, by Consultant surgeons. Patients were allocated to periumbilical or intraumbilical group according to the surgeon's choice. Height, weight, BMI, gender, age and comorbidities of patients were recorded. The comorbidities included diabetes, hypertension, COPD, coronary artery disease. The outcome variables included length of hospital stay, rate of wound complication, intensity of pain in the patient assessed by visual analogue scale, quantity of analgesics required on first postoperative day.

Postoperative umbilical complications included any cases of wound infection, incisional hernia, and hematoma formation. Wound infection was defined as a state of localized erythema, edema, or heat, accompanied by subjective pain, with or without purulent discharge. An incisional hernia was defined as a protrusion or bulge present at or near the umbilical incision.

The recording of post-operative pain was done at 24 hours after the surgery. The evaluation of results was done by student's t-test or Chi-Square test. A P-value  $\leq 0.05$  was considered significant. The approval from Ethics committee was obtained.

### Surgical Technique:

Before initiation of anesthesia, all the patients were administered 1<sup>st</sup> generation cephalosporins IV. Patients were again given antibiotics after termination of surgery. For intraumbilical incision, the umbilical was thoroughly cleaned with the help of cotton swabs by using alcohol. The evacuation of debris was done manually. With the help of betadine, skin preparation was made. Within the depression of umbilicus, a midline incision was given. Skin was retracted slightly on both sides with tissue forceps. The incision was then made till whole length of umbilicus. Since fascia lies directly beneath the skin of umbilicus, by minimal further dissection, approach to peritoneal cavity was made. 11mm trocar was easy to insert as no umbilical ring is more than 10mm in diameter. Laparoscopic using customary techniques was performed. Prevention from contamination of fascia or skin was done by retrieving the appendix from peritoneal cavity with the help of Lap-bag. Single absorbable suture was enough for closing the wound, not needing additional suturing for skin or subcutaneous fat. Full layer suture was made. The approximation of layers was assisted by single suture. A roll of gauze was inserted into the umbilicus, after which bandage was done. In case of periumbilical incision, a U-shaped incision was made

below the umbilicus. The dissection of subcutaneous fat was done and fascia was opened with electro-coagulation. After that, direct trocar was inserted or after insufflation with the help of Veress needle, the trocar was inserted. After completion of appendectomy, wound was closed in a layer to layer manner, while closing fascia, skin and subcutaneous fat separately. A drain was put into the pelvic cavity in case of perforation.

## RESULTS

Two hundred patients were enrolled in this study, both genders. We further categorized the patients as intraumbilical, IU group and periumbilical, PU group. The mean age and BMI of IU group was  $33.17 \pm 2.22$  years and  $22.60 \pm 1.81$  kg/m<sup>2</sup> respectively. Gender distribution observed as n=73 (73%) males and n=27 (27%) females. Hypertension and diabetes was revealed in n=32 (32%) and n=12 (12%) patients for IU group, respectively. While, the mean age and BMI of PU group was  $37.28 \pm 3.01$  years and  $22.58 \pm 1.81$  kg/m<sup>2</sup> respectively. Gender distribution observed as n=29 (29%) males and n=71 (71%) females. Hypertension and diabetes was revealed in n=23 (23%) and n=14 (14%) patients for PU group, respectively. The difference was statistically insignificant except age (p=0.000). (Table. I).

The mean operative time, post-operative hospital stay, morphine equivalent, and visual analogous scale of IU group was  $75.93 \pm 2.87$  minutes,  $8.09 \pm 3.06$  days,  $4.75 \pm 1.37$  mg and  $4.94 \pm 1.38$  respectively. Wound infection, incisional hernia and internal organ injury was observed in n=9 (9.0%), n=3 (3.0%) and n=5 (5.0%) respectively. While, the mean operative time, post-operative hospital stay, morphine equivalent, and visual analogous scale of PU group was  $81.20 \pm 1.92$  minutes,  $6.54 \pm 3.11$  days,  $4.09 \pm 1.45$  mg and  $4.59 \pm 1.80$  respectively. Wound infection, incisional hernia and internal organ injury was observed in n=5 (5.0%), n=6 (6.0%) and n=10 (10.0%) respectively. The difference was statistically significant except visual analogous score (p=0.125), incisional hernia (p=0.306) and internal organ (p=0.179). (Table. 2).

**Table No.I: Demographic Characteristics among the groups**

Variable	IU Group n=100	PU Group n=100	P-value
Age (years)	33.17±2.22	37.28±3.01	0.000
BMI (kg/m <sup>2</sup> )	22.60±1.81	22.58±1.81	0.938
Gender			
Male	n=73 (73%)	n=29 (29%)	0.753
Female	n=27 (27%)	n=71 (71%)	
Hypertension			
Presence	n=32 (32%)	n=23 (23%)	0.154
Diabetes			
Presence	n=12 (12%)	n=14 (14%)	0.854

\*IU intraumbilical, PU= periumbilical, BMI=body mass index

**Table No.2: Demographic Characteristics among the groups**

Variable	IU Group n=100	PU Group n=100	P-value
Operative time (minutes)	75.93±2.87	81.20±1.92	0.000
Post-operative hospital stay (days)	8.09±3.06	6.54±3.11	0.000
Morphine equivalent (mg)	4.75±1.37	4.09±1.45	0.001
Visual analogous score	4.94±1.38	4.59±1.80	0.125
Wound infection	n=9 (9.0%)	n=5 (5.0%)	0.030
Incisional hernia	n=3 (3.0%)	n=6 (6.0%)	0.306
Internal organ	n=5 (5.0%)	n=10 (10.0%)	0.179

## DISCUSSION

There are various management options for the acute appendicitis. Out of the options for surgery of acute appendicitis, the technique of laparoscopic appendectomy has beneficial effects over the conventional surgery says Sauerland S et al<sup>11</sup>. It is believed that where resources and expertise are present and available, diagnostic laparoscopy as well as laparoscopic appendectomy is superior to open appendectomy. There are some trivial clinical effects of this technique, but they are minute and can be ignored. The authors recommend the use of laparoscopy for the diagnosis and surgery of acute appendicitis unless it is contraindicated or not available. It is suggested particularly in obese patients, in young females, and patients who are employed.

Single incision laparoscopy is widely being adapted in the field of surgery. The most common site for access into the abdominal cavity is through umbilicus. However, its shape and anatomy are modified during the procedure. A majority of the population is sensitive and concerned about the physical aspects of their umbilicus. Therefore, it is advised by Iranmanesh et al<sup>12</sup> care must be taken in selecting the patients for the laparoscopic procedure and minimally invasive surgical procedures should be performed in concerned patients. Peritoneal access is crucial step in laparoscopic surgery. It has been observed that intraumbilical incision is convenient and rapid to make. Nonetheless, due to greater risk of wound complication, the periumbilical incision is still in use. A study was done to compare the outcomes of these incisions in laparoscopic cholecystectomy<sup>13</sup>. The operating time and the cosmetic survey score were better in the intraumbilical incision. It was concluded that intraumbilical incision was “safe

and feasible method” to access the peritoneal cavity and it decrease the operating time while providing better cosmetic results to the patients.

Recently the technique of transumbilical laparoscopic assisted appendectomy (TULAA) has been introduced. A study<sup>14</sup> has been performed in pediatric group who were suffering from appendicitis including advanced appendicitis, appendicoliths and retrocecal appendix. As a result, the patients’ average duration of stay in hospital was 1.2 days. There were no postoperative complications. It was cost effective and safe method as compared to conventional laparoscopy.

In the modern era, cosmesis and minimally invasive surgery are gaining more importance. In order to decrease the abdominal trauma and ameliorate the cosmetic effects, surgeons are now using single port laparoscopic appendectomy for acute appendicitis. A study was done upon 43 cases of appendectomy in which the umbilical incision was either infraumbilical or transumbilical<sup>15</sup>. It was observed that although the single port appendectomy needs more operative time, it produces better cosmetic outcomes. It is a feasible technique and can be used as an alternative for treatment of acute appendicitis.

A study by Cloutier AB et al<sup>16</sup> was conducted comparing the efficacy of transumbilical versus periumbilical incision for laparoscopic appendectomy. In terms of postoperative cosmetic outcomes and operative time, no significant difference was observed in both the techniques. The results were alike for all tested outcomes.

When the technique of single incision transumbilical laparoscopy was put to test in appendectomy, it was found that this technique was successful in 73.1% of patients<sup>17</sup>. There was no need to convert it into open surgery. Whereas the time for surgery was recorded as 45.9 minutes and hospital stay was of 1.1 day on average. The rate of wound complication was only 1%. This technique of single incision transumbilical laparoscopy was rendered “safe, feasible and reproducible”.

A similar study was performed by Lee SY et al<sup>18</sup> demonstrating the safety and efficacy of TOPLA (Transumbilical One Port Laparoscopic Appendectomy) over OA (open Appendectomy). The results showed remarkable reduction in operating time (6.15 min) as well as post-operative complications (0%) of TOPLA in comparison to OA which was 118 minutes and 9.8% respectively. Likewise, the need for IV analgesia was also lesser in TOPLA than OA. The technique was established as safe and effective for the surgeon in terms of simplicity and time efficacious as well as for patients in terms of better cosmetic outcomes.

As the umbilicus is deeper than its surrounding structures, it is known to have abundant number of bacteria. Hence, become a risk factor in post-operative complications of laparoscopic appendectomy. Lee JS Et

al<sup>19</sup> compared the rate of wound complications and adverse effects of intraumbilical versus periumbilical incision for laparoscopic appendectomy. The results depicted no differences in the rate of operative time, hospital stay or analgesic requirements among the two groups. Whereas, one case was complicated by wound infection in intraumbilical and three cases were complicated in the periumbilical incision group. It was determined that although these two groups show no aberrations in results, however the technique of intraumbilical incision is regarded as “safe and feasible alternative” for periumbilical incision which is easy to perform and has satisfactory cosmetic outcome. Similar results were obtained when Gogoi et al<sup>20</sup> conducted a study on this comparison. The technique of intraumbilical incision was once again declared safe and feasible, relatively easy to perform with better cosmesis.

## CONCLUSION

There is no difference in the rate of wound complication of intraumbilical or periumbilical incision. Nevertheless, the intraumbilical incision appears to be safer and expedient substitute for periumbilical incision which can be performed with more ease and yields better cosmetic results.

### Author's Contribution:

Concept & Design of Study: Muhammad Amjad Khan  
 Drafting: Humara Gul  
 Data Analysis: Shahid Mansoor Nizami  
 Revisiting Critically: Muhammad Amjad Khan, Humara Gul  
 Final Approval of version: Muhammad Amjad Khan

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. Chow A, Purkayastha S, Nehme J, Darzi LA, Paraskeva P. Single incision laparoscopic surgery for appendicectomy: A retrospective comparative analysis. *Surg Endosc* 2010;24:2567-74.
2. Vidal O, Ginestà C, Valentini M, Martí J, Benarroch G, García-Valdecas Suprapubic single-incision laparoscopic appendectomy: A nonvisible-scar surgical option. *Surg Endosc* 2011;25:1019-23.
3. Holder-Murray J, Zoccali M, Hurst RD, Umanskiy K, Rubin M, Fichera A. Totally laparoscopic total proctocolectomy: A safe alternative to open surgery in inflammatory bowel disease. *Inflamm Bowel Dis* 2012;18:863-8.
4. Pearce NW, Di Fabio F, Teng MJ, Syed S, Primrose JN, Abu Hilal M. Laparoscopic right hepatectomy: A challenging, but feasible, safe and efficient procedure. *Am J Surg* 2011;202:e52-8.
5. Nguyen NT. Open vs. laparoscopic procedures in bariatric surgery. *J Gastrointest Surg* 2004;8:393-5.

6. Zollinger RM, Ellison EC, Zollinger RM. Zollinger's atlas of surgical operations. 9<sup>th</sup> ed. New York: McGraw-Hill Medical; 2011.
7. Kim HH, Ahn SH. The current status and future perspectives of laparoscopic surgery for gastric cancer. *J Korean Surg Soc* 2011;81:151-62.
8. Lee M, Kim SW, Nam EJ, Yim GW, Kim S, Kim YT. Single-port laparoscopic surgery is applicable to most gynecologic surgery: a single surgeon's experience. *Surg Endosc* 2012;26:1318-24.
9. Park KK, Lee SH, Lee SH, Ahn BK, Baek SU. The learning curve by varied operative procedures in laparoscopic colorectal surgery. *J Minim Invasive Surg* 2012;15:44-9.
10. Potter DD, Tung J, Faubion WA, Moir C. Single-incision laparoscopic colon and rectal surgery for pediatric inflammatory bowel disease and polyposis syndromes. *J Laparoendosc Adv Surg Tech A* 2012;22:203-7.
11. Sauerland S, Jaschinski T, Neugebauer EA. Laparoscopic versus open surgery for suspected appendicitis. *Cochrane Database Syst Rev* 2010; (10):CD001546.
12. Iranmanesh P, Morel P, Inan I, Hagen M. Choosing the cosmetically superior laparoscopic access to the abdomen: the importance of the umbilicus. *Surg Endosc* 2011;25:2578-85.
13. Lee JS. Intraumbilical versus periumbilical incision in laparoscopic cholecystectomy: A randomized controlled trial. *Int J Surg* 2016;33:83-87.
14. Shekherdimian S, DeUgarte D. Transumbilical laparoscopic-assisted appendectomy: an extracorporeal single-incision alternative to conventional laparoscopic techniques. *Am Surg* 2011;77(5):557-60.
15. Kim HJ, Lee JI, Lee YS, Lee IK, Park JH, Lee SK, et al. Single-port transumbilical laparoscopic appendectomy: 43 consecutive cases. *Surg Endosc* 2010;24:2765-9.
16. Cloutier AB, Pare A, McFadden N. Periumbilical vs transumbilical laparoscopic incision: A patients' satisfaction-centered randomised trial. *Int J Surg* 2017;43:86-91.
17. Saber AA, Elgamal MH, El-Ghazaly TH, Dewoolkar AV, Akl A. Simple technique for single incision transumbilical laparoscopic appendectomy. *Int Surg* 2010;8(2):128-30.
18. Lee SY, Lee HM, Hsieh CS, Chuang JH. Transumbilical laparoscopic appendectomy for acute appendicitis: a reliable one-port procedure. *Surg Endosc* 2011;25:1115-20.
19. Lee JS, Hong TH, Kim JG. A comparison of the periumbilical incision and the intraumbilical incision in laparoscopic appendectomy. *J Korean Surg Soc* 2012;83:360-6.
20. Rajkhowa K, Gogoi M, Baruah. Periumbilical Incision versus Intraumbilical Incision for Laparoscopic Appendectomy: A Randomized Comparative Study. *Int J Scientific Study* 2016;4(8).

# Frequency of Response with Eltrombopag in Patients with Persistent Immune Thrombocytopenia

Amna Arooj<sup>1</sup>, Madiha Islam<sup>2</sup>, Mona Aziz<sup>3</sup> and Sadia Taj<sup>4</sup>

## ABSTRACT

**Objective:** Determine the frequency of response with eltrombopag in persistent immune thrombocytopenia.

**Design of Study:** Descriptive case series study

**Place and Duration of Study:** This study was conducted at the Department of Hematology, Shaikh Zayed Hospital Lahore from September, 2014 to March, 2015.

**Materials and Methods:** A total of 40 cases of immune thrombocytopenia were included. Socio-demographic data like name, age and sex was taken. Patients were given eltrombopag (25mg/day) for 3 weeks. Platelet count was noted at day 7, day 14 and day 21 of treatment. These tests were performed on hematology analyzer Sysmex XT1800i. Other variables like partial response and no response were also noted.

**Results:** Male patients were 23 (57.5%) while female patients were 17 (42.5%) with mean age was  $32.97 \pm 12.13$  years. The mean platelet count was calculated as  $109.12 \pm 11.29 \times 10^9/L$ . The complete response with eltrombopag in persistent immune thrombocytopenia in 34 (85%) while 6 (15%) had partial response and no cases was recorded with no response.

**Conclusion:** The frequency of response with eltrombopag in persistent immune thrombocytopenia is goods in our population and in future we can use this drug for the management of immune thrombocytopenia.

**Key Words:** Frequency, Persistent immune thrombocytopenia, Eltrombopag

**Citation of articles:** Arooj A, Islam M, Aziz M, Taj S. Frequency of Response with Eltrombopag in Patients with Persistent Immune Thrombocytopenia. Med Forum 2019;30(5):20-22.

## INTRODUCTION

An acquired immune-mediated disorder, Persistent immune thrombocytopenia (ITP), defined as isolated thrombocytopenia (platelet count  $<100 \times 10^9/L$ ) without any obvious underlying or initiating cause that persists for more than 3 months of duration.<sup>1</sup> The prevalence of ITP in adults ranges from 9.5 to 23.6 cases per 1,000,000 per year.<sup>2</sup>

The mainstay of therapy is glucocorticoids followed by splenectomy. Other options that are available for patients with severe illness, are high dose intravenous immunoglobulin and anti-RhD therapy, but are of temporary benefit only. Rituximab, is the drug that shows more durable responses.

<sup>1</sup>. Department of Pathology, Sahiwal Medical College Sahiwal.

<sup>2</sup>. Department of Pathology, M. Islam Medical & Dental College, Gujranwala.

<sup>3</sup>. Department of Hematology & Blood Bank, Shaikh Zayed Medical Complex Lahore.

<sup>4</sup>. Department of Hematology, FMH College of Medicine & Dentistry, Lahore.

Correspondence: Dr. Amna Arooj, Assistant Professor of Pathology, Sahiwal Medical College Sahiwal.

Contact No: 0331-7515457

Email: amnaarooj84@gmail.com

Received: November, 2018

Accepted: February, 2019

Printed: May, 2019

Other drugs like immunosuppressants and cytotoxic agents are less commonly used while danazol may be underutilized.<sup>3</sup> Two novel thrombopoiesis-stimulating agents have been developed that have shown their effect to increase platelet count.<sup>4</sup>

Romiplostim, an injectable thrombopoietin (TPO) peptide agonist and eltrombopag, an oral form of non-peptide thrombopoietin receptor agonist, correcting low platelet count in patients with chronic immune thrombocytopenia.<sup>5</sup>

Thrombopoietin, a cytokine produced in the liver, acts on the thrombopoietin receptors (TPO-R) which are present on the megakaryocytes. As a result, the differentiation of the bone marrow precursor cells occur along the megakaryocytic lineage.<sup>6</sup>

Eltrombopag, in association with metal ion ( $Zn^{2+}$ ) activates the thrombopoietin receptors. Since the interaction between eltrombopag and endogenous thrombopoietin on the the thrombopoietin receptors is non-competitive, their effects are additive.<sup>7</sup> Documented response with eltrombopag in immune thrombocytopenia is 80 to 90%.<sup>8</sup>

Eltrombopag is also being studied in other thrombocytopenic patient populations, including those with hepatitis C, solid tumours, myelodysplastic syndromes, acute myeloid leukaemia and aplastic anaemia.<sup>9</sup>

Eltrombopag is a newly approved drug used in treatment of ITP. It is used when first line therapy fails.

It will provide us with baseline data in our population as well as basis for further research in this regard. No study is available showing its response in Pakistani patients. So we want to see its response in our population.

## MATERIALS AND METHODS

This study that is descriptive case series, was conducted at Hematology Department, Shaikh Zayed Hospital Lahore from 2<sup>nd</sup> September, 2014 to 2<sup>nd</sup> March, 2015 and comprised 40 cases. Patients age >15years, either gender and diagnosed cases of persistent ITP who have completed more than 1 prior drug therapy for immune thrombocytopenia other than eltrombopag were included. All pregnant women with breast feeding to her child, altered renal function and atrial fibrillation were excluded. Patients were given eltrombopag (25mg/day) for 3 weeks. Platelet count was noted at day 7, day 14 and day 21 of treatment. These tests were performed on hematology analyzer Sysmex XT1800i. Other variables like partial response and no response was also noted. The data was entered and analyzed using SPSS-20.

## RESULTS

There were 29 (72.5%) patients between 16-40 years while 11 (27.5%) patients were between 41-60 years with mean age was  $32.97 \pm 12.13$  years. Male patients were 23 (57.5%), while female patients were 17 (42.5%). Thirty four patients (85%) had complete response while 6 patients (15%) had partial response. No case was recorded with absence of response (Table 1).

Mean platelet counts were at day 1 was  $29.3 \pm 8.22 \times 10^9/l$ , day 7 was  $41.5 \pm 9.70 \times 10^9/l$ , day 14 was  $77.7 \pm 11.68 \times 10^9/l$  and day 21 was  $109.12 \pm 11.29 \times 10^9/l$  (Table 2).

Response to eltrombopag was also analyzed among two genders. In Male patients, mean platelet count at Day 1 was  $27.04 \pm 7.88 \times 10^9/l$ , at Day 7 mean platelet count was  $39.73 \pm 8.74 \times 10^9/l$ , at Day 14 mean platelet count was  $78.73 \pm 11.67 \times 10^9/l$  and at Day 21 mean platelet count was  $110.65 \pm 8.58 \times 10^9/l$ .

In Female patients, mean platelet count at Day 1 was  $32.35 \pm 7.88 \times 10^9/l$ , at Day 7 mean platelet count was  $43.88 \pm 10.68 \times 10^9/l$ , at Day 14 mean platelet count was  $76.35 \pm 11.91 \times 10^9/l$  and at Day 21 mean platelet count was  $107.05 \pm 14.18 \times 10^9/l$ .

The mean platelet counts at day 1, showed statistically significant ( $P < 0.05$ ) difference between response of male and female patients while no significant ( $P > 0.05$ ) difference was seen between response of male and female patients at days 7, 14 and 21 (Table 3).

**Table No.1: Demographic status of the patients**

Parameter	No.	%
Age (years)		

16-40	29	72.5
41-60	11	27.5
<b>Gender</b>		
Male	23	57.5
Female	17	42.5
<b>Type of response</b>		
Complete Response	34	85.0
Partial Response	6	15.0
No Response	-	-

**Table No.2: Mean platelet count of persistent immune thrombocytopenia taking eltrombopag before and during therapy (n=40)**

Treatment (day)	Platelet count ( $\times 10^9/l$ )
1	$29.3 \pm 8.22$
7	$41.5 \pm 9.70$
14	$77.7 \pm 11.68$
21	$109.12 \pm 11.29$

**Table No.3: Stratification of mean platelet count of gender according to treatment**

Treatment (day)	Platelet count ( $\times 10^9/l$ )		P value
	Male	Female	
1	$27.04 \pm 7.88$	$32.35 \pm 7.88$	0.04
7	$39.73 \pm 8.74$	$43.88 \pm 10.68$	0.18
14	$78.73 \pm 11.67$	$76.35 \pm 11.91$	0.53
21	$110.65 \pm 8.58$	$107.05 \pm 14.18$	0.32

## DISCUSSION

An acquired immune-mediated disorder, Persistent immune thrombocytopenia (ITP) defined as having isolated thrombocytopenia (platelet count  $< 100 \times 10^9/L$ ) without any obvious underlying and/or initiating cause that persists for more than 3 months of duration.<sup>1</sup> Bussell et al<sup>8</sup> who revealed that response to eltrombopag in immune thrombocytopenia was 80-90% while in the present study it is 85% agreement with the international study. The rise in platelet count  $\geq 50 \times 10^9/l$  or  $\geq 2$  time baseline value is considered response to eltrombopag. Kim and co-workers<sup>10</sup> in a recent trial analyzed in Korean ITP patients, the dose of eltrombopag that is needed to get and maintain safe platelet counts. They recorded that patients who achieved platelet counts  $> 100 \times 10^9/l$  (complete response) were 66.7%, who achieved platelet counts between  $50 \times 10^9/l$  and  $100 \times 10^9/l$  (partial response) were 5.6%, and 27.8% were unable to achieve the target platelet count i.e.  $> 50 \times 10^9/l$  (no response). The present study showed that complete response was seen in 85% and partial response in 15% while absence of response is not seen. In patients who achieved the target platelet count, the median duration of ITP was significantly shorter and concluded that in refractory adult ITP patients, eltrombopag showed excellent treatment outcomes and was well tolerated. The target platelet count was maintained effectively with low-dose eltrombopag.

However, in some patients, especially in longer cases of ITP or who are heavily pre-treated, longer or higher-dose of treatment is required to maintain the target count of platelets.

Saleh et al<sup>11</sup> reported that 79% were white, 15% Asian and 6% belong to other ethnic groups. Reduction in symptoms like bleeding and sustained elevation of platelet counts along with use of ITP medications were observed for prolonged periods of time (months) in many patients, that confirmed the extension of eltrombopag response in the pivotal 6-week and 6-month trials. Overall response is seen in 80–88 % of cases with well tolerated treatment with eltrombopag. This figure closely resembles our study response in 85% of cases.

Cheng et al<sup>12</sup> also reported that 75% were white, 16% were Asian and 10% belonged to other ethnic groups. This study in patients with chronic immune thrombocytopenia during a 6-month periods, compared the once daily eltrombopag response versus placebo. Patients in the eltrombopag group, who showed response to treatment at least once during the study was 79%, in comparison with patients in the placebo group who were 28%. The odds of response to treatment throughout the 6 months period were more in the eltrombopag group patients in comparison with the patients in the placebo group. The results are close to response rate 85% in our study. The findings of our study provide us with baseline data in our population as well as basis for further research in this regard while no local study was available showing its response in Pakistan. We found higher efficacy in our population.

## CONCLUSION

The frequency of response to eltrombopag in persistent immune thrombocytopenia is good in our population and in future we can use this drug for the management of ITP.

### Author's Contribution:

Concept & Design of Study: Amna Arooj  
 Drafting: Madiha Islam  
 Data Analysis: Mona Aziz, Sadia Taj  
 Revisiting Critically: Amna Arooj, Madiha Islam  
 Final Approval of version: Amna Arooj

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. Rodeghiero F, Stasi R, Gernsheimer T. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. *Blood* 2009; 113(11): 2386-93.
2. Abrahamson PE, Hall SA, Tepie FM, Fanny S, Gold M, Logie J. The incidence of idiopathic thrombocytopenic purpura among adults: a population based study and literature review. *Eur J Haematol* 2009;83(2):83-89.
3. Rice L. Treatment of immune thrombocytopenic purpura: focus on eltrombopag. *Biologics* 2009;3: 151-5.
4. Pecci A, Gresele P, Klersy C, Savoia A, Noris P, Fierro T. Eltrombopag for the treatment of the inherited thrombocytopenia deriving from MYH9 mutations. *Blood* 2010;116:5832-7.
5. Bussel JB, Provan D, Shamsi T. Effect of eltrombopag on platelet counts and bleeding during treatment of chronic idiopathic thrombocytopenic purpura: a randomised, double-blind, placebo-controlled trial. *Lancet* 2009;373 (9664):641-8.
6. Sharma V, Randhawa H, Sharma A, Aggarwal S. Eltrombopag – an oral thrombopoietin agonist. *Eur Rev Med Pharmacol Sci* 2012;16:743-6.
7. Erickson-Miller CL, Delorme E, Tian SS, Hopson CB, Landis AJ, Valoret EI, SE. Preclinical activity of eltrombopag (SB-497115), an oral, nonpeptide thrombopoietin receptor agonist. *Stem Cells* 2009; 27:424-30.
8. Bussel JB, Saleh MN, Basey SY, Mayer B, Arning M, Stone NL. Repeated use of eltrombopag in patients with chronic immune thrombocytopenia. *Br J Haematol* 2013;60(4):538-46.
9. Chawla SP, Staddon AP, Messam C, Graham AM, Mostafa Kamel YM. An open label, dose-ranging study to assess the safety, efficacy, and pharmacokinetics of eltrombopag in treating thrombocytopenia in patients with advanced sarcomas receiving doxorubicin and ifosfamide. *J Clin Oncol* 2010; 28(Suppl 15): 334.
10. Kim Y, Lee S, Jeong S, Ahn J, Yang D. Efficacy and safety of eltrombopag in adult refractory immune thrombocytopenia. *Blood Res* 2015; 50(1):19–25.
11. Saleh MN, Bussel JB, Cheng G, Meyer O, Bailey CK, Arning M, Brainsky A. Safety and efficacy of eltrombopag for treatment of chronic immune thrombocytopenia: results of the long-term, open-label EXTEND study. *Blood* 2013; 121(3): 537-45.
12. Cheng G, Saleh MN, Marcher C. Eltrombopag for management of chronic immune thrombocytopenia (RAISE): a 6-month, randomized, phase 3 study. *Lancet* 2011; 377(9763): 393-402.

# Etiology and Presentation of Stroke in Hospitalized Children

Farrukh Saeed, Amna Iqtidar, Farhan Zahoor and Muhammad Asif Siddiqui

## ABSTRACT

**Objective:** This study was aimed to note the main underlying causes and presentation of stroke amongst hospitalized children.

**Study Design:** A retrospective study.

**Place and Duration of Study:** This study was conducted at the Department of Pediatrics, Services Hospital, Lahore from March 2016 to March 2018.

**Materials and Methods:** A total of 62 children admitted with stroke during the study period, aged one to 15 years, having focal acuteneural impairment established by brain imaging, were analyzed. Demographic characteristics including age and gender along with clinical presentation and neuroimaging findings of all the study participants were noted. Etiologies like prenatal diseases, CHD, hematological disorders, trauma as well as infections of CNS were also recorded.

**Results:** Out of a total of 62 children with stroke, 36 (58.1%) were male and 26 (41.9%) female. There were 9 (14.5%) children below the age of 1 years, 36 (58.1%) between 1 to 5 years, 8 (12.9%) from 5 to 10 years and 9 (14.5%) above 10 years of age. Mean age was noted to 4.5 years with standard deviation of 2.4 years. There were 28 (45.2%) children who belonged to urban areas while 34 (44.8%) to rural area. There were 52 (83.9%) children who presented with weakness, 41 (66.1%) with raised intracranial pressure while seizures were seen to be a presenting feature 37 (59.7%). Commonest cause of stroke was noted to be hemorrhagic stroke due to trauma in 22 (35.5%) and vascular disease in 17 (27.4%).

**Conclusion:** Hemorrhagic stroke due to trauma, coagulopathy and vasculopathy were found to be the most common etiologies in children with stroke. Preventive strategies involving measures to address the causes of stroke in children along with early diagnosis and treatment will certainly reduce its burden amongst children.

**Key Words:** Stroke, hemorrhagic stroke, vascular disease, coagulopathy

**Citation of articles:** Saeed F, Iqtidar A, Zahoor F, Siddiqui MA. Etiology and Presentation of Stroke in Hospitalized Children. Med Forum 2019;30(5):23-26.

## INTRODUCTION

Stroke is described as rapid decline of cerebral blood flow that goes on to result in impairment of functions related to brain.<sup>1</sup> In the past few decades, a rise has been noted in the prevalence of stroke around the world. Global incidence of stroke in pediatric population is calculated to be 13 to 16 cases per 100000.<sup>2</sup> In North America, stroke's incidence is estimated to be 2.5-2.7 per 100000 in pediatric population while France represents an incidence of 13 per 100000 cases in children.<sup>3,4</sup>

In the United States, it is estimated to be one of the top ten diseases to be blamed for childhood mortality. Pakistan holds noteworthy share of stroke that is contributing significantly to economic burden as well as

occupancy at healthcare facilities.<sup>5</sup> Mortality rate in children with stroke ranges between 2 to 11% while persistent neurological deficit is recorded in about 70% of pediatric population with stroke.<sup>6</sup>

Diagnosis of stroke in children is not always prompt and in a country like Pakistan, timely access to acute MRI and pediatric anesthesia is not always available all the time. There are no stroke centers of any type of standardized care for strokes in children in our settings. Moreover, it has been observed widely around the world that causes of stroke in children differ clearly as it is different in terms of etiology, physiology as well as natural history when compared to adults.<sup>7</sup> Thrombophilia, sickle cell anemia, infections, acquired or congenital embologenic heart diseases are noted as most common causes of stroke in children. In children, Stroke may go on to cause death while cognitive-motor disabilities as well as seizure spanning long durations (1 day or more) are other important factors to consider while dealing stroke. Congenital heart disease is known to be the commonest risk factor associated with ischemic and hemorrhagic stroke in children.<sup>8</sup> Coagulopathy and thrombophilia are also recorded to be an important risk factor associated with arterial ischemic stroke. In children, metabolic disorders as

Department of Pediatrics Med, Services Hospital, Lahore.

Correspondence: Dr. Farrukh Saeed, Senior Registrar of Pediatrics Medicine, Services Hospital, Lahore.

Contact No: 03457131588

Email: dr.farrukhsaeed@yahoo.com

Received: December, 2018

Accepted: March, 2019

Printed: May, 2019



well as injuries progressing to infarction are not seen frequently but these conditions cannot be overlooked.<sup>9</sup> In the recent years in Pakistan, not much work has been done to find out the underlying causes as well as presentation of stroke in Pediatric population. So, we did this study to note the main underlying causes and clinical features of stroke amongst hospitalized children.

## MATERIALS AND METHODS

This study was a retrospective analysis from March 2016 to March 2018, from Department of Pediatrics, Services Hospital, Lahore. Approval from institutional ethical and research committee was taken for this study. A total of 62 children admitted with stroke during the study period, aged one to 15 years, having focal acuteneural impairment established by brain imaging, were analyzed.

Detailed general physical as well as systemic examination was done. Investigations like peripheral smear, serumelectrolytes, CSF examination and neuroimaging like cranial ultrasound and CT scan were done. Demographic characteristics including age and gender along with clinical presentation and neuroimaging findings of all the study participants were noted. Etiologies like prenatal diseases, CHD, hematological disorders, trauma as well as infections of CNS were also recorded.

## RESULTS

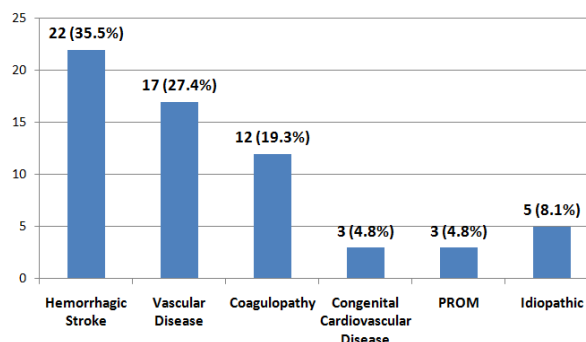
Out of a total of 62 children with stroke, 36 (58.1%) were male and 26 (41.9%) female. Male to female ratio was noted as 1.4/1. There were 9 (14.5%) children below the age of 1 years, 36 (58.1%) between 1 to 5 years, 8 (12.9%) from 5 to 10 years and 9 (14.5%) above 10 years of age. Mean age was noted to 4.5 years with standard deviation of 2.4 years. There were 28 (45.2%) children who belonged to urban areas while 34 (44.8%) to rural area.

**Table No.1: Signs and Symptoms at Presentation Amongst Children with Stroke**

Signs and Symptoms	Cases (%)
Weakness	52 (83.9%)
Hemiplegia / hemiparesis	45 (72.6%)
Monoplegia	7 (11.3%)
Raised Intracranial Pressure	41 (66.1%)
Irritability	30 (48.4%)
Nausea & Vomiting	6 (9.7%)
Headache	5 (8.1%)
Seizures	37 (59.7%)
Fever	38 (61.3%)
Cranial Nerve Palsies	16 (25.8%)
Aphasia	4 (6.5%)
Comatose	15 (25.0%)

There were 52 (83.9%) children who presented with weakness, 41 (66.1%) with raised intracranial pressure while seizures were seen to be a presenting feature 37 (59.7%). Fever was noted to be present in 38 (61.3%) whereas 15 (25.0%) reported in a state of coma.

Commonest cause of stroke was noted to be hemorrhagic stroke due to trauma in 22 (35.5%). Vascular disease, coagulopathy, congenital cardiovascular disease, and premature rupture of the membranes (PROM) were noted in 17 (27.4%), 12 (19.3%), 3 (4.8%), 3 (4.8%) cases respectively whereas 5 (8.1%) cases had idiopathic causes.



**Figure No.1: Causes of Stroke Amongst Children with Stroke**

## DISCUSSION

Stroke contributes significantly towards morbidity and mortality along with causing major restraints to quality of life. Stroke has long been thought to be uncommon amongst children but figures in the last few decades are indicating that its presence is being recognized more around the world.<sup>10,11</sup> We noted 62 cases of stroke amongst children in a study period of 3 years. A study from Ayub Medical College<sup>12</sup> spanning 2 years and 10 months recorded 46 cases whereas if we note the stats 1985 to 1993 from Stroke Registry of France,<sup>13</sup> they documented 28 stroke cases amongst children.

In the present retrospective study, we noted that stroke was more common in males (58.1%) as compared to females. Our results were quite consistent with a recent study from Iran<sup>14</sup> where they found 53% of children having stroke as male. A study from China<sup>15</sup> in 2015 evaluating children with stroke, also noted 60% male in their findings. Pretty similar male to female ration in comparison to our study has also been noted previously where the researchers noted this to be 1.4:1.<sup>16</sup>

In the current work, it was noted that 45 (72.6%) children were below the age of 5 years. Keihani DZ et al from Iran<sup>16</sup> also found that 86% of the children with stroke were less than 6 years of age. Tavassoli A et al<sup>17</sup> in their clinical survey regarding cerebrovascular disease in children found 2 to 5 year old to be the most common age amongst children with stroke. Our results were also comparable to another local study<sup>12</sup> found meanage of onset related to stroke in children was

found to be 3 years while a study from Saudi Arabia<sup>18</sup> having a duration of more than 10 years evaluating 104 children with stroke also found similar findings regarding age of children with stroke.

In this study, we noted 52 (83.9%) children having weakness, 41 (66.1%) raised intracranial pressure, seizures in 37 (59.7%) while 15 (25.0%) reported as comatose. Our results are quite consistent with those of Saima B et al where in a local study<sup>14</sup> analyzing 46 children with stroke, they found limb weakness as presenting feature in 80% while seizures in 61% and coma in 22%. Pediatric Ischemic Stroke Registry of Canada<sup>19</sup> documented hemiparesis in 51% of cases while they also noted seizures to be in 48% children with stroke. Tham EH et al<sup>20</sup> also reported seizures in 58% cases while hemiparesis and altered level of consciousness were found to be 39% each in children with stroke.

Hemorrhagic stroke due to trauma was the most frequent cause of stroke in our study affecting 35.5% children, followed by vascular disease (27.4%) and coagulopathy 19.3% being the other most frequent causes. Hemorrhagic stroke due to trauma has also been noted as the commonest cause affecting 27% cases of stroke in children in a study done in the neighboring Iran.<sup>14</sup> A study done by Gulati et al from India<sup>21</sup> noted head trauma and arterial dissection in 26% cases of children with brain infarction. A study done by Cicconi S and coworkers<sup>22</sup> recorded spontaneous intraparenchymal hemorrhage and nontraumatic subarachnoid hemorrhages as the most common causes of stroke. Vascular disease was found to be another common cause observed in our study, found in 27.4% cases. Keihani DZ et al<sup>14</sup> also found vascular disease in 20% cases with stroke while the same study also noted vasculopathy to be in 24% of cases.

We found coagulopathy in 19.3% of children which is very near to the findings from Iran<sup>14</sup> while our results were different from another study conducted in Iran<sup>17</sup> where they found prothrombotic disorders to be in only 8% of children with stroke. Higher contribution of prothrombotic disorders ranging around 50% have also been noted in the past in children with stroke.<sup>23</sup>

Past few years have seen a rapid advancement regarding stroke in children in the shape of research as well as trials assessing clinical care. Lot of efforts are being put to better understand the underlying pathology to devise appropriate strategies for the right management. Likewise, it has also been advocated that more detailed in to cerebral arteriopathies will surely give us more insight to form better treatments. Early identification of risk factors and underlying pathologies regarding stroke in pediatric population is the best way to handle this problem.<sup>24</sup>

## CONCLUSION

Hemorrhagic stroke due to trauma, coagulopathy and vasculopathy were found to be the most common etiologies in children with stroke. Preventive strategies involving measures to address the causes of stroke in children along with early diagnosis and treatment will certainly reduce its burden amongst children.

### Author's Contribution:

Concept & Design of Study:	Farrukh Saeed
Drafting:	Amna Iqtidar
Data Analysis:	Farhan Zahoor, Muhammad Asif Siddiqui
Revisiting Critically:	Farrukh Saeed, Amna Iqtidar
Final Approval of version:	Farrukh Saeed

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. Rosa M, De Lucia S, Rinaldi VE, Le Gal J, Desmarest M, Veropalumbo C, et al, Titomanlio. Pediatric arterial ischemic stroke: acute management, recent advances and remaining issues. *Ital J Pediatr* 2015;41:95.
2. Mallick AA, O'Callaghan FJ. The epidemiology of childhood stroke. *Eur J Paediatr Neurol* 2010; 14(3):197-205.
3. Schoenberg BS, Mellinger JF, Schoenberg DG. Cerebrovascular disease in infants and children: a study of incidence, clinical features, and survival. *Neurol* 1978;28:763-8.
4. Broderick J, Talbot GT, Prenger E, Leach A, Brott T. Stroke in children within a major metropolitan area: the surprising importance of intracerebral hemorrhage. *J Child Neurol* 1993;8:250-5.
5. Chung B, Wong V. Pediatric stroke among Hong Kong Chinese subjects. *Pediatrics* 2004;114(2): e206-12.
6. Bernard TJ, Goldenberg NA, Armstrong-Wells J, Amlie-Lefond C, Fullerton HJ. Treatment of childhood arterial ischemic stroke. *Ann Neurol*. 2008;63(6):679-96.
7. The Epidemiology of Stroke in a Developing Country (Pakistan). *J Neurol Stroke* 2018;8(1): 00275.
8. DeVeber G. Arterial ischemic strokes in infants and children: an overview of current approaches. *Semin Thromb Hemost* 2003;29:567-573.
9. Mandalenakis Z, Rosengren A, Lappas G, Eriksson P, Hansson P, Dellborg M. Ischemic stroke in children and young adults with congenital heart disease. *J Am Heart Assoc* 2016; 5:e003071.

10. Stroke Association. The nation Stroke statistics January 2017. Together we can conquer stroke. Zh Nevrol Psikhiatr Im S SKorsakova 2003;(Suppl 8): 4-9.
11. Wang W, Jiang B, Sun H, Ru X, Sun D, et al. Prevalence, Incidence and Mortality of Stroke in China: Results from a Nationwide Population-Based Survey of 480, 687 Adults. *Circulation* 2017;35(8): 759-771.
12. Saima B, Syed YH, Syed RA, Sadia B, Tahir S. Siddiqui. Childhood strokes: epidemiology, clinical features And risk factors Ayub Med Coll Abbottabad 2011;23(2):69-71.
13. Giroud M, Lemesle M, Gouyon KB, Nivelon JL, Milan C, Dumas R. Cerebrovascular disease in children under 16 years of age in the city of Dijon, France: a study of incidence and clinical features from 1985 to 1993. *J Clin Epidemiol* 1995;48: 1343–8.
14. Keihani DZ, Noori SF, Akbari AP, Farahani Z, Tehrani F, Shariat M. Incidence and Etiology of Stroke among Hospitalized Children: A Case-Series Study. *Iran J Child Neurol*. Winter 2019; 13(1): 65-70.
15. Gao YB. Risk factors and imaging characteristics of childhood stroke in China. *J Child Neurol* 2015;30(3):339-43.
16. Shi KL, Wang JJ, Li JW, Jiang LQ, Mix E, Fang F, et al. Arterial ischemic stroke: experience in Chinese children. *Pediatr Neurol* 2008;38(3): 186-90.
17. Tavassoli A, Ghofrani M. Clinical Survey of Cerebrovascular Disease in Children. *Iran J Pediatr* 2008; 18(Suppl 1):53-58.
18. Salih MA, Abdel-Gader AM, Al-Jarallah AA, Kentab AY, Alorainy IA, Hassan HH, et al. Stroke in Saudi children: Epidemiology, clinical features and risk factors. *Saudi Med J* 2006;27 Suppl 1:S12-20.
19. de Veber G. The Canadian Pediatric ischemic stroke study group. Canadian pediatric ischemic stroke registry: analysis of children with arterial ischemic stroke. *Ann Neurol* 2000;48:526.
20. Tham EH, Tay SK, Low PS. Factors predictive of outcome in childhood stroke in an Asian population. *Ann Acad Med Singapore* 2009;38 (10):876-81.
21. Gulati S, Karla V. Stroke in children. *Indian J Pediatr* 2003; 70:639-648.
22. Ciccone S, Cappella M, Borgna-Pignatti C. Ischemic Stroke in infants and children: practical management in emergency. *Stroke Res Treat* 2011; 2011:736965.
23. Simma B, Martin G, Müller T, Huemer M. Risk factors for pediatric stroke: consequences for therapy and quality of life. *Pediatr Neurol* 2007; 37(2):121-6.
24. Kirton A, deVeber G. Paediatric stroke: pressing issues and promising directions. *The Lancet Neurol* 2015;14(1):92-102.

# Sickle Cell Trait and Disease in Anaemic Patients, Visiting Health Care Centre, KFU, Al Hasa

Hussain Mohammed Alhiwaishil<sup>1</sup>, Ashok Kumar<sup>2</sup>, Ali Hussain Alrufayi<sup>3</sup>, Ali Abdulkarim Alsuliman<sup>4</sup> and Chetan Lal<sup>2</sup>

## ABSTRACT

**Objective:** To determine the frequency of sickle cell trait and disease in anaemic patients of Al Hasa.

**Study Design:** Descriptive / cross-sectional study

**Place and Duration of Study:** This study was conducted at the At health Care Centre, King Faisal University, Al Hasa, from June to November 2016.

**Materials and Methods:** Anaemic patients, diagnosed by blood complete picture, were included in the study. Total 638 anaemic patients were investigated for sickle cell trait and disease, which consisted of 230 children (100 males and 130 females), and 408 adults (210 males and 198 females). The blood samples of these patients were analyzed by using both, the sickle cell screening kit and the haemoglobin electrophoresis. The data were analysed by using SPSS 18.

**Results:** 80 (12.5%) out of 638 investigated patients were positive for sickle cell trait, among which 32 were children (10 males and 22 females) and 48 were adults (26 males and 22 females). 20 (3.1%) out of 638 investigated patients were positive for sickle cell disease, among which 6 were children (1 male and 5 females) and 14 were adults (10 males and 4 females).

**Conclusion:** We found a significant frequency of sickle cell trait and disease in anaemic patients of our region Al Hasa, which indicates the urgent need of screening and counselling programs in this region to prevent further transmission of this familial disorder to new generations.

**Key Words:** Anaemia, frequency, sickle cell disease, sickle cell trait

**Citation of articles:** Alhiwaishil HM, Kumar A, Alrufayi AH, Alsuliman AA, Lal C. Sickle Cell Trait and Disease in Anaemic Patients, Visiting Health Care Centre, KFU, Al Hasa. Med Forum 2019;30(5):27-30.

## INTRODUCTION

Sickle cell disorder is a group of inherited disorders of red blood cells which contain abnormal haemoglobin called sickle haemoglobin (Hb S).<sup>1</sup> Individuals who have both copies of abnormal haemoglobin genes (Hb SS) are termed as sickle cell disease (SCD) patients. Individuals who are affected with one copy of sickle haemoglobin and the other copy of normal haemoglobin (Hb AS) are termed as sickle cell carriers.

<sup>1</sup>. Department of Medicine, King Faisal University, Al Hasa, Saudi Arabia.

<sup>2</sup>. Department of Medicine, Aimst University, Malaysia.

<sup>3</sup>. Department of Microbiology, Federal Postgraduate Medical Institute, Lahore.

<sup>4</sup>. Department of Pharmacy, Qassim University, Buraidah, Saudi Arabia.

Correspondence: Hussain Mohammed Alhiwaishil, College of Medicine, King Faisal University, Al Hasa, Saudi Arabia.  
Contact No: +966542509525  
Email: prephsor@hotmail.com

Received: October, 2018  
Accepted: February, 2019  
Printed: May, 2019

The carrier state is often referred to as sickle cell trait (SCT). The SCD patients may present with diverse clinical manifestations, ranging from asymptomatic with mild anaemia to systemic illnesses which are caused due to haematological and vaso-occlusive events and infectious crises.<sup>2,3</sup> SCD patients may also develop various life threatening systemic illnesses, such as, pulmonary hypertension, cardiac failure,<sup>4</sup> renal diseases<sup>5</sup> and skull bone infarction with epidural haematoma.<sup>6</sup> Many SCD patients suffer from leg ulcers<sup>7</sup> and acute & chronic bone pains, which result due to sickle cell crisis.<sup>8</sup>

Sickle cell disorder is considered as a major public health problem in certain parts of the world which include the Middle East, sub-Saharan Africa, India, Eastern coast of the America and Western Europe.<sup>9</sup> In the middle East, Kingdom of Saudi Arabia (KSA) is well-known for its high prevalence of familial haemoglobinopathies, and the sickle cell disorder is one of those. It is prevalent throughout the KSA, being most common in the Eastern and Southern provinces.<sup>10</sup> The data on this disorder is scarce and back-dated due to very limited research in KSA. Due to lack of knowledge, many new generations are born with this disorder. Due to associated complicated clinical outcomes of this disorder, the families of the patients

spend a huge amount of their earnings to the hospitals. Therefore, it is very important to know the updated prevalence of this disorder.

In the current study, we determined the frequency of this disorder in anaemic patients of Al Hasa, which is the largest city in Eastern province of KSA. These patients belonged to King Faisal University, which included the staff, students and their families. Hence, literate people and their families were included in this study. We chose the literate group to know the prevalence and awareness among these people, who would further make awareness and do counseling to the common people of this region to control the further transmission of this familial disorder to the new upcoming generations.

## MATERIALS AND METHODS

This prospective study was conducted at Health Care Center of King Faisal University (KFU), Al Hasa city from June to November 2016. For ethical consideration, we obtained the ethical approval from ethical committee of KFU under the letter No. 9/31/89. The patients' consent was taken at the Health Care Center, KFU. The patients belonged to KFU, which included the staff, students and their families. Total 638 anaemic patients, diagnosed by performing blood complete picture (blood C.P) at Health Care Center of KFU were included in the study. Patients under the age of 14 years were considered children. The blood samples were analyzed first by using sickle cell screening test kit 'HbS-Solubility Screening' (Helena Bioscience Europe), and then confirmed by performing haemoglobin electrophoresis using BIO RAD System-D10. The controls, provided by the manufacturer, were run in parallel.

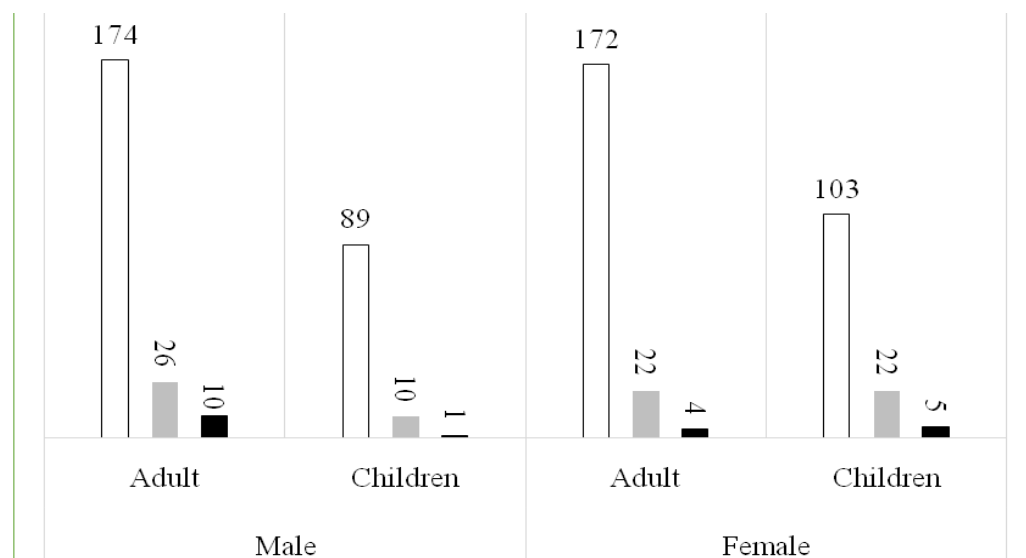
Briefly, for screening, 2ml venous blood was collected in an EDTA bottle and mixed gently. From this sample, 20µl blood was taken in a test tube and 2ml reagent mixture was added and mixed well as per the kit manufacturer's instruction. The mixture was allowed to stand for 3-5 minutes and examined for turbidity. The positive and the negative controls were run in parallel with the test samples. A turbid reaction denoted a positive result (i.e., the lines on the provided viewing chart could not be seen when viewed through the sample tube). A negative result was obtained with a clear reaction (i.e., the lines on the viewing chart were clearly visible when viewed through the sample tube). Furthermore, to differentiate between SCT and SCD, the test tubes were centrifuged at 1200g without brake for 5 minutes. Red precipitate on top of yellow solution indicated homozygous HbS (sickle cell disease), while red precipitate on top of pink solution indicated heterozygous HbS (sickle cell trait).

For further confirmation of SCT and SCD, the positive samples were analysed by performing haemoglobin electrophoresis, using BIO RAD System-D10, which confirmed the final diagnosis of SCT and SCD.

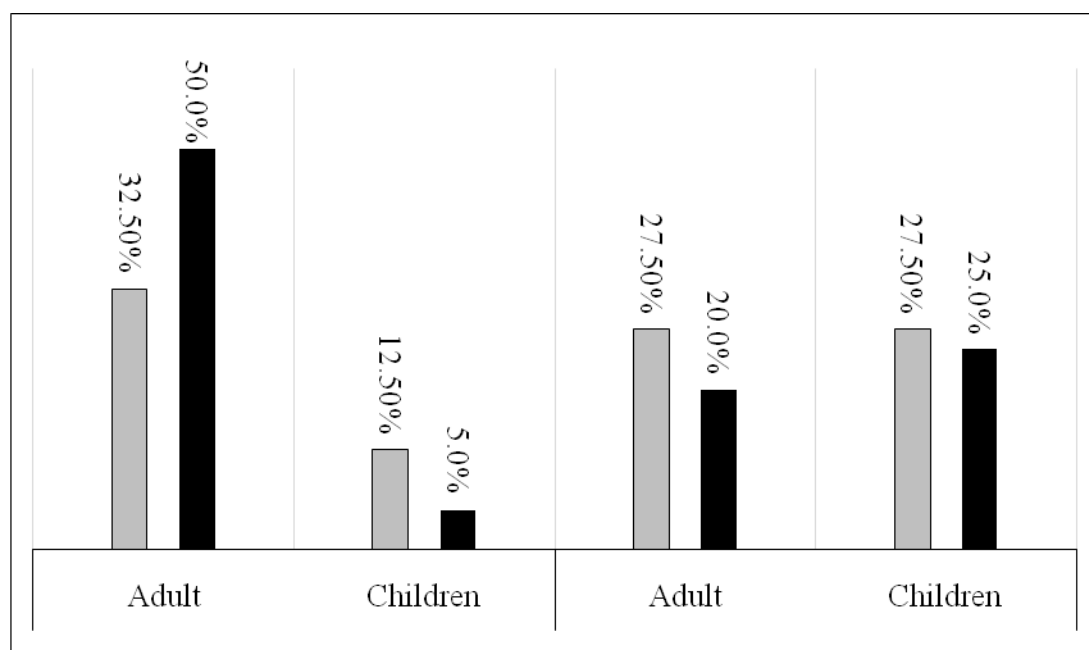
The data were analysed by using SPSS 18.

## RESULTS

Among total 638 investigated anaemic patients, 80 (12.5%) were positive for SCT and 20 (3.1%) for SCD. Among those 80 positive patients for SCT, 32 were children (10 males and 22 females), and 48 were adults (26 males and 22 females). From 20 positive patients for SCD, 6 were children (1 male and 5 females) and 14 were adults (10 males and 4 females). The prevalence of SCT and SCD in number of patients, based on age and gender groups is described in Figure 1.



**Figure No.1.**Number of patients with sickle cell trait (SCT) and sickle cell disease (SCD), based on age and gender groups. Grey bar: SCT, Black bar: SCD, White bar: Negative for SCT & SCD.



**Figure No.2: Percentage of patients with sickle cell trait (SCT) and sickle cell disease (SCD) among individual groups. Grey bar: SCT, Black bar: SCD.s**

The prevalence of SCT and SCD in percentage among individual group is described in Figure 2. Thus, we had 4 groups, i.e., female children, female adults, male children and male adults. The highest prevalence of SCD was found among male adults, which was 10 among 210 total male adults (4.7%). The second most common group was female children, which was 5 among total 130 children (3.8%). The third common group was female adults, which was 4 among total 198 female adults (2%), and the fourth group was male children which was 1 among total 100 male children (1%).

## DISCUSSION

In this study, we investigated the frequency of SCD and SCT among anaemic patients who belonged to the literate people and their families of KFUPM, Al Hasa. It was quite surprising that the frequency of this disorder was high among even literate people. We determined significant frequency of this disorder, i.e., 3.1% SCD and 12.5% SCT among our investigated anaemic patients. Overall, we did not find a significant difference in the frequency among individual group, based on age and gender. This is justifiable with the fact that this is an autosomal disorder which affects the both genders equally and the patients may be diagnosed at early or later stage of life. Similarly, another study also reported no significant difference in the frequency of this disorder among various groups.<sup>11, 12</sup> Saudi Arabia is a large country with approximately 32 million population, living in an area of 2,149,690 km<sup>2</sup>. The data on this disorder among Saudi population is scattered

and back dated. Al-Qurashi<sup>11</sup> reported a prevalence of SCD in five main regions of Saudi Arabia, which was 0.06% in Central, 0.12% in Western, 1.45% in Eastern, 0.0% in Northern, and 0.24% in Southern regions. Another study in KSA also showed almost the same prevalence for SCD (0.26%) and for SCT (4.2%).<sup>13</sup> Ziad Ahmed<sup>14</sup> reported overall 0.2% prevalence of SCD and 4.3% of SCT in KSA. An old data of 1998 from Al Hasa region, reported by Nasserullah<sup>15</sup> showed considerable difference in prevalence of this disorder among neonates. He reported the prevalence of 2.35% for SCD and 28.21% for SCT in Qatif city, and 1.08% for SCD and 20.02% for SCT in Al Hasa city. A study on the screening of sickle cell disorder in 2004 showed higher prevalence of this disorder in our region than the other regions of KSA, which was 1.2% for SCD and 17% for SCT.<sup>16</sup>

On the basis of general prevalence, our results slightly differ from other studies conducted in Al Hasa region. As we chose a restricted group of literate people and their families, it was surprising that the prevalence of this disorder was even higher. Various factors may be possible for this, for example, lack of awareness, large family size and consanguineous marriages as many of the patients gave this history. These factors were previously described as the possible causes of sickle cell disorder in KSA.<sup>17</sup> Although our study was conducted on a relatively smaller number of patients in comparison to the other large sample-size studies, this prevalence is highly significant because only the literate people and their families were included and these people visited the Health Care Center just in 2016. Therefore, our updated findings indicate that there is a

an urgent need to organize the awareness, screening and genetic counseling programs of this disorder not only among the literate people, but also in whole Al Hasa region so that further transmission of this inherited disorder to the next generations can be avoided.

## CONCLUSION

We found a significant frequency of sickle cell disorder among literate people and their families. Our research recommends the urgent need of awareness, screening and counselling programs of this disorder on higher level in Al Hasa region in order to prevent the further transmission of this disorder to the next generations.

**Acknowledgement:** We are thankful to the staff of healthcare center, King Faisal University and Dr Hany Aly Hassan for the technical support.

### Author's Contribution:

Concept & Design of Study:	Hussain Mohammed Alhiwaishil
Drafting:	Ashok Kumar, Ali Hussain Alrufayi
Data Analysis:	Ali Abdulkarim Alsuliman, Chetan Lal
Revisiting Critically:	Hussain Mohammed Alhiwaishil, Ashok Kumar
Final Approval of version:	Hussain Mohammed Alhiwaishil

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. Rees DC, Williams TN, Gladwin MT. Sickle-cell disease. *The Lancet* 2010;376(9757):2018-31.
2. El-Hazmi MA. Clinical and haematological diversity of sickle cell disease in Saudi children. *J Tropical Pediatr* 1992;38(3):106-12.
3. Panepinto JA, Pajewski NM, Foerster LM, Sabnis S, Hoffmann RG. Impact of family income and sickle cell disease on the health-related quality of life of children. *Quality of Life Res* 2009;18(1):5.
4. Klings ES, Machado RF, Barst RJ, Morris CR, Mubarak KK, Gordeuk VR, et al. An official American Thoracic Society clinical practice guideline: diagnosis, risk stratification, and management of pulmonary hypertension of sickle cell disease. *Am J Respiratory and Critical Care Med* 2014;189(6):727-40.
5. Bolarinwa R, Akinlade K, Kuti M, Olawale O, Akinola N. Renal disease in adult Nigerians with sickle cell anemia: a report of prevalence, clinical features and risk factors. *Saudi J Kidney Dis Transplant* 2012;23(1):171.
6. Arends S, Coebergh JA, Kerkhoffs JL, van Gils A, Koppen H. Severe unilateral headache caused by skull bone infarction with epidural haematoma in a patient with sickle cell disease. *Cephalalgia* 2011;31(12):1325-8.
7. Delaney K-MH, Axelrod KC, Buscetta A, Hassell KL, Adams-Graves PE, Seamon C, et al. Leg ulcers in sickle cell disease: current patterns and practices. *Hemoglobin* 2013;37(4):325-32.
8. Taylor LEV, Stotts NA, Humphreys J, Treadwell MJ, Miaskowski C. A review of the literature on the multiple dimensions of chronic pain in adults with sickle cell disease. *J Pain and Symptom Manage* 2010;40(3):416-35.
9. Piel FB, Patil AP, Howes RE, Nyangiri OA, Gething PW, Dewi M, et al. Global epidemiology of sickle haemoglobin in neonates: a contemporary geostatistical model-based map and population estimates. *The Lancet* 2013;381(9861):142-51.
10. El-Hazmi MA. Heterogeneity and variation of clinical and haematological expression of haemoglobin S in Saudi Arabs. *Acta haematologica* 1992;88(2-3):67-71.
11. Al-Qurashi MM, El-Mouzan MI, Al-Herbish AS, Al-Salloum AA, Al-Omar AA. The prevalence of sickle cell disease in Saudi children and adolescents. A community-based survey. *Saudi Med J* 2008;29(10):1480-3.
12. Kamble á, Chaturvedi P. Epidemiology of sickle cell disease in a rural hospital of central India. *Ind Pediatr* 2000;37(4):391-6.
13. Al-Odaib AN, Abu-Amro KK, Ozand PT, Al-Hellani AM. A new era for preventive genetic programs in the Arabian Peninsula. *Saudi Med J* 2003;24(11):1168-75.
14. Memish ZA, Saeedi MY. Six-year outcome of the national premarital screening and genetic counseling program for sickle cell disease and  $\beta$ -thalassemia in Saudi Arabia. *Annals of Saudi Med* 2011;31(3):229.
15. Nasserullah Z, Al AJ, Abu HS, Al GQ, Al SN, Al AA, et al. Neonatal screening for sickle cell disease, glucose-6-phosphate dehydrogenase deficiency and  $\alpha$ -thalassemia in Qatif and Al Hasa. *Annals Saudi Med* 1998;18(4):289-92.
16. AlHamdan NA, AlMazrou YY, AlSwaiddi FM, Choudhry AJ. Premarital screening for thalassemia and sickle cell disease in Saudi Arabia. *Genetics Med* 2007;9(6):372.
17. El-Mouzan MI, Al-Salloum AA, Al-Herbish AS, Qurachi MM, Al-Omar AA. Regional variations in the prevalence of consanguinity in Saudi Arabia. *Saudi Med J* 2007;28(12):1881-4.

# Prevalence of Anxiety and Depression among the Patients Attending Surgical Ward at Public Sector Tertiary Care Hospitals in Karachi

Atif Mahmood<sup>1</sup>, Atif Jawad<sup>2</sup>, Ali Maqbool<sup>3</sup>, Hamza Akhtar<sup>5</sup>, Safdar Ali<sup>5</sup>  
and Faria Khan<sup>4</sup>

## ABSTRACT

**Objective:** To highlight the prevalence of depression and anxiety among patients admitted in a surgical ward of a hospital.

**Study Design:** Cross-sectional study

**Place and Duration of Study:** This study was conducted at the Department of Surgery at Major Tertiary Care Hospitals in Karachi, from March 2018 to September 2018.

**Materials and Methods:** A written informed consent was obtained from each and every patient. A total of 250 questionnaires were distributed of which 210 were returned (Response rate = 84%). But only 198 were complete and thus included in the study. Patients were enrolled by non-probability convenient sampling majority of which were postoperative (n=178). The patients of both sexes who were greater than 15 years of age were included in the study. The Urdu version of Hospital Anxiety and Depression Scale (HADS) was used to measure the severity of anxiety and depression. The score obtained from each patient was used to categorize non-cases (0-7), mild anxiety and mild depression (8-11), moderate anxiety and moderate depression (12-16) and severe anxiety and severe depression (17 and above) cases.

**Results:** The studied patients comprised of 144 (72.7%) males and 54 (27.3%) females. The mean age of the patients was  $31.36 \pm 12.31$ . The mean score of HADS anxiety was found to be  $8.49 \pm 3.47$  whereas for depression, the mean score was  $8.44 \pm 3.39$ . Out of 198, 60 patients were identified as non-cases of anxiety and 73 as non-cases of depression whereas 138 and 125 were determined to be cases of anxiety and depression respectively. The duration of the disease was found to be significantly associated with the HADS scores for anxiety and depression (p value= <0.001).

**Conclusion:** The study was conclusive that staying in hospital and undergoing a surgical procedure does produce anxiety and depression in otherwise healthy individuals and it was also found that duration of disease had a significant impact on the psychological state of the patient.

**Key Words:** HADS, Anxiety, Depression, Surgical procedures. Hospital anxiety

**Citation of articles:** Mahmood A, Jawad A, Maqbool A, Akhtar H, Ali S, Khan F. Prevalence of Anxiety and Depression Among the Patients Attending Surgical Ward at Public Sector Tertiary Care Hospitals in Karachi. Med Forum 2019;30(5):31-35.

## INTRODUCTION

Depression is a condition in which a person feels discouraged, sad, hopeless, unmotivated, or disinterested in life in general. Depression is the most

common psychiatric disorder and is common in hospitalized patients<sup>1,2</sup>. Depression and anxiety are approximated to effects about 480 million people worldwide<sup>1,3,4</sup>. Most developing countries including Pakistan have high ratio of depression and anxiety due to rapid growth of population, lack of basic facilities as a result of low socio economic level. Psychological disorders are not only related to a poor adjustment to hospitalization distress<sup>5</sup>, but is associated with adverse events and unsatisfactory outcomes.<sup>2</sup>

Admission to hospital and the prospect of surgery is accepted as extremely anxiety-provoking resulting in behavioral and cognitive sequel which can have far reaching effects on recovery. Studies have explored the relationship between psychological factors and post-operative anxiety, leaving depression relatively unexplored<sup>6</sup>.

The objective of this study was to study the prevalence of depression and anxiety among post-operative

<sup>1</sup>. Department of Physiology / Prosthodontics<sup>2</sup> / Oral Biology<sup>3</sup> / Anatomy<sup>4</sup>, Bhitai Dental and Medical College, Mirpurkhas

<sup>5</sup>. Department of Surgery, SMBBMC, Lyari.

Correspondence: Dr. Atif Jawad, Associate Professor of Prosthodontics, Bhitai Dental and MC, Mirpurkhas.  
Contact No: 0300-8544867  
Email: atif\_jawad@hotmail.com

Received: December, 2018  
Accepted: March, 2019  
Printed: May, 2019



patients of the surgical ward of public sector tertiary care hospitals and also to see its association with duration of disease using the hospital anxiety and depression scale (HADS).

## MATERIALS AND METHODS

This cross-sectional study was conducted in the post-operative patients of department of Surgery at major tertiary care hospitals in Karachi, from March 2018 to September 2018. A total of 250 questionnaires were distributed of which 210 were returned (Response rate = 84%). But only 198 were complete and thus included in the study. Patients were enrolled by non-probability convenient sampling majority of which were postoperative (n=178). The severity of anxiety and depression was determined by the Hospital Anxiety and Depression Scale (HADS)(7). The patients of both sexes who were greater than 15 years were included in the study and they were divided into four groups (I=15-25 years, II=26-40 years, III=41-55 years, IV=>55years), furthermore age was also asked as a continuous variable. The patients fulfilling inclusion criteria were administered Urdu version of Hospital Anxiety and Depression Scale.

HAD Scale was basically designed for detecting the states of hospital acquired anxiety and depression. It is considered to be effective in determining the emotional problems among the admitted patients. In 1983, this scale was invented by Zigmond and Snaith and it consists of 14 questions. It is a self-report measure for anxiety and depression used in clinical practice(7). The score obtained from each patient was used to categorize non-cases (0-7), mild anxiety and mild depression (8-11), moderate anxiety and moderate depression (12-16) and severe anxiety and severe depression (17 and above).

Statistical Package for Social Sciences (SPSS) (version 17) was used for the analysis of the data. Frequencies tables and bar chart was drawn to show the distribution of the variables. Chi square test was used to determine the association between the duration of disease and depression and anxiety. Written informed consent was taken from each and every patient and anonymity of the data was ensured. The study was approved from the Ethics Review Committee (ERC) of Bhitai Dental and Medical College, Mirpurkhas

## RESULTS

Out of the 198 patients who returned the completely filled questionnaire, 144 (72.7%) were males and 54 (27.3%) females. Minimum age of presentation was 19 years and maximum age was 65 years; mean age was  $31.36 \pm 12.3$ . Most of our patients (n=81, 40.9 %) were among the age group of 15-25 years. (Table I)

The educational status of the enrolled patients was mixed. n=41 (20.7%) were illiterate, n=30 (15.7%) had primary education, n=46 (23.2%) had secondary

schooling, n=57 (28.8%) were intermediate whereas n=24 (12.1%) were graduate. (Table I)

Majority of the patients were employed (n=90, 45.5%). Majority of the patients had the illness for less than 3 years (n= 142, 72.7%). (Table I) The mean score of HADS anxiety was found to be  $8.49 \pm 3.47$  whereas for depression, the mean score was  $8.44 \pm 3.39$ . Out of 198, 138 and 125 subjects were identified as cases of anxiety and depression respectively. (Table 2)

The association of duration of disease with HADS anxiety scores showed that the patients with disease for less than 3 years were mostly found to be border line n=61 (43.0%), n=50 (35.2%) were non-cases, n=31 (21.8%) were moderate and none of the patient was found to be severe. The patients with duration of disease from 3-5 years were mostly found to be borderline (n=16, 35.6%), n=12 (26.7%) were moderate, n=10 (22.2%) were non-cases, n=7 (15.6%) were found to have severe anxiety. While among those patients who had disease for greater than 5 year were shown to be severely anxious (n=10, 90.9%), n=1 (9.1%) was found to be moderate but none of the patients with prolonged history of disease were non case or border line. Mean HADS score anxiety was found to  $8.49 \pm 3.47$ ; p value was highly significant  $<0.001$ . (Table 3)

**Table No.I: Demographics of the studied subjects (N=198)**

Parameters Studied	Classification	Frequency	%tage
Age in groups (years)	15-25	81	40.9
	26-40	78	39.4
	41-55	31	15.7
	>55	8	4.0
Gender	Male	144	72.7
	Female	54	27.3
Duration of Disease (years)	Less than 3 years	142	71.7
	3-5 years	45	22.7
	Greater than 5 years	11	5.6
Educational Status	Illiterate	41	20.7
	Primary	30	15.2
	Secondary	46	23.2
	Intermediate	57	28.8
	Graduate	24	12.1
Occupational Status	Unemployed	56	28.3
	Employed	90	45.5
	Student	47	23.7
	Self employed	5	2.5

The association of duration of disease with HADS depression score patients for patients with disease less than 3 years were mostly found to be non-cases (n=61, 43.0%), n=54 (38.0%) were borderline, n=25 (17.6%)

were moderate, n=2 (1.4%) had severe depression. And those with duration of disease in between 3-5 years were mostly (n=18, 40%) border line, n=12 (26.7%) were non cases, n=10 (22.2%) were moderate, n=5 (11.1%) were found to have severe depression. While patients with duration of disease greater than 5 year n=9 (81.8%) of them were severely depressed, n=2 (18.2%) were border line and none of them were moderate and non-cases. Mean HADS score depression found to be  $8.44 \pm 3.39$ , p value was highly significant <0.001. (Table 4)

**Table No.2: Descriptive Statistics of Studied variables**

Study Variables	Mean ( $\pm$ SD)	95% CI	Range (Min – Max)
Age (in years)	31.36 (12.31)	29.64 – 33.09	53 (12-65)
HADS Scoring Anxiety	8.49 (3.47)	8.0 – 8.98	14 (1-15)
HADS scoring Depression	8.44 (3.39)	7.96- 8.91	20 (0-20)

**Table No.3: Association of HADS Anxiety Scores with Duration of the disease**

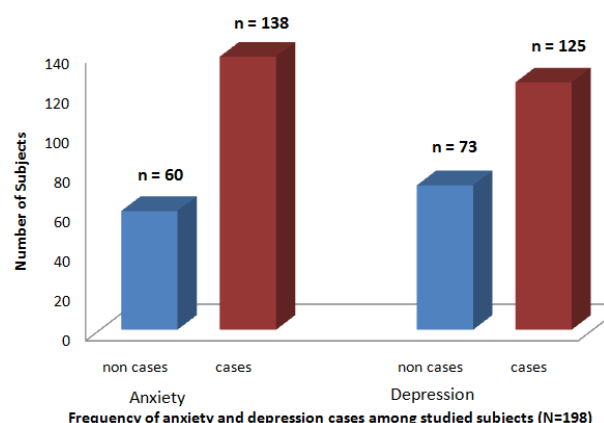
		HADS Anxiety Scores									P value*
		Non Case		Borderline		Moderate		Severe		n	
		n	%	n	%	N	%	n	%		
Duration of the Disease	Less than 3 yrs.	50	35.2	61	43.0	31	21.8	0	0	142	0.000
	3 – 5 years	10	22.2	16	35.6	12	26.7	7	15.6	45	
	Greater than 5 yrs.	0	0	0	0	1	9.1	10	90.9	11	
	Total	60	30.3	77	38.9	44	22.2	17	8.6	198	

\*p value less than 0.05 = significant, less than 0.01= very significant, less than 0.001=highly significant

**Table No.4: Association of HADS Depression Scores with Duration of the disease**

HADS Depression scores											
		Non Case		Borderline		Moderate		Severe		n	P value*
		n	%	n	%	N	%	n	%		
Duration of the Disease	Less than 3 yrs.	61	43.0	54	38.0	25	17.6	2	1.4	142	
	3 – 5 years	12	26.7	18	40.0	10	22.2	5	11.1	45	
	Greater than 5 yrs.	0	0	2	18.2	0	0	9	81.8	11	
	Total	73	36.9	74	37.4	35	17.7	16	8.1	198	

\*p value less than 0.05 = significant, less than 0.01= very significant, less than 0.001=highly significant



**Figure No.1: Frequency of anxiety and depression cases among the studied subjects (N=198)**

## DISCUSSION

The study showed that the prospect of surgery in itself was a very stressful state, after effects of which caused marked increase in anxiety and depression which increased with increased duration of disease or probably with increased duration of hospital stay as well. According to the previous studies, the ratio increases remarkably in hospitalized elderly patients<sup>3,4</sup>. The

activities of daily living were also affected in certain patients due to symptoms of after surgery and long stay in the hospitals<sup>8,9,10</sup>.

A study conducted by Gillies et al.(1999) studied 351 adolescents undergoing elective surgery. They were surprised to find that although depression on the Hospital Anxiety and Depression scale was less than 4% pre-operatively and it rose to 29% post-operatively, and patients with depression were significantly more likely to experience moderate to severe pain post-operatively. This study does not study the difference between the depression and anxiety score in pre and post-operative states but all mean scores of depression and anxiety found in the study showed moderate on both<sup>11</sup>.

Another study was conducted in Silakot, Pakistan in 2017<sup>12</sup>. The compared the anxiety and depression in patients about to undergo elective or emergency surgery by dividing them in to two groups and recorded anxiety and depression at week 0 and 3. Their findings showed that anxiety was present in only 10.93% subjects at week 0 and 29.87% at week 3 among those undergoing elective surgery while depression was present in 9.98% and 32.1% respectively at week 0 and 3 in similar patients. This comparison was lacking in the current

study and is a good prospect for those who wish to conduct future research in this area.

In this study, anxiety and depression varied considerably with the duration of disease. Understandably anxiety was more marked than depression with significantly more patients scoring as 'cases' for depression than the normal population range of 11-22%<sup>13,14</sup>. It was likely that the advent of illness and the fear and anxiety associated with surgery were reflected in these scores. In another study, 33% patients showed evidence of subclinical depression which is also the case in the present study in which the depression and anxiety was 63.1% and 69.6% respectively among the studied subjects<sup>15</sup>.

Our results generally confirm the findings of previous studies that there are high rates of psychological problems in patients attending even the out-patient departments. Two hundred patients attending out-patient Department of Dermatology, Jinnah Hospital, Lahore were studied for Hospital Anxiety and Depression<sup>16</sup>. 20% cases of depression and 28% cases of anxiety were found in the total sample, using cut off point as 11 or more on HAD Scale.

The relationship between anxiety and pain has previously been identified<sup>17</sup> and psychological stress, measured over several post-operative days, revealed that anxiety and pain are positively correlated<sup>18,19</sup>. It is important to emphasize that these findings do not explain whether anxiety and depression make pain worse or whether the experience of pain leads to anxiety and depression<sup>20</sup>. Whilst it is not possible to identify the nature of the relationship between anxiety, depression and pain from the data, it seems from patients report that these different variables had a cumulative effect. A similar study shows the same result of high frequency of anxiety and depression<sup>21</sup>.

## CONCLUSION

Anticipating surgery is understandably a big source of anxiety and depression but one would expect that levels would subside after surgery. The present study revealed that nearly a third of the sample experienced high levels of anxiety and depression after surgery. This anxiety and depression was significantly related to the duration of the disease as well.

### Author's Contribution:

Concept & Design of Study:	Atif Mahmood
Drafting:	Atif Jawad, Ali Maqbool
Data Analysis:	Hamza Akhtar, Sfdar Ali, Faria Khan
Revisiting Critically:	Atif Mahmood, Atif Jawad
Final Approval of version:	Atif Mahmood

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. Shoar S, Naderan M, Aghajani M, Sahimi-Izadian E, Hosseini-Araghi N, Khorgami Z. Prevalence and determinants of depression and anxiety symptoms in surgical patients. *Oman Med J* 2016;31(3):176.
2. Stundner O, Kirksey M, Chiu YL, Mazumdar M, Poultsides L, Gerner P, et al. Demographics and perioperative outcome in patients with depression and anxiety undergoing total joint arthroplasty: a population-based study. *Psychosomatics* 2013; 54(2):149-57.
3. Hellstadius Y, Lagergren J, Zylstra J, Gossage J, Davies A, Hultman C, et al. Prevalence and predictors of anxiety and depression among esophageal cancer patients prior to surgery. *Diseases of the Esophagus* 2016;29(8):1128-34.
4. Vincent T. Stress Management: Health vs. Unhealthy. *Mich BJ* 2012;91:54.
5. Tully PJ, Baker RA. Depression, anxiety, and cardiac morbidity outcomes after coronary artery bypass surgery: a contemporary and practical review. *J Geriatric Cardiol: JGC.* 2012;9(2):197.
6. Salehi A, Javanbakht M, Ezzatababdi MR. Stress and its determinants in a sample of Iranian nurses. *Holistic Nursing Pract* 2014;28(5):323-8.
7. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta psychiatrica scandinavica.* 1983;67(6):361-70.
8. Detroyer E, Dobbels F, Verfaillie E, Meyfroidt G, Sergeant P, Milisen K. Is preoperative anxiety and depression associated with onset of delirium after cardiac surgery in older patients? A prospective cohort study. *J Am Geriatrics Soci* 2008; 56(12):2278-84.
9. Tully PJ, Baker RA, Knight JL. Anxiety and depression as risk factors for mortality after coronary artery bypass surgery. *J Psychosomatic Res* 2008;64(3):285-90.
10. Tully PJ, Baker RA, Turnbull D, Winefield H. The role of depression and anxiety symptoms in hospital readmissions after cardiac surgery. *J Behavioral Med* 2008;31(4):281-90.
11. Gillies ML, Smith LN, Parry-Jones WL. Postoperative pain assessment and management in adolescents. *Pain* 1999;79(2-3):207-15.
12. Latif A, Khan RMS, Nawaz K. Depression and anxiety in patients undergoing elective and emergency surgery: Cross-sectional study from Allama Iqbal Memorial Teaching Hospital, Sialkot. *Morbidity and Mortality* 2017;8:9.
13. Rentsch D, Dumont P, Borgacci S, Carballeira Y, Archinard M, Andreoli A. Prevalence and treatment of depression in a hospital department of internal medicine. *General Hospital Psychiatr* 2007;29(1):25-31.

14. Mata DA, Ramos MA, Bansal N, Khan R, Guille C, Di Angelantonio E, et al. Prevalence of depression and depressive symptoms among resident physicians: a systematic review and meta-analysis. *JAMA* 2015;314(22):2373-83.
15. Hermanns N, Kulzer B, Krichbaum M, Kubiak T, Haak T. How to screen for depression and emotional problems in patients with diabetes: comparison of screening characteristics of depression questionnaires, measurement of diabetes-specific emotional problems and standard clinical assessment. *Diabetologia*. 2006; 49(3):469-77.
16. Aslam R, Qadir A, Asad F. Psychiatric morbidity in dermatological outpatients: an issue to be recognized. *J Pak Assoc Dermatologists* 2007;17(4):235-9.
17. Johnston M, Vögele C. Benefits of psychological preparation for surgery: a meta-analysis. *Annals Behavioral Med* 1993;15(4):245-56.
18. Seers K. Perceptions of pain. *Nursing Times*. 1987;83(48):37-9.
19. Granot M, Ferber SG. The roles of pain catastrophizing and anxiety in the prediction of postoperative pain intensity: a prospective study. *The Clinical J Pain* 2005;21(5):439-45.
20. Desbiens NA, Wu AW, Broste SK, Wenger NS, Connors AF, Lynn J, et al. Pain and satisfaction with pain control in seriously ill hospitalized adults: findings from the support research investigations. *Critical Care Med* 1996;24(12): 1953-61.
21. Shakoor A, Shaheen JA, Khan JI. Association of anxiety and depression with acne: evaluation of pathoplastic effect of adolescence on this comorbidity. *J Pak Assoc Dermatologists* 2012; 22(4).

# Pattern of Medico-Legal Deaths at Abbasi Shaheed Hospital Autopsy Based 6 Years Study

Roohi Ehsan<sup>1</sup>, M. Faiz<sup>2</sup>, M. Irfan<sup>1</sup>, Wasiq Ahmed<sup>1</sup>, Raffat Rasool<sup>1</sup> and Summaiya Tariq<sup>1</sup>

## ABSTRACT

**Objective:** To determine the frequency, sex, and cause of death in medico-legal autopsies conducted at Abbasi Shaheed Hospital.

**Study Design:** Determination / analytic study.

**Place and Duration of Study:** This study was conducted at the Abbasi Shaheed Hospital from January 2012 till December 2017.

**Materials and Methods:** A 6 years case study involving the medico-legal deaths autopsied at Abbasi Shaheed Hospital. Bodies were first examined externally and then internally by dissection of body cavities. The results were collected on a structured proforma from the respective institution and were statistically analyzed using SPSS version 15.

**Results:** Out of a total of 5131 autopsies conducted during the period of study in Abbasi Shaheed Hospital, firearm injuries were the most common cause of death followed by road traffic accident, asphyxia, assault, burn, police encounter, explosion, poisoning, fall, electrocution and others. Majority of victims being male with male to female ratio of 10:1.

**Conclusion:** Frequency in relation to cause of death & autopsied revealed firearms injury accounting for 58.83% deaths followed by road traffic accident at 19.78%, asphyxia at 4.78% and assault at 3.73%.

**Key Words:** Medico-legal, Autopsy, Abbasi Shaheed Hospital, Karachi, Firearm Injury

**Citation of articles:** Ehsan R, Faiz M, Irfan M, Ahmed W, Rasool R, Tariq S. Pattern of Medico-Legal Deaths at Abbasi Shaheed Hospital Autopsy Based 6 Years Study. Med Forum 2019;30(5):36-39.

## INTRODUCTION

The word Autopsy, Necropsy and Postmortem examination are synonymous. The term "Autopsy" originates from ancient "Autopsia" which is derived from "Autos", i.e. Self and "Opis" i.e. to see for oneself. "Autopsia" means "seeing with one's own eyes".<sup>1</sup>

Autopsy entails examination of the dead body with a glimpse of penetrating primarily for the cause of death. Autopsy has to be chaperon by a well trained and experienced doctor in the terrain of Forensic Medicine/ Forensic Pathology in all cases of sudden, suspicious and unexpected deaths particularly those resulting due to violence.<sup>2</sup> The Cause of death for legal purpose can only be inclined by the autopsy surgeon who is licit to perform the medico-legal autopsies under his perquisite as a registered medical practitioner and can give affirmation at any inquest.<sup>3</sup>

<sup>1</sup>. Department of Forensic Medicine & Toxicology / Pathology<sup>2</sup>, Karachi Medical & Dental College, Karachi.

Correspondence: Roohi Ehsan, Associate Professor, Head of Forensic Medicine & Toxicology, Karachi Medical & Dental College, Karachi.

Contact No: 0333-2528545

Email: roohimurtaza@yahoo.com

Received: November, 2018

Accepted: March, 2019

Printed: May, 2019

This study focused on medico-legal autopsy as hospital autopsy is not common in our country. It is more than 700 years, since the first medico-legal autopsy was toted out in Bologna.<sup>4</sup> The number and array of medico-legal deaths has inflated tremendously in recent years in relation to an increase in crime.<sup>5</sup> However our six years study shows an initial rise in the first three years and then a decline in the number of medico-legal autopsies in the later three years. As per legal procedure of our country, all medico- legal deaths have a need to be investigated by the police/ magistrate and a final resolution by the courts.<sup>6</sup> The investigators require some cardinal dubiety to be answered by a medical man like cause, manner, fatal period and time since death. The answer of this particular catechism is only achievable with an unfolded and meticulous autopsy.<sup>7</sup> Such autopsies as per rule are conducted at mortuaries christen by the Provincial government and by a Prosecutor, nominated by the Health Department, known as an Authorized medical officer.<sup>8</sup> Sometimes deceased are buried as per routine liturgy without any umbrage of suspicion, but cause of death at later stage becomes controversial, requiring resolution and becomes a cause of concern for police. The investigators request for disinterment of the grave and conduction of autopsy on exhumed bodies.<sup>9</sup>

The WHO recommended a verbal autopsy tool currently being utilized in resource-constrained settings for the cause of death surveillance.<sup>10</sup> Verbal autopsy connote conducts a standardized interview with the family of deceased and interprets the data amassed in

order to construe a possible cause of death.<sup>11</sup> Musing in Pakistan show that among all medico-legal deaths autopsied, firearms have become the weapon of choice. A cramming from Dera Ismail Khan District reported 341 medico legal autopsies conducted over the years 2007 and 2008, where firearms caused 59% of the homicidal death.<sup>12</sup> Hussain et al proclaimed 633 medico-legal autopsies escorted in Peshawar during 2004.<sup>13</sup> The preeminent purpose of this study is to persuade the frequency and causes of medico legal autopsies at Abbasi Shaheed Hospital, Karachi.

## MATERIALS AND METHODS

This study covers the period from January 2012 to December 2017 which includes all the cases of medico-legal deaths autopsied at Abbasi Shaheed Hospital. A detailed study was conducted to determine the cause of death. The external examination followed by internal examination in accordance with the adopted Robert Virchow's technique. Findings were noted as per study design and cause of death given by gross examination, chemical examination and histo-pathological examination. Conventional X-rays and CT Scans were done whenever and wherever required. Results were collected from the institution records and were statistically analyzed using SPSS Version 15. The frequency and percentages were calculated for all categorical variables including frequency, gender and cause of medico-legal deaths.

## RESULTS

A total of 5131 medico-legal autopsies were reported and autopsied during the study period at Abbasi Shaheed Hospital, Karachi. Medico-legal deaths autopsied were 1131, 1140, 1142, 700, 494 and 524 in the year 2012, 2013, 2014, 2015, 2016 and 2017 respectively. (Table 1)

Frequency in relation to cause of death revealed firearm injuries to account for leading number of deaths (58.83%) followed by road traffic accidents (19.78%), asphyxia (4.78%), assault (3.73%), thermal injuries (3.7%), police encounter (2.16%), explosives (1.71%), fall (1.18%), poison (1.16%) electrocution (1.09%) and others (1.8%) respectively (Table 2) representing frequency and percentage in relation to cause of death respectively).

The frequency of cause of medico-legal deaths in relation to years during the study period of 2012 – 2017 shows that in the first three years the total number of cases are higher which then reduced in number in the next three years of the study (Table 3).

Frequency of medico-legal deaths in relation to months during the study period shows that September accounts for the leading month followed by May, January, July, February, April, March, August, June, November, December and October (Table 4).

Gender distribution shows that males formed a significant fraction of the 4671 victims but females account for only 460 of the cases. This shows male dominance (Table 5).

**Table No.1: Total number of medico-legal deaths autopsied (2012 – 2017)**

Year	Number of medico-legal death autopsied
2012	1131
2013	1140
2014	1142
2015	700
2016	494
2017	524

**Table No.2: Total frequency and percentage of cause of medico-legal deaths**

Cause of Death	Frequency	Percentage %
Firearm injury	3019	58.83
Road traffic Accident	1015	19.78
Asphyxia	247	4.81
Assault	194	3.78
Burn/Thermal	190	3.7
Police encounter	111	2.16
Explosives/Blast	88	1.71
Fall	61	1.18
Poison	60	1.16
Electrocution	56	1.09
Others	90	1.8
Total	5131	100

**Table No.3: Frequency of cause of medico-legal deaths in relation to year during the study period**

	2012	2013	2014	2015	2016	2017
Firearm injury	690 (61%)	798 (70%)	797 (69.7%)	371 (53%)	173 (35%)	190 (36.2%)
Road traffic accident	188(1 6.2%)	143(1 2.5%)	162(1 4.1%)	165(2 3.5%)	180(3 6.4%)	177(3 3.7%)
Asphyxia	50(4. 4%)	68(5. 96%)	31(2. 7%)	26(3. 7%)	26(5. 26%)	46(8. 7%)
Assault	30(2. 6%)	29(2. 5%)	45(3. 9%)	21(3 %)	41(8. 2%)	28(5. 3%)
Burn	124(1 0.9%)	5(0.4 3%)	24(2. 1%)	5(0.7 1%)	5(1.0 1%)	27(5. 1%)
Police encounter	–	–	6(0.5 2%)	63(9 %)	30(6. 07%)	12(2. 2%)
Explosives/Blast	11(0. 97%)	48(4. 2%)	13(1. 1%)	10(1. 42%)	3(0.6 0%)	3(0.5 7%)
Fall	14(1. 23%)	16(1. 4%)	7(0.6 1%)	9(1.2 8%)	7(1.4 %)	8(1.5 %)
Poison	9(0.7 9%)	17(1. 49%)	19(1. 66%)	11(1. 57%)	3(0.6 0%)	3(0.5 7%)
Electrocution	6(0.5 3%)	11(0. 96%)	12(1. 05%)	8(1.1 4%)	6(1.2 1%)	13(2. 4%)
Others	9(0.7 9%)	5(0.4 1%)	26(2. 25%)	11(1. 56%)	20(4. 02%)	17(3. 24%)
Total	1131	1140	1142	700	494	524

**Table No. 4: No. of medico-legal deaths in relation to months during the study period**

Months	No. of Male cases	No. of Female cases	Total
January	437	70	507
February	423	36	459
March	383	33	416
April	405	24	429
May	447	34	481
June	364	35	399
July	424	27	451
August	373	52	425
September	519	36	555
October	280	31	311
November	318	36	354
December	298	45	343

**Table No.5: Medico-legal deaths in relation to gender during the study period (2012-2017)**

Gender	Total no. of cases	Male to Female Ratio
Male	4671	10:1
Female	460	

## DISCUSSION

In this study 5131 medico-legal deaths were autopsied at one of the tertiary care hospital of Karachi City "Abbasi Shaheed Hospital" during the period of January 2012 to December 2017. A study from Rawalpindi reported a total of 215 medico legal deaths followed by autopsy during the year 1997.<sup>12</sup> Marri et al reported 662 medico- legal autopsies in Khyber Medical College, Peshawar during 2002.<sup>14</sup> In other cities of Pakistan nearly 600 cases are autopsied per year.<sup>15</sup> Yousfani et al reported 697 medico legal autopsies conducted during the period of January 2006 to December 2008.<sup>16</sup>

From this 6 years study we have observed that the cases autopsied were 1131, 1140, 1142, 700, 494 and 524 in the year 2012, 2013, 2014, 2015, 2016 and 2017 respectively.(Table 1). A study from Kuala Lumpur, Malaysia reported a total of 2,762 medico-legal autopsies conducted over a period of five years.<sup>17</sup> Our study shows that the number of autopsies in the initial 3 years of study was higher and in the next 3 years there was a general decline in the number of cases but an increase in the police encounter cases seen in the years 2015, 2016 and 2017. However a decline of firearm cases is seen in these 3 years which favors the efficient measures taken to decrease the rapidly growing crime within the city and better develop the law and order situation of the Karachi City.

This study reported firearms to account for majority of the causes of deaths i.e. 58.83%. Death by firearms whether homicidal, suicidal, or accidental is above all other causes at international, national as well as at local

level. A study from England and Wales reported firearms to account for less than 10% of homicide and less than 5% of suicides in man and is most unusual in woman.<sup>18</sup> In Australia, firearm deaths comprise of 7.3% of all Injury deaths.<sup>19</sup> In Nigeria, four years study, 1999-2002 at Kano Teaching Hospital shows 12.5% fatality by firearm injuries.<sup>20</sup> Within Pakistan majorly deaths occur due to firearms. A two year study in Bahawalpur from January 01, 1997 to December 31, 1999 showed death by firearms as 44.1%.<sup>21</sup>

Road Traffic deaths autopsied (19.78%) second to firearms in our study. In Assam, India from January 01, 1999 to December 31, 2003, out of a total of 7,852 medico-legal autopsies, 1872 (23.84%) were of road traffic accident victims.<sup>22</sup> Generally causes of road traffic deaths include cell phone use by drivers, eating while driving, driving under influence of alcohol, over speeding, recklessness, rough roads, under age drivers and failure to follow the traffic laws.

Most of the bodies autopsied were of male. In most of the studies, including our study the male to female ratio appears higher 10:1. This might be due to violence, aggressiveness, involvement in different conflicts that develop a male towards becoming a victim or a murderer.

## CONCLUSION

In relation to cause of death in medico-legal deaths autopsied in the study, it was revealed that firearm injuries outnumber the other causes followed in descending order as road traffic accidents, asphyxia, assault, burns and other cases respectively. We also observed the male dominance in the study. Due to the betterment of law and order in the city frequency of medico-legal deaths autopsied has decreased in later years of the study.

### Author's Contribution:

Concept & Design of Study:	Roohi Ehsan
Drafting:	M. Faiz
Data Analysis:	Wasiq Ahmed, Raffat Rasool, Summaiya Tariq
Revisiting Critically:	Roohi Ehsan, M. Irfan
Final Approval of version:	Roohi Ehsan

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. Rothenberg K. The Autopsy through History. In: Embarras A, Pass AD, editors. Forensic Science. Ipswich MA: Salem Press;2008.p.100.
2. Qasim AP, Awan ZA, Ansari AJ. Critical Appraisal of Autopsy Work. APMC 2016;10(4): 194-202.

3. Parikh CK. Parikh's Text Book of Medical Jurisprudence & Toxicology; 5<sup>th</sup> ed. 1990.p114, 385, 551, 582-3.
4. Vij K. Textbook of Forensic Medicine and Toxicology, Principles and Practice. 5<sup>th</sup> ed. 2011.p.17
5. Mirza FH, Hassan Q, Naz R, Khan M. Spectrum of Medico-legal Deaths in Metropolis of Karachi: An Autopsy Based Study. Pak J Med Dentist 2013;2(4): 4-9.
6. Asgher A. Information to the police and their powers to investigate. The Code of Criminal Procedures 1898. 4 ed. Karachi: Pioneer Book House; 2004.p.84-7.
7. Joseph HD. Medicolegal death investigation. In: Dolinak D, Matshes E, Lew E's Forensic pathology; principles and practice. Oxford: Elsevier Academic Press; 2005.p.1-64
8. Memon MU, Khalil ZH, Aziz K, Kaheri GQ, Khalil IR. Audit of cases autopsied in the mortuary of Khyber Medical College Peshawar during the year 1999. Ann King Edward Med Coll 2001; 7(3): 190-193.
9. Awan NR. Autopsy and exhumation, In: Awan NR's principles and practice of forensic medicine. Lahore: M Istiaq Printers; 2009.p.130.
10. World Health Organization. Verbal Autopsy Standards: Ascertaining and attributing causes of death [http://www.who.int/healthinfo/statistics/verbalautopsystandards/en%5D.
11. Burton JL, Underwood J. Clinical, educational, and epidemiological value of autopsy. Lancet 2007;369(9571):1471-80.
12. Mian AR, Majid A, Malik MM, Zaheer M, Gorava SU. Analysis of unnatural death in Rawalpindi during 1997. Pak Armed Forces Med J 1999; 49(1):68-70.
13. Hussain Z, Shah MM, Afridi HK, Arif M. Homocidal deaths by firearms in Peshawar: an autopsy study. J Ayub Med Coll Abbottabad 2006;18(1):44-47.
14. Marri MZ, Bashir Z, Munawar AZ, Khalil ZH, Khalil IU. Analysis of homicidal deaths in Peshawar, Pakistan. J Ayub Med Coll Abbottabad 2006; 18(4):30-33.
15. Memon MU, Khalil ZH, Aziz K, Kaheri GQ, Khalil IR. Audit of cases Autopsied in the Mortuary of Khyber Medical College Peshawar during the year 1999. Ann King Edward Med Uni 2001;9:190-3.
16. Yousfani GM, Memon MU. Spectrum of Unnatural Deaths in Hyderabad: An Autopsy Based Study. J Dow Univ Health Sci 2010;4(2):54-57.
17. Kumar V, Li AK, Zaniat AZ, Lee DA, Salleh SA. A study of homicidal deaths in medico-legal autopsies at UMMC, Kuala Lumpur. J Clin Forensic Med 2005;12(5):254-257.
18. Chapman J, Milroy CM. Firearm deaths in Yorkshire and Humberside. Forensic Sci Int 1992;57(2):181-191
19. Harrison J, Moller J, Bordeaux S. Injury by firearms Australia 1994. [Online] 1996 [cited 2009 Mar 11] Available from- <http://www.nisu.flinders.edu.au/data/phonebook/queries/guninjuries94.php>.
20. Ochicha O, Muhammad AZ, Nwokedi EE, Umar AB. A review of medico-legal deaths in Kano. Niger Postgrad Med J 2003;10(1):16-18.
21. Ali SMA, Rizvi SI, Ali MA, Chaudry TH. Weaponry patterns in the homicidal deaths in Bahawalpur. The Professional 2000;7(4):514-516.
22. Singh YN, Bairagi KK, Das KC. An epidemiological study of road traffic accident victims in medicolegal autopsies. JIAFM 2005; 27(3).ISSN 971-973.



# New Onset Post-Operative Seizures Associated with

Onset Post-Operative  
Seizures with  
Ventriculoperitoneal Shunts

## Ventriculoperitoneal Shunts; A Retrospective Study

Muhammad Aamir Saghir, Muhammad Samir Irfan Wasi and Syed Sheeraz ur Rehman

### ABSTRACT

**Objective:** To establish the frequency of post-operative seizures in patients treated with ventriculoperitoneal shunt, either first or revised, so that the role of post procedural prophylactic anti-epileptic drug administration could be established.

**Study Design:** Retrospective observational study

**Place and Duration of Study:** This study was conducted at the Liaquat National Hospital, Karachi from January 2010 to December 2017.

**Materials and Methods:** The sampling technique used was retrospective non-probability sampling. The sample size for this study was 76 and was calculated using WHO sample size calculator.

The Inclusion criteria were established that included patients operated with VP shunt within the duration mentioned above. Patients above the age of 60 years, having history of seizures previous to the procedure, and history of previous cerebral trauma were excluded from the study.

**Results:** The mean age of the patients was found to be  $26.7 \pm 18.74$ . The results of this study reveal that out of the 76 patients included in the study 2 (2.63%) patients developed new onset seizures associated with ventriculoperitoneal shunt. None of the patients received Levitracetam or any other antiepileptic drug prophylactically in the post-operative period.

**Conclusion:** It is concluded from this study that new onset seizures are a relatively non significant risk in the post operative management and care of patient and anti epileptics do not have a significant role in preventing such episode.

**Key Words:** Ventriculoperitoneal shunt, Seizures, Anti epileptics

**Citation of articles:** Saghir MA, Wasi MSI, Rehman SS. New Onset Post-Operative Seizures Associated with Ventriculoperitoneal Shunts; A Retrospective Study. Med Forum 2019;30(5):40-43.

### INTRODUCTION

It has been estimated that 0.59 to 1 per 1000 live births are affected by hydrocephalus, which is an accumulation of abnormal amount of CSF fluid in ventricles<sup>1</sup>. Dandy classified hydrocephalus into two types, nearly a century ago in 1922, i.e. communicating and non-communicating hydrocephalus.<sup>2</sup> Ventriculoperitoneal shunt has been regarded as the treatment of choice for such patients with either communicating or non-communicating type of hydrocephalus, since many years but is associated with a wide range of complications. Over 30,000 procedures to treat hydrocephalus are performed in the United States annually.<sup>3,4</sup>

Department of Neurosurgery, Liaquat National Hospital, Karachi.

Correspondence: Muhammad Aamir Saghir, Consultant Neurosurgeon, Liaquat National Hospital, Karachi.

Contact No: 03032573949

Email: draamirlnh@yahoo.com

Received: January, 2019

Accepted: March, 2019

Printed: May, 2019

Shunts constitute one of the most difficult management in neurosurgical practice. Nevertheless it is widely accepted by neurosurgeons because of the ease of conduction and good capacity of peritoneum to reabsorb fluid.<sup>2</sup>

Endoscopic third ventriculostomy is an alternative surgical treatment option but is associated with significant failure rates mostly due to the steep learning curve.<sup>5</sup>

The complications associated with ventriculoperitoneal shunt can be divided into mechanical and infective. The mechanical complications include obstruction, disconnection and migration of the instrumentation. This complication can occur in either the ventricular or peritoneal end of the shunt system.

On the other hand, the infective complications include abscess, meningitis, ventriculitis and skin necrosis. In addition to these complications seizures, subdural collection and craniosynostosis can also occur secondary to introduction of a shunt system and its sequel. Abdominal complications include inguinal hernia, hydrocele, ascites, pseudocyst formation, perforation of a viscus or extrusion of the shunt, intestinal volvulus and obstruction.<sup>6</sup> One of the less common and less studied complications associated with VP shunts procedure is post operative seizures.

The procedure involves inserting the ventricular catheter through a burr hole and direct it as such to place the tip of this catheter at the foramen of Monroe.<sup>7</sup> It has been postulated previously in studies that the procedure described involves cerebral tissue compromise and could potentially cause post operative seizures.

In a recent series it was shown that 84.5% of the patients in which ventriculoperitoneal shunt was complicated by infection or malfunction, revision of shunt was required at least once.<sup>8</sup> These revised shunt procedures predispose the patients with hydrocephalus to seizures because of repeated cerebral trauma<sup>9</sup>. This has been the reason behind use of prophylactic anti epileptic drugs post operatively in several neurosurgical centres.

In our study we aim to determine the frequency of new onset post-operative seizures in patients treated with ventriculoperitoneal shunt, either first or revised, so that the role of post procedural prophylactic anti-epileptic drug administration could be established.

## MATERIALS AND METHODS

This is a retrospective observational study. The sampling technique used was retrospective non-probability sampling.

The sample size for this study was 76 and was calculated using WHO sample size calculator.

This study was conducted in Liaquat National Hospital, Karachi Pakistan from January 2010 to December 2017. in which cases operated with ventriculoperitoneal shunt by a single neurosurgeon were studied. All cases included were operated within the time frame mentioned above and were followed post operatively for seizures.

**Inclusion Criteria:** The Inclusion criteria were established that included patients operated with VP shunt within the duration mentioned above.

**Exclusion Criteria:** Patients above the age of 60 years, having history of seizures previous to the procedure, on prophylactic antiepileptic pre or post op and history of previous cerebral trauma were excluded from the study. Study was started after formal approval from the departmental members and institute. Records of the patient matching the inclusion criteria were retrieved and reviewed from the HIMS (Hospital Information Management System). A predesigned performa was used to make the entries which were later transferred to the SPSS by the principal researcher ensuring patient confidentiality at all times.

All patients were operated by a senior neurosurgeon and the same instrumentation was used in all the patients. The procedure involved abdominal incision for peritoneal end of the shunt system. A semicircular incision was given over the point of insertion 3 cm above and behind the upper pole of respective pinna. After dissection of subcutaneous tissue upto the

periosteum, burr hole was made. After that the dural layer was incised and cauterized. Ventricular end of the catheter was inserted at right angle to all planes targeting the lateral ventricle and checked for drainage of CSF. Peritoneal end was placed upto the abdominal incision previously given. Reservoir of the system was attached and CSF flow was checked multiple times during each procedure. Wounds were closed in multiple layers taking care that the tubing system does not intermingle with the sutures. All procedures were done using Medtronic ventriculoperitoneal shunt system®.

**Operational Definition:** New onset seizures were defined as seizures occurring post operatively after ventriculoperitoneal with no previous history of any type of fits preoperatively.

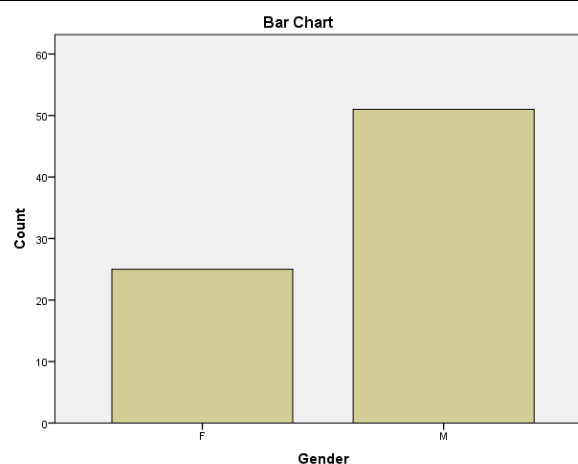
Data was analyzed using SPSS version 23 using descriptive statics where applicable. Descriptive statics included means and percentages. Chi-square was used as a test of significance. P value of <0.05 was considered significant.

## RESULTS

A total of 76 patients were included in the study in accordance with the inclusion criteria. Out of 76, 51(67.1%) were male and 25 (32.9%) were female (Graph 1) with male is female ratio of 2:1.

**Table No.1: Gender Comparison with Variables**

Variables	p-value
New Onset Of seizures	0.041
Shunt Side	0.98
Redo Case	0.98



**Graph No.1: Bar chart.**

The mean age of the patients was  $26.7 \pm 18.74$  with maximum age of 65 and minimum age of 2 and mode of 9. Out of 76 patients only 2 (2.63%) patients developed new onset seizures post operatively. The sample included both the paediatric and adult age groups with 26 (34.21%) patients being in paediatric age group and 50 (65.76%) patients being in the adult one.

All the patients that developed new onset seizures (2.63%) were of paediatric age group without any previous episodes. All the three patients presented with seizure episodes during the post operative period before discharge. None of these patients were on prophylactic anti epileptics. None of the patients, in their pre or postictal phase, developed meningism. Gender based analysis using chi square was also insignificant when compared using new onset of seizures, shunt side and redo cases as shown in Table 1.

## DISCUSSION

Walter Dandy's classification for hydrocephalus being either communicating or non communicating, has long been used among the neurosurgical community.<sup>10</sup> Ventricular shunts have been used widely to divert the flow of CSF in both of these forms of hydrocephalus. Over the years massive advancements have occurred in the techniques and instrumentation for diversion of CSF flow. Nulsen, Spitz and Holter were the first to develop the modern form of shunts.<sup>11</sup> Since the introduction of endoscopic techniques for diverting CSF through third ventriculostomy, there have been debate over the justified use of shunt over ETV. However evidence suggests that both are viable options in the management of both forms of hydrocephalus. The fact, however, remains that ETV adds the added advantage of avoiding placement of foreign body within the ventricular system.<sup>12</sup>

Ventriculoperitoneal shunt has been used effectively by neurosurgeons throughout the world but complications related to shunt do occur commonly<sup>13,14</sup>, the most common being obstruction and infection. According to Farid Khan et al the frequency of overall shunt malfunction was found to be 15.4%. In the same study, the frequency of shunt revision was 14.1%.<sup>15</sup> One of the less common complications of ventriculoperitoneal shunt includes new onset seizures secondary to shunt. There have been some studies that reported an increased frequency of seizures associated with the ventricular shunt although there is no convincing data available yet.<sup>16, 17</sup>

Our study reveals a non significant risk of new onset seizures (2.36%) in patients that underwent ventriculoperitoneal shunt. The gender also has no influence on the new onset of seizures. Marie Bourgeois et al reveal a thirty two percent frequency of seizures post ventriculoperitoneal shunt but their study has multiple limitations including the fact that new onset seizures are not classified<sup>18</sup>. Our study specifies new onset seizures in post operative VP shunt patients and relates the etiology to presence of foreign body through the cerebral cortex into the ventricular system. Dennis el Johnson put forth in his study that seizures are seldom an indication for malfunction of shunt.<sup>19</sup> This may describe the rare new onset seizures that are falsely associated with the presence of foreign body

through the cortex. Hydrocephalus is not commonly recognized as a cause of seizures in any age group, thus indicating that shunt malfunction (causing recurrence of hydrocephalus) would not likely be an etiology for seizures.

This study provides evidence for the unjustified use of anti epileptics prophylactically in the post operative period after ventriculoperitoneal shunt. The most common complications of VP shunt including infection and obstruction of shunt have been a major concern in the research projects around the world; however, new onset seizures have been a rare sought complication and much less studied. The increasing use of prophylactic antiepileptics for post operative new onset seizures among patients with ventriculoperitoneal shunt should incite large scale studies to be carried out discussing the avoidance of extravagant use of anti epileptics as it might be cause and cost effective for the patients simultaneously.

## CONCLUSION

In our study we conclude that new onset post operative seizures are a non significant risk in post operative period of patients undergoing shunt procedure. A neurosurgeon must take into account all aspects of the complications and thus prophylactic use of anti epileptics in post operative period of ventricular shunt should be avoided as it would be cause and cost effective simultaneously.

### Author's Contribution:

Concept & Design of Study:	Muhammad Aamir Saghir
Drafting:	Muhammad Samir Irfan Wasi
Data Analysis:	Syed Sheeraz ur Rehman
Revisiting Critically:	Muhammad Aamir Saghir, Muhammad Samir Irfan Wasi
Final Approval of version:	Muhammad Aamir Saghir

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. Munch TN, Rostgaard K, Rasmussen ML, Wohlfahrt J, Juhler M, Melbye M. Familial aggregation of congenital hydrocephalus in a nationwide cohort. *Brain* 2012;135(Pt 8):2409-15.
2. Dandy WE. Anoperative procedure for hydrocephalus. *Johns Hopkins Hosp Bull* 1922; 33: 189-190.
3. Bondurant CP, Jimenez DF. Epidemiology of cerebrospinal fluid shunting. *Pediatr Neurosurg* 1995;23:254-9.

4. Patwardhan RV, Nanda A. Implanted ventricular shunts in the United States: The billion-dollar-a-year cost of hydrocephalus treatment. *Neurosurg* 2005; 56:139–45.
5. Agarwal N, Shukla RM, Agarwal D, Gupta K, Luthra R, Gupta J, et al. Pediatric Ventriculoperitoneal Shunts and their Complications: An Analysis. *J Ind Assoc Pediatr Surg* 2017;22(3): 155-157.
6. Agarwal N, Shukla RM, Agarwal D, Gupta K, Luthra R, Gupta J et al. . Pediatric Ventriculoperitoneal Shunts and their Complications: An Analysis. *J Ind Assoc Pediatr Surg* 2017;22(3): 155-157.
7. Kulkarni AV, Riva-Cambrin J, Browd SR, Drake JM, Holubkov R, Kestle JR, et al. Endoscopic third ventriculostomy and choroid plexus cauterization in infants with hydrocephalus: a retrospective Hydrocephalus Clinical Research Network study. *J Neurosurg Pediatr* 2014;14(3):224-9.
8. A.Rashid Choudhury. Avoidable factors that contribute to the complications of ventriculoperitoneal shunt in childhood hydrocephalus. *Child's Nerv Syst* 1990; 6: 346-349
9. Stone JJ, Walker CT, Jacobson M, Phillips V, Silberstein HJ. Revision rate of pediatric ventriculoperitoneal shunts after 15 years. *J Neurosurg Pediatr* 2013;11(1):15-9.
10. Tully HM, Kukull WA, Mueller BA. Clinical and Surgical Factors Associated With Increased Epilepsy Risk in Children With Hydrocephalus. *Pediatr Neurol* 2016;59:18-22.
11. Dandy WE. Extirpation of the choroid plexus of the lateral ventricles in communicating hydrocephalus. *Ann Surg* 1918; 68:569–579
12. Nulsen FE, Spitz EB. Treatment of hydrocephalus by direct shunt from ventricle to jugular vein. *Surgical forum* 1951: 399–403.
13. Lo P, Drake JM. Shunt malfunctions. *Neurosurg Clin N Am* 2001; 12: 695–701.
14. Drake JM, Kestle JR, Tuli S. CSF shunts 50 years on—past, present and future. *Childs Nerv Syst* 2000; 16: 800–4.
15. Khan F, Rehman A, Shamim MS, Bari ME. Factors affecting ventriculoperitoneal shunt survival in adult patients. *Surg Neurol Int* 2015 Feb 13;6:25.
16. Kulkarni AV, Riva-Cambrin J, Butler J, Browd SR, Drake JM, Holubkov R et al. Outcomes of CSF shunting in children: comparison of Hydrocephalus Clinical Research Network cohort with historical controls: clinical article. *J Neurosurg Pediatr* 2013; 12(4):334-8.
17. Talwar D, Baldwin MA, Horbatt CI. Epilepsy in children with meningomyelocele. *Pediatr Neurol* 1995; 13:29–32.
18. Bourgeois M, Sainte-Rose C, Cinalli G, Maixner W, Malucci C, Zerah M, et al. Epilepsy in children with shunted hydrocephalus. *J Neurosurg* 1999; 90(2):274-81.
19. Johnson DL, Conry J, O'Donnell R. Epileptic seizure as a sign of cerebrospinal fluid shunt malfunction. *Pediatr Neurosurg* 1994; 24:223–228.

# Levetiracetam in Neonates Having Refractory Seizure

Farhan Zahoor<sup>1</sup>, Beenish Bashir Mughal<sup>1</sup>, Bushra Madni<sup>2</sup>, Kaleem Akhtar Malhi<sup>3</sup> and Farrukh Saeed<sup>1</sup>

## ABSTRACT

**Objective:** To evaluate the efficacy of add on oral levetiracetam in neonates having refractory seizure.

**Study Design:** A prospective clinical trial

**Place and Duration of the Study:** This study was conducted at the Department of Pediatrics, Services Hospital, Lahore from June 2018 to March 2019.

**Materials and Methods:** We analyzed 60 neonates visiting neonatal emergency with seizure, who did not respond to initial intravenous (IV) phenobarbital or subsequent addition of IV phenytoin. We went on to use oral levetiracetam as an add on therapy. Oral levetiracetam as gavage as a starting dose of 10 to 20 mg per kg and gradual increase to 40 to 50 mg per kg if a repeat of seizure occurred according to clinical signs and then, persistence or complete control of seizure was monitored. Chi square test was applied to the effect of study variables on the response of levetiracetam and p value < 0.05 was considered as statistically significant.

**Results:** Out of a total of 60 neonates, most were 40 (66.7%) male, had gestational age status as term 38 (43.3%), delivered by cesarean section (CS) 39 (65.0%), aged less than or equal to 7 days 42 (70.0%). Tonic seizure was found to be the most frequent type, in 19 (31.7%) while 18 (30.0%) had idiopathic as the commonest underlying cause of seizure. There were 56 (93.3%) neonates who went on to positively respond to add on therapy of oral levetiracetam.

**Conclusion:** Oral levetiracetam as an add on therapy was found to have excellent response in neonate having seizure after the failure of 1<sup>st</sup> line treatment options.

**Key Words:** Neonatal Seizure, Levetiracetam, Idiopathic, Response.

**Citation of articles:** Zahoor F, Mughal BB, Madni B, Malhi KA, Saeed F. Response of Add-On Oral Levetiracetam in Neonates Having Refractory Seizure. Med Forum 2019;30(5):44-47.

## INTRODUCTION

Seizure is described as sudden alteration in behavior, sensory or autonomic function which are related to dysfunction of paroxysmal electrical activity of brain.<sup>1-</sup>

<sup>3</sup>Neonates are said to be affected more in comparison to children of any other age, estimating about 1 to 5 per 1000 live births.<sup>4,5</sup> In children, variation persists in reported prevalence of seizures due to difference in definitions and well as challenges in timely diagnosis but still a yearly prevalence of around 1% is noted around the world.<sup>6,7</sup> Neonatal seizure is noted to be one of the most frequent cause of admissions while the pattern of disease vary greatly.<sup>8</sup>

In neonates, seizures are classified in to various types like subtle, clonic, tonic, spastic as well as myoclonic.<sup>9,10</sup> Asphyxia as well as hypoxic-ischemic encephalopathy (HIE) are known to be the most common causes of seizure in neonates, accounting 50% to 75% of cases. Infectious diseases, metabolic disorders, injuries, intracranial hemorrhages and abnormalities related to structure of the brain are some of the other known causes of seizures in neonates.<sup>11,12</sup>

It has also been noted commonly that central nervous system (CNS) premature neonates exhibit non-specific response. Most seizures involving neonates have good outcome while some may go on to develop complications of transient or chronic nature.<sup>13</sup> The brain is noted to develop in the first few years that is why frequent seizure can alter the development as well as learning potential due to structural changes related to brain.<sup>6</sup> That is why it is imperative to aim inhibition of seizures by adopting efficacious drugs.

Lots of antiepileptic options are available to tackle seizures, mainly depending upon the etiological factors suspected.<sup>14</sup> Phenobarbital followed by phenytoin are considered to be the 1<sup>st</sup> line treatment options for neonatal seizure.<sup>6</sup> Phenobarbital accompanies powerful anticonvulsive benefits but low toxicity that is why WHO holds it as 1<sup>st</sup> line treatment option for generalized, tonic, clonic and partial seizures.<sup>15,16</sup>

<sup>1</sup>. Department of Paediatrics, Services Hospital, Lahore.

<sup>2</sup>. Department of Paediatrics, Shalamar Medical and Dental College, Lahore.

<sup>3</sup>. Department of Paediatrics, The Children's Hospital and The Institute of Child Health, Lahore.

Correspondence: Dr. Farhan Zahoor, Assistant Professor of Paediatrics, Services Hospital, Lahore.

Contact No: 0333-4272862

Email: drf.zahoor@gmail.com

Received: March, 2019

Accepted: April, 2019

Printed: May, 2019

It has also been noticed that around 40% of seizures do not respond with either phenobarbital and phenytoin that presents a space for the addition of other anti-convulsive drugs.<sup>17,18</sup> Topiramate, levetiracetam and lamotrigine are some of the newer recommended antiepileptic options available for the treatment of neonatal seizure. Levetiracetam as an add on therapy has been studied recently and was found to yield good result as 1<sup>st</sup> line add on therapy.<sup>19</sup> Levetiracetam has a non-hepatic metabolism and addition of no drug interaction without any major complications or neurotoxic effects<sup>20,21</sup> makes it a valuable choice to test in our local population. To shed more light on this new drug, we planned this study to evaluate the efficacy of add on oral levetiracetam in neonates having refractory seizure.

## MATERIALS AND METHODS

This prospective clinical trial was conducted at The Department of Pediatrics, Services Hospital, Lahore, from 1<sup>st</sup> June 2018 to 31<sup>st</sup> March 2019. We analyzed all neonates visiting neonatal emergency with seizure were enrolled. Inclusion criteria was all those neonates who did not respond to initial intravenous phenobarbital or subsequent addition of intravenous phenytoin, and were went on to have oral levetiracetam as an add on therapy for refractory seizure. Finally, 60 neonates having refractory seizure met the inclusion criteria and were included in the study while neonates with electrolyte

imbalance, presenting with hypoglycemia or not meeting the inclusion criteria, were excluded.

Informed consent was sought from parents / guardians of all the study participants. Approval from institutional Ethical and Research Committee was granted.

Oral levetiracetam as gavage as a starting dose of 10 to 20 mg per kg and gradual increase to 40 to 50 mg per kg<sup>19</sup> if a repeat of seizure occurred according to clinical signs and then, persistence or complete control of seizure was monitored.

Age, gender, types of delivery, gestational age, type and causes of seizures along with response of levetiracetam was noted in control of seizure in all the neonates. SPSS version 21 was used for data analysis. All the qualitative variables like gender, types of delivery, types and causes of seizure were presented as frequencies and percentages while quantitative variables like age were presented in the form of mean and standard deviation. Chi square test was applied to the effect of study variables on the response of levetiracetam and p value < 0.05 was considered as statistically significant.

## RESULTS

Out of a total of 60 neonates, there were 40 (66.7%) male and 20 (33.3%) female. According to the gestational age of neonates, 22 (36.7%) were preterm and 38 (43.3%) term.

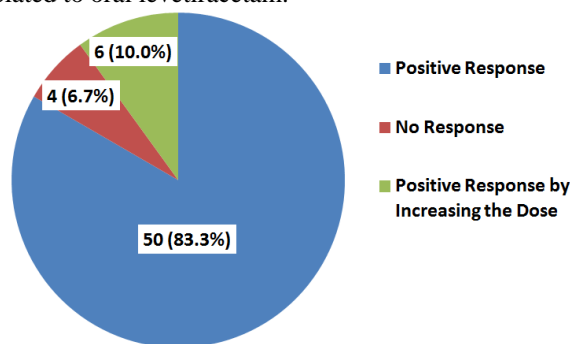
**Table No.1: Distribution of Response of Levetiracetam and Characteristics of Neonates**

Characteristics		Response to Levetiracetam (n=60)			P Value
		Positive Response (n=50)	No Response (n=4)	Positive Response by Increasing Dose (n=6)	
Gender	Male	32 (64.0%)	2 (50.0%)	4 (66.7%)	0.842
	Female	18 (36.0%)	2 (50.0%)	2 (33.3%)	
Preterm (<37 weeks)		20 (40.0%)	1 (25.0%)	1 (16.7%)	0.471
Term (>37 weeks)		30 (60.0%)	3 (75.0%)	5 (83.3%)	
Type of Delivery	NVD	18	1 (25.0%)	2 (33.3%)	
	CS	32	3 (75.0%)	4 (66.7%)	
Postnatal Age (days)	<7	36 (72.0%)	3 (75.0%)	3 (50.0%)	0.152
	8-14	2 (4.0%)	1 (25.0%)	2 (33.3%)	
	15-21	5 (10.0%)	0 (0%)	1 (16.7%)	
	22-28	7 (14.0%)	0 (0%)	0 (0%)	
CNS Infection	Yes	1 (2.0%)	0 (0%)	1 (16.7%)	0.155
	No	49 (98.0%)	4 (100%)	4 (13.3%)	
Type of Seizure	Tonic	14 (28.0%)	3 (75.0%)	2 (33.3%)	0.630
	Subtle	5 (10.0%)	0 (0%)	1 (16.7%)	
	Spastic	13 (26.0%)	0 (0%)	1 (16.7%)	
	Clonic	7 (14.0%)	0 (0%)	0 (0%)	
	Mixed	11 (22.0%)	1 (25.0%)	2 (33.3%)	
Underlying Disease					
HIE		14 (28.0%)	0 (0%)	2 (33.3%)	0.264
Brain Malformation		9 (18.0%)	2 (50.0%)	0 (0%)	
IEM		7 (14.0%)	2 (50.0%)	2 (33.3%)	
IVH		4 (8.0%)	0 (0%)	0 (0%)	
Idiopathic		16 (32.0%)	0 (0%)	2 (33.3%)	

There were 39 (65.0%) neonates who were delivered by cesarean section (CS) while 21 (35.0%) by normal vaginal delivery (NVD). Majority, 42 (70.0%) of the neonates were aged less than or equal to 7 days. Only 2 (3.3%) neonates were found to have CNS infection. Tonic seizure was found to be the most frequent, in 19 (31.7%) neonates while spastic 14 (23.3%), 6 (10.0%) subtle, 7 (11.7%) clonic and mixed form was noted in 14 (23.3%). In terms of underlying causes of seizure in studied neonates, 18 (30.0%) were idiopathic, 16 (26.7%) had HIE, 11 (18.3%) brain malformation, 11 (18.3%) inborn errors of metabolism (IEM) and 4 (6.7%) intraventricular hemorrhage (IVH).

In terms of response of levetiracetam, 50 (83.3%) neonates were noted to have positive response (complete control of seizures) while 6 (10.0%) more achieved complete cessation of seizure with increase in dosage of oral levetiracetam, whereas 4 (6.7%) neonates did not respond to the studied treatment.

When neonates having positive response to levetiracetam, with no response and response by increasing the dosage were compared within different study variables, no significance was found in terms of response ( $p > 0.05$ ). We did not notice any side effects related to oral levetiracetam.



**Figure No.1: Response of Levetiracetam Amongst All the Neonates**

## DISCUSSION

In the current study, we included those neonates who did not respond to 1<sup>st</sup> line treatment options. We noticed that a total of 56 (93.3%) neonates went on to positively respond to add on therapy of oral levetiracetam while only 4 (6.7%) did not respond at all, even after increasing the dosage. Not much work has been done in the recent past to evaluate the effectiveness of levetiracetam in neonates presenting with seizures. This study was aimed to evaluate the newer options like levetiracetam to help clinicians picking up effective and modern option while facing seizures in neonates. No real work was found specifically analyzing oral levetiracetam so the result of this study will surely add to the little knowledge that currently exist in this regards. The results of the present study in terms of positive response are very consistent to a study conducted by Mollamohammadi M et al in Iran<sup>19</sup> also analyzed the

response of oral levetiracetam in 42 neonates with seizures, found an overall positive response of 95%.

Levetiracetam has been studied well in IV form for control of seizure in neonates. A study analyzing 38 neonates,<sup>22</sup> IV levetiracetam was administered as 1<sup>st</sup> line therapy in comparison to IV phenobarbital and the results proved that IV levetiracetam turned out to have better efficacy for the control of neonatal seizures versus IV phenobarbital. In another study conducted by Khan O and colleagues,<sup>23</sup> IV levetiracetam was used in a dosage of 10-50 mg/kg, and was found to subside seizure in all neonates while all of them got discharged on oral levetiracetam.

In the present study, we did not notice any significant relationship between levetiracetam response rate and any of the studied variables. Our findings in these aspects were very similar to what has been found earlier as well. We did not notice any side effects related to oral levetiracetam which is very consistent with the previous findings.<sup>19</sup>

## CONCLUSION

Oral levetiracetam as an add on therapy was found to have excellent response in neonate having seizure after the failure of 1<sup>st</sup> line treatment options. Further studies having bigger sample size assessing the response of various forms of levetiracetam are needed to authenticate the findings of the current research that will be hugely beneficial for the treatment of seizure in neonates.

### Author's Contribution:

Concept & Design of Study:	Farhan Zahoor
Drafting:	Beenish Bashir Mughal, Bushra Madni
Data Analysis:	Kaleem Akhtar Malhi, Farrukh Saeed
Revisiting Critically:	Farhan Zahoor, Beenish Bashir Mughal
Final Approval of version:	Farhan Zahoor

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. Johnston MV. Seizure in childhood. In: Behrman RE, Kliegman RM, Jenson HB, editors. Nelson Textbook of Pediatrics. 17th ed. Philadelphia: Saunders; 2004.p.1993-2009.
2. Menkes JH, Sarnat BH perinatal asphyxia and trauma. In: Menkes JH, Sarnat HB, Maria BL, editors. Child neurology. 6<sup>th</sup> ed. Philadelphia: Lippincott Williams & Wilkins; 2000.p. 919-1007.
3. Arzimanoglou A, Guerrini R, Aicardi J. Aicardi's infantile spasm and related syndromes. In: Arzimanoglou A, Guerrini R, Aicardi J, editors.

- Philadelphia: Lippincott Williams & Wilkins; 2004.p.235-40.
4. vanRooij LG, Hellström-Westas L, de Vries LS. Treatment of neonatal seizures. *Seminars in Fetal and Neonatal Medicine* 2013;4(18):209-215.
  5. Glass HC. Neonatal seizures: advances in mechanisms and management. *Clinics in Perinatology* 2014;41(1):177-90.
  6. Hellstrom-westas L, Blennow G, Lindroth M, Rosen I, Svenningsen NW. Low risk of seizure recurrence after early withdrawal of antiepileptic treatment in the neonatal period. *Arch Dis Child* 1995;72:P 97-101.
  7. Mohamad A, Mikati, Abeer J, Hani. Seizure in Childhood, Nelson: Pediatrics, 2, 20<sup>th</sup> ed. Philadelphia;2015.p.2823.
  8. Hauser WA. The prevalence and incidence of convulsive disorders in children. *Epilepsia* 1994; 35(Suppl. 2):1-6.
  9. Serdaroglu A, Ozkan S, Aydin K, Gucuyener K, Tezcan S, Aycan S. Prevalence of epilepsy in Turkish children between the ages of 0 and 16 years. *J Clin Neurol* 2004;19:271-5.
  10. Hauser WA. Seizure disorders: The changes with age. *Epilepsia* 1992; 33(Suppl. 4):6-14.
  11. Volpe JJ. Neonatal seizures: current concepts and revised classification. *Pediatrics* 1989;84(3):422-8.
  12. Robert M. Kliegman, Bonita F. Stanton, Joseph W. Staeme, Nina F. Schor. Nelson: Pediatrics. 20<sup>th</sup> ed. Philadelphia;2015.p.2849-54.
  13. Brunquell PJ, Glennon CM, Dimario FJ, Lever T, Eisefeld L. Prediction of outcome based on clinical seizure type in newborn infants. *J Pediatr* 2004; 140: 707-12.
  14. Donovan M, Griffin B, Kharoshankaya L, Cryan J, Boylan G. Pharmacotherapy for neonatal seizures: current knowledge and future perspectives. *Drugs* 2016;76(6):647-61.
  15. Ross J. Baldessarini and Frank I. Tarazi pharmacotherapy of psychosis and mania. In: Goodman LS, editor. Goodman and Gilman's the pharmacological basis of therapeutics. 11<sup>th</sup> ed. New York: McGraw-Hill;1996.p.478-85.
  16. Lerman-Sagie T, Lerman P. Phenobarbital still has a role in epilepsy treatment. *J Child Neurol* 1999; 14(12):820-1.
  17. Sedighi M, Asadi F, Moradian N, Vakiliamini M, Moradian M. Efficacy and safety of levetiracetam in the management of seizures in neonates. *Neurosciences (Riyadh)* 2016;21(3):232-5.
  18. Treiman DM, Meyers PD, Walton NY. A comparison of four treatments for generalized convulsive status epilepticus. Veterans Affairs Status Epilepticus Cooperative Study Group. *N Engl J Med* 1998;339:792-8.
  19. Mollamohammadi M, Amirhoseini ZS, Saadati A, Pirzadeh Z, et al. Oral Levetiracetam as Add-On Therapy in Refractory Neonatal Seizures. *Iran J Child Neurol*. Autumn 2018; 12(4):103-110.
  20. Shoemaker MT, Rotenberg JS. Levetiracetam for the treatment of neonatal seizures. *J Child Neurol* 2007;22:95-98.
  21. Mruk AL, Garlitz KL, Leung NR. Levetiracetam in neonatal seizures: a review. *J Pediatr Pharmacol Therapeutics* 2015;20(2):76-89.
  22. Ramantani G, Ikonomidou C, Walter B, Rating D, Dinger J. Levetiracetam: safety and efficacy in neonatal seizures. *Eur J Paediatr Neurol* 2011;15: 1-7.
  23. Khan O, Chang E, Cipriani C, Wright C, Crisp E, Kirmani B. Use of intravenous levetiracetam for management of acute seizures in neonates. *Pediatr Neurol* 2011;44:265-9.



# Efficacy and Safety of Ferric Carboxymaltose for Iron-Deficiency Anemia (IDA) in Postpartum Women: An Observational Study

Shahina Ishtiaq<sup>1</sup>, Urooj Malik<sup>1</sup>, Minahil Majid<sup>1</sup>, Muhammad Athar Khan<sup>2</sup>, Mehreen Yousaf Rana<sup>1</sup> and Rozina Khaskheli<sup>1</sup>

## ABSTRACT

**Objective:** To assess the efficacy and safety of ferric caboxymaltose in postpartum women with iron deficiency anemia using single dose infusion in a tertiary care hospital.

**Study Design:** A single center, single-arm observational study

**Place and Duration of Study:** This study was conducted at the Ziauddin Hospital Keamari, Karachi which is affiliated with Ziauddin University, Karachi from April, 2014 and November, 2014.

**Materials and Methods:** A single center, single-arm observational study was conducted at Ziauddin Hospital Keamari, Karachi which is affiliated with Ziauddin University between April, 2017 and November, 2017. A total of 60 women 10 days or less after delivery with postpartum Hb less than 9g/dl diagnosed as iron deficiency anemia. The dosage of ferric carboxymaltose was fixed as 1000mg diluted in 100 ml normal saline infused in 30 minutes or less, for all the patients. CBC, serum iron, serum ferritin, TIBC were performed prior to administration of ferric carboxymaltose and then repeated after week 2 and week 4. The primary efficacy end point was the change in Hb from baseline to week 4. Secondary efficacy endpoints included change in Hb and other serum iron parameters. A secondary outcome measure was occurrence of adverse events from baseline to week 4.

**Results:** There was a statistically significant improvement in haemoglobin levels over a period of 4 week (day 0 - 14  $p < 0.001$ , day 0 - 28  $p < 0.001$ ). The mean MCV was not found to be statistically significant between baseline and week 2 and week 4 ( $p = 0.158$ ,  $p = 0.658$ ). We found a statistically significant improvement in TSAT and serum ferritin from baseline to week 2 and week 4 ( $p < 0.001$ ).

**Conclusion:** In conclusion, ferric carboxymaltose seems to be the drug of choice if I/V iron treatment during postpartum period becomes necessary. Our study shows that the tolerance of ferric carboxymaltose in pregnancy is excellent, and prevalence of side effects is low, in the postpartum period.

**Key Words:** Post partum anemia, iron deficiency anemia, blood loss

**Citation of articles:** Ishtiaq S, Malik U, Majid M, Khan MA, Rana MY, Khaskheli R. Efficacy and Safety of Ferric Carboxymaltose for Iron-Deficiency Anemia (IDA) in Postpartum Women: An Observational Study. Med Forum 2019;30(5):48-51.

## INTRODUCTION

Anemia is defined by World Health Organization as hemoglobin of less than 12g/dl. It is a global public health issue<sup>1,2</sup> and its most common cause is iron deficiency<sup>3</sup>. Postpartum anemia occurs in 50-80% of mothers in the developing countries<sup>4</sup> and is common even in the developed world.<sup>5,6</sup>

<sup>1</sup>. Department of Obstet and Gynae, Ziauddin University, Karachi.

<sup>1</sup>. Department of Community Medicine, Liaquat Medical College & Dentistry, Karachi.

Correspondence: Muhammad Athar Khan, Associate Professor of Community Medicine, Liaquat Medical College & Dentistry, Karachi.

Contact No: 0323-2135932

Email: matharm@yahoo.com

Received: September, 2018

Accepted: March, 2019

Printed: May, 2019

Iron deficiency is most prevalent in the developing countries<sup>7</sup>. Furthermore postpartum anemia is associated with depression in the postpartum period, stress, anxiety, cognitive impairment and poor mother child bonding with consequent delay in the infant development<sup>8,9</sup>. Mothers who are anemic also have increased risk of infections including infections of breast and urinary tract, delayed healing of the wounds and diminished supply of milk<sup>10,11</sup>. Postpartum anemia in postpartum patients is caused primarily by inadequate iron intake prior to and during pregnancy<sup>2</sup>, and by peripartum blood loss.<sup>12,13</sup>

Patients with postpartum anemia have a longer average length of hospital stay, are more likely to receive a blood transfusion, and there is an increased hospital cost. For many decades the mainstay of treatment of iron deficiency anemia has been oral or conventional parenteral iron and red blood cell (RBC) transfusions. However, oral iron supplementation can lead to significant gastrointestinal side effects resulting in non-compliance in many patients. The conventional

parenteral iron supplements including iron sorbitol citrate, and iron sucrose are associated with allergic reactions which may prove to be lethal. Moreover multiple doses make parenteral iron non-convenient for the patient. The risks for blood transfusion are well established and it should be avoided whenever possible<sup>14</sup>.

Ferric carboxymaltose (FCM) is a newer dextran-free iron formulation with a near neutral pH, physiological osmolality and increased bioavailability which allows for single dose, short fifteen minute infusion time and higher dosing (upto 1000 mg). These properties make ferric carboxymaltose an attractive alternative to iron sucrose in terms of risk profile, efficacy, patient comfort and convenience, staff and institutional resource utilization. It facilitates effective treatment of iron deficiency as well as rapid replacement of iron stores.

Postpartum anemia is widespread in Pakistan, but there is paucity of local studies and there is a serious need for developing a proper protocol and management strategy for treatment of anemic mothers. This will help in reduction of morbidity associated with anemia and improve maternal health situation in our country. The total drug infusion concept with third-generation parenteral iron molecules is convenient for the patient and can save resources in the health care system, especially when compared with oral therapy and blood transfusions.

## MATERIALS AND METHODS

A single center, single-arm observational study was conducted at Ziauddin Hospital Keamari, Karachi which is affiliated with Ziauddin University between April, 2014 and November, 2014. An institutional review board approved the study protocol for the center prior to initiation. All subjects gave written informed consent before enrollment. A total of 60 subjects was considered as sufficiently powered to detect differences in Hb levels at week 4 versus baseline ( $\alpha = 0.05$ , two-sided; 90% power). Women 10 days or less after delivery with postpartum Hb less than 9g/dl diagnosed as iron deficiency anemia, with peripheral smear showing microcytic hypochromic anemia, low serum ferritin levels and intolerance to oral iron supplementation were enrolled in our study after they gave informed consent. Patients with concomitant severe hepatic, cardiovascular or renal disorder, asthma or atopic allergy, severe psychiatric disorders, severe infection, and who had received parenteral iron therapy or blood transfusion for anemia within last 20 days were excluded from this study.

After obtaining informed consent patients were administered ferric carboxymaltose. The dosage of ferric carboxymaltose was fixed as 1000mg diluted in 100 ml normal saline infused in 30 minutes or less, for all the patients. CBC, serum iron, serum ferritin, TIBC

were performed prior to administration of ferric carboxymaltose and then repeated after week 2 and week 4. All laboratory data for efficacy analysis were collected and analyzed at the hospital laboratory. A pre designed Performa was filled that included patients bio data and initial and subsequent hematological values.

The primary efficacy end point was the change in Hb from baseline to week 4. Secondary efficacy endpoints included change in Hb and other serum iron parameters. A secondary outcome measure was occurrence of adverse events from baseline to week 4. Adverse events were classified using the Medical Dictionary for Regulatory Activities Terminology. For the purpose of this study, allergic reactions (hypersensitivity) were classified by grade according to the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE), Version 3.0. An AE was classified as serious if it met any one of the following: death, life-threatening, hospitalization, disability, or important medical events. The data was analyzed using SPSS version 19. Paired t-test and Wilcoxon signed-rank test was used to compare the changes in parameters from baseline to week 2 and 4. A p-value  $<0.05$  was considered as significant.

## RESULTS

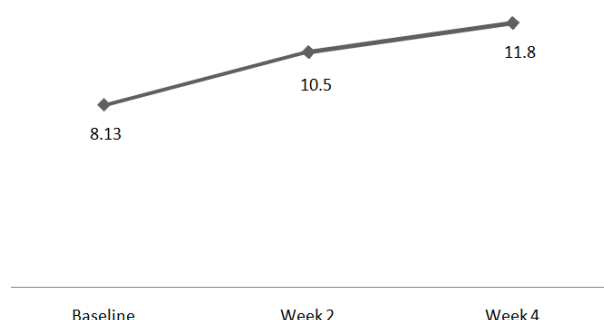
A total of 60 post-partum women who delivered at our tertiary care hospital were included in the study. Most common age group included women between 28-32 years of age ( $n = 26$ , 43.3%). About 55% ( $n=33$ ) of women were multigravida and 45% ( $n=27$ ) were primigravida. At screening (day 0), mean hemoglobin, mean MCV, mean TSAT and mean serum ferritin were  $8.13 \pm 0.9$  g/dL,  $79.8 \pm 9.5$  fL, 9.7% and 52.7 ng/ml. At day 14, mean hemoglobin, mean MCV, mean TSAT and mean Serum ferritin were  $10.5 \pm 1.2$  g/dL,  $82.6 \pm 15.4$  fL, 25.8% and 777.3 ng/ml. At day 30, mean hemoglobin, mean MCV, mean TSAT and mean Serum ferritin were  $11.8 \pm 1.02$  g/dL,  $80.9 \pm 19.5$ , 26.3% and 316.1 ng/ml.

**Table No. 1: Demographic Characteristics of Study Participants (n=60)**

<b>Age (years)</b>	Mean $\pm$ sd	32.1 $\pm$ 4.3
<b>Gravidity</b>	Mean $\pm$ sd	2.1 $\pm$ 1.2
<b>Parity</b>	Mean $\pm$ sd	1.6 $\pm$ 0.8
<b>Delivery Method n(%)</b>		
Vaginal		38 (63.3)
Caesarean		18 (30)
Forceps		03 (5)
Vacuum		01 (1.7)
<b>Weight (kg)</b>	Mean $\pm$ sd	72.4 $\pm$ 17.8

There was a statistically significant improvement in haemoglobin levels over a period of 4 week (day 0 - 14  $p < 0.001$ , day 0 - 28  $p < 0.001$ ) Figure 1. The mean MCV was not found to be statistically significant between baseline and week 2 and week 4 ( $p = 0.158$ ,  $p = 0.658$ )

but still a small rise of 1.1 fL. We found a statistically significant improvement in TSAT and serum ferritin from baseline to week 2 and week 4 ( $p < 0.001$ ). Other parameters like TIBC and Iron showed marked improvement after FCM administration.(Table 2).



**Figure No. 1: Hemoglobin values before and after treatment**

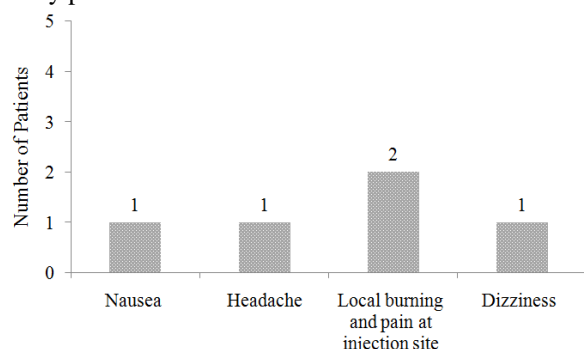
**Table No.2: Hematological values at baseline, week 2 and week 4(n=60)**

Parameters		Screening				
		Baseline	Week 2	P value*	Week 4	P value**
Hemo-globin	g/dL	8.13	10.5	<0.001	11.8	<0.001
MCV	fL	79.8	82.6	0.158	80.9	0.658
TSAT	%	9.7	25.8	<0.001	26.3	<0.001
S. ferritin	ng/ml	52.7	777.3	<0.001	316.1	<0.001

\* Baseline and week 2

\*\*Baseline and week 4

During the first 24 hours of the treatment period in the study subjects, The most common treatment-emergent adverse events after receiving FCM were nausea (3.3%), headache (5%), palpitations (5%) and dizziness (1.6%)Figure 2.However, no serious ADR was reported in any patient.



**Figure No.2: Treatment Related Adverse Events**

## DISCUSSION

Postpartum anemia is a common problem in our population. In the vast majority of patients the

underlying cause is iron deficiency as a result of either noncompliance of patients with iron preparation or a non-booked status during pregnancy. Occurrence of postpartum hemorrhage further complicated the picture. The conventional treatment is either blood transfusion, iron supplementation in the form of oral iron or multiple doses of intravenous iron which is largely dependent on patient's compliance. Use of ferric carboxymaltose provides us the opportunity to treat iron deficiency anemia with a large dose of intravenous iron in a single administration. This is important as the patient can be loaded with iron during her hospital stay and thus is independent of the patient's compliance. However, safety and tolerability of this preparation is important in addition to its efficacy. Since the oral compliance is a problem in post partum females the 1000mg dose seems a promising option in order to maintain the hemoglobin level, and meet the iron need in lactation.

In this study we found that after a single dose administration of ferric carboxymaltose the mean hemoglobin increased from 8.13 on day 0 to 10.69 on day 10 and 11.64 on day 30 which means an increase of 2.56g/dl after 10 days and 3.51g/dl after 4 weeks. This is in accordance with the study done by Froessler who found an increase in hemoglobin levels at 3 and 6 weeks post infusion of ferric carboxymaltose ,however his cohort was of pregnant mothers<sup>15</sup>.Setu Rathood reports the mean increase in Hb after 2 weeks as 3.2 g/dL and 4.4 g/dL at 6 weeks In post partum females, after they received ferrous carboxymaltose<sup>16</sup>.

In our study we found that the rise in ferritin at day 30 was 238.5microgram above the baseline and the mean end of trial (day 30). Mean T SAT (transferrin saturation) was 25.36% after 30 days as compared to 10.69% of baseline.Vikrant has also reported similar trends in T SAT. In his subjects the TSAT increased from baseline of 19.5 % to 25.5 % at follow up<sup>17</sup>.Baillie reported that serum ferritin increased in the ferrous carboxymaltose treatment group<sup>18</sup>.Our results are also consistent with the results of a meta-analysis which showed an end-of-trial increase over oral iron of hemoglobin and ferritin<sup>19</sup>.We did not find any adverse reactions in our study subjects. Vikrant also didn't find any significant minor or major side effects in his study participants. Overall, both drugs (FCM & IS) did not show any serious ADR and these are expected events that are reported in previous literature.<sup>20-23</sup>

## CONCLUSION

Intravenous ferric carboxymaltose was safe and well tolerated and an effective treatment option for postpartum and postoperative anemic women. Advantages included achievement of normal haemoglobin levels in a shorter duration, single administration with no relevant clinical safety concerns and a single dose infusion can avoid multiple visits.

**Author's Contribution:**

Concept & Design of Study: Shahina Ishtiaq, Urooj Malik, Minahil Majid  
 Drafting: Muhammad Athar Khan  
 Data Analysis: Minahil Majid, Mehreen Yousaf Rana, Rozina Khaskheli  
 Revisiting Critically: Muhammad Athar Khan, Shahina Ishtiaq, Mehreen Yousaf Rana, Rozina Khaskheli  
 Final Approval of version: Shahina Ishtiaq, Urooj Malik, Minahil Majid

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

**REFERENCES**

- World Health Organization. Anemia prevention and control. Geneva, Switzerland: World Health Organization; 2011.
- Somdatta P, Reddaiah VP, Singh B. Prevalence of anaemia in the postpartum period: a study of a North Indian village. *Trop Doct* 2009;39:211–215.
- Bodnar LM, Cogswell ME, Scanlon KS. Low income postpartum women are at risk of iron deficiency. *J Nutr* 2002;132:2298–3021.
- Milman N. Postpartum anemia: definition, prevalence, causes, and consequences. *Ann Hematol* 2011;90:1247–1253.
- Bodnar LM, Scanlon KS, Freedman DS, Siega-Riz AM, Cogswell ME. High prevalence of postpartum anemia among low-income women in the United States. *Am J Obstet Gynecol* 2001;185:438–443.
- Pehrsson PR, Moser-Veillon PB, Sims LS, Suitor CW, Russek-Cohen E. Postpartum iron status in nonlactating participants and nonparticipants in the special supplemental nutrition program for women, infants, and children. *Am J Clin Nutr* 2001;73:86–92.
- Zimmerman MB, Hurrell RF. Nutritional iron deficiency. *Lancet* 2007;370:511–520.
- Beard JL, Hendricks MK, Perez EM, et al. Maternal iron deficiency anemia affects postpartum emotions and cognition. *J Nutr* 2005;135:267–272.
- Corwin EJ, Murray-Kolb LE, Beard JL. Low hemoglobin level is a risk factor for postpartum depression. *J Nutr* 2003;133:4139–4142.
- Gibbs RS. Clinical risk factors for puerperal infection. *Obstet Gynecol* 1980;55:178–184.
- Henly S, Anderson C, Avery M. Anemia and insufficient milk in first time mothers. *Birth* 1995;22:87–92.
- Rakesh PS, Jamkhandi D, Manjunath K, George K and Prasad J. Determinants of postpartum anemia among women from a rural population in southern India. *Int J Women Health* 2014; 6: 395–400.
- Sserunjogi L, Scheutz F, Whyte SR. Postnatal anaemia: neglected problems and missed opportunities in Uganda. *Health Policy Plan* 2003; 18:225–231.
- Shander A, Javidroozi M, Ozawa S, et al. What is really dangerous: anaemia or transfusion? *Br J Anaesth* 2011;107(1):41–59.
- Froessler B, Collingwood J, Hodyl NA, Dekker G. Intravenous ferric carboxymaltose for anaemia in pregnancy. *BMC Pregnancy Childbirth* 2014; 14:115.
- Rathod S, Samal S K, Mahapatra P C, and Samal S. Ferric carboxymaltose: A revolution in the treatment of postpartum anemia in Indian women. *Int J Appl Basic Med Res* 2015;5(1):25–30.
- Vikrant. S, Parashar A. The safety and efficacy of high dose ferric carboxymaltose in patients with chronic kidney disease: A single center study. *Indian J Nephrol* 2015;25(4):213–221.
- Bailie GR. Efficacy and safety of ferric carboxymaltose in correcting iron-deficiency anemia: a review of randomized controlled trials across different indications. *Arzneimittelforschung* 2010;60(6a):386-98
- Moore RA, Gaskell H, P, Allan J. Meta-analysis of efficacy and safety of intravenous ferric carboxymaltose (Ferinject) from clinical trial reports and published trial data. *BMC Blood Disord* 2011;11:4.
- Rathod S, Samal SK, Mahapatra PC, Samal S. Ferric carboxymaltose: a revolution in the treatment of postpartum anemia in Indian women. *Int J Appl Basic Med Res* 2015;5(1):25–30
- Ferinject (ferric carboxymaltose) [Internet]. Electronic Medicine compendium (eMC). Surrey, England: Electronic Medicine compendium, DataPharm; 2016a;29. <https://www.medicines.org.uk/emc/medicine/24167>.
- Breymann C, Gliga F, Bejenariu C, Strizhova N. Comparative efficacy and safety of intravenous ferric carboxymaltose in the treatment of postpartum anemia. *Int J Gynaecol Obstet* 2008; 110:267–78.
- Seid MH, Derman RJ, Baker JB, Banach W, Goldberg C, Rogers R. Ferric carboxymaltose injection in the treatment of postpartum iron deficiency anemia: a randomized controlled clinical trial. *Am J Obstet Gynecol* 2008;199 (4):435.

# Study of Biochemical, Hematological & Clinical Profile of Dengue Fever Patients in a Tertiary Care Hospital in Northern Pakistan

Mohsin Shafi<sup>1</sup>, Syed Shahmeer Raza<sup>3</sup>, Zarmina Hussain<sup>1</sup>, Fatima<sup>5</sup> and Syed Muhammad Owais<sup>4</sup>

## ABSTRACT

**Objective:** To assess the changes in biochemical and hematological profiles of the patients with dengue and to evaluate the effects of the patient's co-morbidities on the outcome.

**Study Design:** Descriptive / observational and retrospective study

**Place and Duration of Study:** This study was conducted at the Medical Ward of Hayatabad Medical Complex, Peshawar from August 2017 to October 2017.

**Materials and Methods:** This study was carried on a total of 470 patients. Biochemical tests namely ALT, AST and Creatinine along with full blood count were carried out. SPSS 20 was used for statistical analysis.

**Results:** Biochemical markers such as AST and ALT showed a wide degree of deviation from the mean while platelets and WBC counts were markedly decreased. Fever, Headache and Myalgia was the most common presenting complaints whereas Capillary leak, Acute Respiratory Distress Syndrome and Multi organ failure were the major complications. Diabetes mellitus, malaria and coronary artery disease were reported to be the major co-morbidities.

**Conclusion:** Dengue is a matter of global health concern and has become increasingly hard to manage and control over the last decade. It is a public health care issue and needs to be addressed in due time. Moreover, our study highlights the importance of admission and timely management of dengue patients with comorbid, which are lethal if not managed properly. So routine biochemical tests should be carried out to rule out these.

**Key Words:** Dengue; Pleural Effusion; Capillary leak; Epidemic

**Citation of articles:** Shafi M, Raza SS, Hussain Z, Fatima, Owais SM: Study of Biochemical, Hematological & Clinical Profile of Dengue Fever Patients in a Tertiary Care Hospital in Northern Pakistan. Med Forum 2019;30(5):52-55.

## INTRODUCTION

Dengue Fever presents with headache, fever, joint pain, skin rash and a variety of other signs and symptoms.<sup>1-3</sup> Dengue shock syndrome (DSS) is due to excessive bleeding and low blood pressure. In such cases fluid replacement therapies or transfusions may be required. Dengue is a mosquito-borne viral disease spread by the female Aedes aegypti. Rainfall, temperature and

unplanned urbanization are risk factors for the spread of dengue.<sup>4-6</sup>

The very first cases of dengue hemorrhagic fever (DHF) were documented in Thailand and Philippines during the 1950s.<sup>7</sup> Dengue fever was considered to be prevalent in endemic areas but it has been transferred to other parts of the world due to trade and tourism.<sup>8</sup> Pakistan has had a few dengue epidemics in the recent past since the first one in 1994 and is now prevalent in all provinces of the country.<sup>9,10</sup> In 2010 over 21,000 people were affected by dengue in Pakistan, of which 16,000 were reported only from the capital of Punjab, Lahore.<sup>11,12</sup> A substantial surveillance system and fumigation lead to a control over this issue. This time the province of Khyber Pakhtunkhwa is under the attack of this fatal yet manageable medical condition. It is still an uphill task to clinically diagnose and identify the patients of dengue. In the absence vaccine for dengue fever, preventive strategies have to be used to counter the problem.<sup>13</sup> Goal of the study is identification of causes which can predict the severity of the disease and the outcome of patients with dengue infection. The main objective of this study is to assess the changes in biochemical and hematological profiles

<sup>1</sup>. Department of Pathology / Pathology<sup>2</sup>, Khyber Medical College, Peshawar.

<sup>3</sup>. Department of Forensic Medicine / Biochemistry<sup>4</sup>, North West School of Medicine, Peshawar.

<sup>5</sup>. Department of Medicines, Hyatabad Medical Complex, Peshawar.

Correspondence: Dr. Mohsin Shafi, Assistant Professor of Pathology, Khyber Medical College, Peshawar.

Contact No: 0321-9009689

Email: mohsinshafi@gmail.com

Received: December, 2018

Accepted: February, 2019

Printed: May, 2019

of the patients with dengue and to evaluate the effects of the patient's co-morbidities on the outcome. It will help us in improving the diagnosis and management amongst the patients and point out factors which can help in identifying patients more likely to develop severe disease.<sup>14-16</sup>

## MATERIALS AND METHODS

We planned to carry out the assessment of the biochemical, hematological and clinical profile of patients presenting with dengue during the recent outbreak in the parts of Peshawar, Pakistan. This descriptive observational and retrospective study was carried on a total of 470 patients admitted in the various medical wards from August 2017 to October 2017. The study was carried out in the department of Medicine of Hayatabad Medical Complex, Peshawar. The subject under observation were admitted patients brought to the hospital with a variety of clinical complaints that required evaluation and admissions. All the patients with dengue NS1 positive / Dengue IgM positive hospitalized in the Medical Unit were studied by analyzing case records. A standard proforma was devised to fulfill the study objectives information was gathered on demographic, haematological profile, biochemical tests, management, comorbidities, use of blood and platelet transfusions and the outcome. The data was collected and analyzed on SPSS 20 and MS Excel. The results were displayed in a tabulated form and interpretations were made.

## RESULTS

A total of 470 patients were included in the study. The patients presented with a variety of signs and symptoms as shown in table 1. All the 470 patients presented with fever while bleeding was present in 100 patients. Biochemical parameters (ALT, AST and Creatinine) and hematological parameters (Hb, WBC, Platelets and HCT) are shown in Table 2. Amongst the hematological markers, Platelet count and Hematocrit show a Mean and Standard Deviation as follows: Hemoglobin (gm/dl) =  $11.0 \pm 1.49$  and PLT (/cmm) =  $70000 \pm 40000$ . This particularly wide range of standard deviation with which the platelet count is noted, can be instrumental in Dengue patients especially in those with dengue hemorrhagic syndrome and comorbid. Capillary leaks (Pleural effusion and ascites) was the most common complication in these patients as 170 patients had them while only 20 patients had renal failure, 15 had hepatic dysfunction and 10 had encephalopathy as shown in Table 3. Table 4 shows the comorbidities present in the patients. Diabetes mellitus was the most common comorbidity present in 50 (10.64%) cases. Only 150 (31.9%) of the patients required platelet therapy while 320 (68.1%) were given symptomatic treatment. Of the total 470 patients, 445 (94.7%) recovered while 25 (5.3%) died.

**Table No.1 Frequency of different Symptoms and Signs that patients had at presentation.**

Sign and Symptoms	Number of Cases
Fever	470
Headache	350
Myalgia	450
Vomiting	400
Skin Rash	150
Bleeding	100
Breathlessness	120
Abdominal Pain	170

**Table No.2 Biochemical and Hematological parameters of the dengue patients. (n=470)**

Parameter	Mean $\pm$ SD	Reference Range
Hemoglobin (gm/dl)	$11.0 \pm 1.49$	13-18
RBC (Millions/cmm)	$5.1 \pm 0.32$	4.5 – 6.5
WBC (/cmm)	$6000 \pm 2300$	4000 – 11,000
PLT (/cmm)	$70000 \pm 40000$	150,000 – 400,000
HCT	$42 \pm 3$	40-52
AST (IU/ml)	$112.8 \pm 60$	05-42
ALT (IU/ml)	$115 \pm 45$	05-42
Creatinine (mg/dl)	$1.05 \pm 0.25$	0.7 – 1.3

**Table No.3 Frequency of different complications that patients developed due to dengue fever.**

Complication	Number of Cases
Hepatic Dysfunction	15
Renal Failure	20
Multi Organ Failure	30
Encephalopathy	10
Acute Respiratory Distress Syndrome (ARDS)	40
Capillary leak (P. Effusion/ Ascites)	170

**Table No.4 Frequency of different comorbidities in dengue patients fever.**

Comorbidities	Number of Cases
Diabetes Mellitus	50
Malaria	30
Coronary Artery Disease	30
Pregnancy	20
Hypertension	15

## DISCUSSION

This study describes different aspects of clinical profile such as the frequency and severity of signs and symptoms, their biochemical status throughout the illness, the co-morbidities and how these affect the overall clinical outcome of patients. Dengue is emerging as a major health concern throughout the world in the recent decade because it is widespread

geographically and affecting many countries causing major epidemics.

This research was done in post monsoon months (August to October) as the epidemics are reported in many areas of the country from the month of August to October and the number of cases tends to fall afterwards as the temperature falls. A study conducted in Khyber Pakhtunkhwa showed a significant rise in the number of patients admitted with Dengue fever in the hospitals in 2013 also.<sup>17</sup> Out of 470 hospitalized patients included in this study, fever was the most common symptom at the time of presentation with a frequency of 100%. The frequency of other symptoms at the time of presentation was in the order of myalgia 95% , vomiting 85% , headache 74% , abdominal pain 36% , skin rash 31% , breathlessness 25% and bleeding 21% (including hematemesis , melena, gum bleeding and epistaxis. Congruent pattern was also seen in a study conducted during Faisalabad epidemic 2014.<sup>18</sup>

A study reveals that these five signs/symptoms predict the prognosis of dengue. These include: vomiting/ nausea, abdominal pain, skin rashes, bleeding, and hepatomegaly.<sup>19</sup> Sixty percent (60%) of the patients included in our study had different complications over the period of stay at the hospital with the most common being capillary leak i.e. abdominal ascites and pleural effusion affecting 36% of the patients. Other complications reported were Acute respiratory distress syndrome 8%, multiple organ failure 6%, renal failure 4.2%, hepatic dysfunction 3%, encephalopathy 2%.

In the hematological and biochemical parameters of the patients bicytopenia was more pronounced in majority of the patients with a significant decrease in WBC counts and Platelet counts below the normal ranges. In the initial phase there is a quick fall in WBC's count when compared with platelet count. In the convalescent phase, WBC count increase was preceded by platelet increase after 72 – 96 hours. Similar findings were observed in a retrospective study conducted in Punjab Pakistan.<sup>20</sup> It suggested that WBC counts is also a good indicator of recovery from Dengue infection rather than focusing on Platelet counts only.<sup>20</sup> A rise in Hematocrit was observed in majority of patients and was more pronounced in patients who had complications as DHF and DSS. AST and ALT were raised in patients with hepatic dysfunction. Creatinine was only raised in patients with acute kidney injury as a complication of DSS. With proper patient care and timely management of complications the overall outcome was found to be satisfactory with majority of the patients recovering from the illness in a period of 5-7 days of admission in the hospital.

It is seen that mortality rate is increased when patients have comorbidities like acute kidney injury, respiratory failure, coagulopathy and results in increased stay in hospitals. Similar findings were also evident in a study conducted in 2014.<sup>21</sup> 94.7% of the hospitalized patients recovered from the illness completely and were in a good state of health at the time of discharge from

hospital while 5.3% of the patients expired. Our study shows that majority of the patients admitted to the hospital could be treated only with symptomatic treatment and fluid therapy and rehydration as per WHO guidelines without platelets transfusion with only 31.9% requiring platelets transfusion as a treatment modality. The reason behind platelets transfusion in these patients was sudden drop in platelet count over a period of 24 hrs, platelet counts below 10000/cmm, DHF and DSS. Therefore this study suggests that fluid therapy and symptomatic treatment is the preferred modality of treatment and majority of the patients respond well and improve whereas platelets transfusion is not only related with its own side effects such as transfusion reaction but had no additional benefit in preventing severe bleeding or decreasing time to stop bleeding. Similar findings were observed in a randomized control trial conducted in Pakistan in 2013.<sup>22</sup>

Patients with a past history of any illness are more at risk of developing complications. Diabetes and hypertension were common co morbid in the middle aged patients but these did not pose any difficulty in the overall management of dengue fever in general. We found that any patient having uncontrolled hypertension alone or along with uncontrolled diabetes led to DSS. Similar results were obtained in a study from Taiwan.<sup>23</sup> Malarial parasite was positive in many of the patients diagnosed with dengue fever. The coexisting dengue and malaria infection in significant number of patients throws light on the need of carrying out MP as a routine investigation in dengue patients.<sup>24,25</sup> Diarrhea as a common finding in patients with Dengue fever, which still needs to be evaluated thoroughly to find out the cause. Coronary artery disease and stroke in elderly patients darken the already gruesome picture of managing these patients. Pregnant women have increasingly been reported to present with dengue. This poses a threat for both the mother and baby. One limitation was that as this was a retrospective study, because of which some important information could not be obtained but this would pave path for further research in the medical condition under consideration.

## CONCLUSION

Dengue is a matter of global health concern and has become increasingly hard to manage and control over the last decade. It is a public health care issue and needs to be addressed in due time. Moreover, our study highlights the importance of admission and timely management of dengue patients with comorbidities, which are lethal if not managed properly. This studies stresses the importance of carrying out routine biochemical tests to rule out comorbidities. Further research including level 1 studies are needed in this field to establish a better understanding of the subject.

**Author's Contribution:**

Concept & Design of Study: Mohsin Shafi, Syed Shahmeer Raza  
 Drafting: Zarmina Hussain  
 Data Analysis: Zarmina Hussain, Fatima  
 Revisiting Critically: Syed Muhammad Owais, Syed Shahmeer Raza  
 Final Approval of version: Mohsin Shafi

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

**REFERENCES**

- Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, et al. The global distribution and burden of dengue. *Nature* 2013; 496(7446):504-7.
- Jahan F. Dengue Fever (DF) in Pakistan. *Asia Pacific Family Medicine* 2012;10(1):1-4.
- Jawad KA, Masood S, Tassawar H, Inam B, Waheeduz ZT. Outbreak of Dengue Hemorrhagic Fever in Karachi. *Pak Armed Forces Med J* 2001; 51(2):94-98.
- Guzman MG, Halstead SB, Artsob H, Buchy P, Farrar J, Gubler DJ, et al. Dengue: a continuing global threat. *Nature Reviews Microbiol* 2010; 8(12supp):S7-16.
- Vezzani D, Carbajo AE. *Aedes aegypti*, *Aedes albopictus*, and dengue in Argentina: current knowledge and future directions. *Memórias do Instituto Oswaldo Cruz* 2008;103(1):66-74.
- Oishi K, Saito M, Mapua CA, Natividad FF. Dengue illness: clinical features and pathogenesis. *J Infection Chemotherap* 2007;13(3):125-33.
- Brady OJ, Gething PW, Bhatt S, Messina JP, Brownstein JS, Hoen, et al. Refining the global spatial limits of dengue virus transmission by evidence-based consensus. *PLoS neglected tropical diseases* 2012;6(8):e1760.
- O'Brien D, Tobin S, Brown GV, Torresi J. Fever in returned travelers: review of hospital admissions for a 3-year period. *Clin Infect Dis* 2001;33(5):603-9.
- Chan YC, Salahuddin NI, Khan J, Tan HC, Seah CL, Li J, et al. Dengue haemorrhagic fever outbreak in Karachi, Pakistan, 1994. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1995;89(6):619-20.
- Ahsan T. Dengue fever: a regular epidemic?. *JPMA* 2008;58(1):1-2.
- Khan E, Hasan R. Dengue infection in Asia; A regional concern. *J Post Grad Med Inst* 2011;26(1): 1-6.
- Ramzan M, Ansar A, Nadeem S. Dengue epidemics: knowledge perhaps is the only key to success. *Journal of Ayub Medical College Abbottabad* 2015;27(2):402-6.
- Qadir S, Ahmad I, Akhtar MN, Naeem H. Knowledge, attitude and practice about dengue fever among local population. *Gomal Med Sci* 2015; 13(2):87-90.
- Vaughn DW, Green S, Kalayanarooj S, Innis BL, Nimmannitya S, Suntayakorn S, et al. Dengue viremia titer, antibody response pattern, and virus serotype correlate with disease severity. *J Infect Dis* 2000;181(1):2-9.
- Johansson MA, Dominici F, Glass GE. Local and global effects of climate on dengue transmission in Puerto Rico. *PLoS Neglected Tropical Dis* 2009;3 (2):e382.
- Riaz H. Pakistan reigns in "breakbone fever". *Pakistan reins in "breakbone fever"*. *CMAJ* 2013;185 (5): E215-E216.
- Ali A, Rehman H, Nisar M, Rafique S, Ali S, Hussain A, et al. Seroepidemiology of dengue fever in Khyber Pakhtunkhwa, Pakistan. *Int J Infect Dis* 2013;17(7):e518-23.
- Raza FA, Rehman S, Khalid R, Ahmad J, Ashraf S, Iqbal M, et al. Demographic and clinico-epidemiological features of dengue fever in Faisalabad, Pakistan. *PloS One* 2014;9(3):e89868.
- Zhang H, Zhou YP, Peng HJ, Zhang XH, Zhou FY, Liu ZH, et al. Predictive symptoms and signs of severe dengue disease for patients with dengue fever: a meta-analysis. *BioMed Research Int* 2014;2014.<http://dx.doi.org/10.1155/2014/359308>
- Rasool F, Ahmad M, Masood I, Khan HM. Evaluating Relationship Between White Blood Cells and Platelets During Recovery Phase In Dengue Hemorrhagic Fever Cases In Punjab, Pakistan: A Retrospective Study. *Value in Health* 2014;17(7):A536-7.
- Khalil MA, Tan J, Khalil MA, Awan S, Rangasami M. Predictors of hospital stay and mortality in dengue virus infection-experience from Aga Khan University Hospital Pakistan. *BMC Research Notes* 2014;7(1):473.
- Assir MZ, Kamran U, Ahmad HI, Bashir S, Mansoor H, Anees SB, et al. Effectiveness of platelet transfusion in dengue Fever: a randomized controlled trial. *Transfusion Medicine and Hemotherapy* 2013;40(5):362-8.
- Pang J, Salim A, Lee VJ, Hibberd ML, Chia KS, Leo YS, et al. Diabetes with hypertension as risk factors for adult dengue hemorrhagic fever in a predominantly dengue serotype 2 epidemic: a case control study. *PLoS Neglected Tropical Dis* 2012; 6(5):e1641.
- Guzmán MG, Alvarez M, Rodriguez R, Rosario D, Vázquez S, Valdés L, et al. Fatal dengue hemorrhagic fever in Cuba, 1997. *Int J Infect Dis* 1999;3(3):130-5.
- Anders KL, Nguyet NM, Chau NV, Hung NT, Thuy TT, Farrar J, et al. Epidemiological factors associated with dengue shock syndrome and mortality in hospitalized dengue patients in Ho Chi Minh City, Vietnam. *Am J Tropical Med Hygiene*. 2011;84(1):127-34.



# Compliance in Type 2 Diabetic Patients Treated with SGLT2 Inhibitors in a Tertiary Care Hospital Peshawar Pakistan

Type 2 Diabetic Patients Treated with SGLT2 Inhibitors

Jamaluddin<sup>1</sup>, Nizamuddin<sup>2</sup>, Manzoor Khan<sup>1</sup>, Shafaq Naz<sup>3</sup>, Amjad Mustafa<sup>4</sup> and Waheed Iqbal<sup>2</sup>

## ABSTRACT

**Objective:** To evaluate the adherence to treatment in type 2 diabetic patients using SGLT2 inhibitors.

**Study Design:**

**Place and Duration of Study:** This study was conducted at the Department of Medicine, Khyber Teaching Hospital Peshawar from August 2018 to January 2019.

**Materials and Methods:** Total 260 diabetic patients, with mean age of  $47 \pm 1.26$  years, were enrolled in the study by non-probability consecutive sampling. After taking informed consent and recording the demographic profile of the patients, SGLT2 inhibitors were given for the treatment of T2DM. Necessary data was collected regarding the compliance of patients to these drugs after 2 months. The statistical analysis was done using SPSS version 20.0 and graph were constructed with graphpad prism software.

**Results:** In total 260 patients, 182 (70%) were male and 78 (30%) were female. Poor compliance (adherence to therapy) was recorded in 60 (23.07%) of patients, while in 200 (76.93%) patients shows good drug compliance. No significant association was observed in patients' compliance with different age group. Similarly, gender makes no difference in compliance to treatment however, female patients shows slightly increase noncompliance as compared to males with OR, 95% CI 1.07(0.55-2.08). Polyuria was the main adverse event for noncompliance of the patient to SGLT-2 inhibitors.

**Conclusion:** Compliance to SGLT-2 inhibitors in our study in 76.93% which may be increased by proper counselling the patients. Furthermore, multiple studies may be conducted with large sample size to further strengthen our findings and to identify other adverse events as well.

**Key Words:** Type-2 Diabetes Mellitus, SGLT 2 inhibitors, drug compliance

**Citation of articles:** Jamaluddin, Nizamuddin, Khan M, Naz S, Mustafa A, Iqbal W. Compliance in Type 2 Diabetic Patients Treated with SGLT2 Inhibitors in a Tertiary Care Hospital Peshawar Pakistan. Med Forum 2019;30(5):56-58.

## INTRODUCTION

Type-2 diabetes mellitus is a multifactorial disorder, which account for more than 93% of cases worldwide. Either insulin deficiency or insulin resistance causes it but in majority of cases both of these mechanism may be involved<sup>1</sup>. DM is considered as the mother of all metabolic disease.

<sup>1</sup>. Department of Medicine, Khyber Teaching Hospital, Peshawar.

<sup>2</sup>. Department of Pharmacology, Khyber Medical College, Peshawar.

<sup>3</sup>. Department of Medicine, Naseer Teaching Hospital, Peshawar.

<sup>4</sup>. Department of Pharmacology, KIMS Kohat.

Correspondence: Dr. Waheed Iqbal, Chemist, Department of Pharmacology, Khyber Medical College, Peshawar.

Contact No: 0334-9190299

Email: waheediqbal22@gmail.com

Received: February, 2019

Accepted: April, 2019

Printed: May, 2019

Robust research is going on the treatment strategies for the management of diabetes mellitus and different drugs option are used so for either alone or in combination with other drugs and even insulin. Most of these drugs are using the body insulin for their final action, which may be either increasing its secretion or increasing its sensitivity.

The new anti-diabetic drugs, which have been used for a few years around the world and recently marketed in Pakistan, are sodium-glucose co-transporter 2 (SGLT-2) inhibitors. SGLT-2 inhibitors, which are also called as gliflozine, include Dapagliflozine (Dapa), Empagliflozine (Empa) and Canagliflozine (Cana)<sup>2,3</sup>. We have used Dapa and Empa in our patients. These drugs basically inhibit the absorption of glucose from the glomeruli by blocking SGLT-2 transport system in the glomeruli<sup>4,5</sup>. By this mechanism, its decrease the blood glucose level by increasing its removal in urine. By this mechanism, these drugs also improve blood pressure and congestive state in CCF patients<sup>6,7</sup>. At the same time, it increases the frequency of urine, which is also one of the most bothersome symptoms of diabetes mellitus itself<sup>8,9</sup>. This increase frequency of micturition, recurrent urinary tract infection and so many other adverse effects make it comparatively bad option for many patients, especially young working slot<sup>7,8</sup>. And

most of the time compliance issue occurs with continuation of these drugs<sup>10,11</sup>.

In spite of these significant adverse effects of SGLT-2 inhibitors, little is known about the compliance related to these drugs on both national and international level. To fill this gap, this study was conducted to know about the compliance of these drugs.

## MATERIALS AND METHODS

This study was mainly conducted in the department of internal medicine, KMC/KTH Peshawar. Duration of study was 6 months, starting from August 2018 to January 2019. Total 260 patients, having T2DM were selected. The group age were 35 and plus years, comprising 70%(182)males and 30%(78) females patients. To avoid any confounders, all Patients with heart failure, ascites, and chronic renal and liver diseases were excluded from the study. The study design was descriptive- cross sectional.

**Data Collection:** After getting approval from ethical committee KMC/KTH and informed consent from the patients, total 260 patients with T2DM, which were fulfilling the criteria for inclusion/exclusion, were enrolled in a consecutive manner. All cases were documented from the medical outdoors department of KTH Peshawar. Demographic information like names, gender and age were recorded. All these patients were prescribed SGLT-2 inhibitors for their T2DM. They were followed for two months and information regarding adherence to the use of these drugs were recorded.

**Data Analysis:** SPSS version 20.0 was used to analyze the data. Chi-square test was done to determine any possible association between categorical values. Similarly, univariate analysis was done to determine age related difference in compliance. P-value <0.05 was considered significant. The graphs were constructed using graph pad prism version 6.0.

## RESULTS

In these 260 studied cases, there were 182 (70%) male and 78 (30%) female, having mean age of  $47 \pm 1.26$  years with minimum age of 35 years. Out of these 260 patients, n=52(20%) patients were in age group 35-45 years old, n=104(40%) patients were in 45-55 years old, n=78(30%) patients were in 55-65 years old, n=26(10%) patients were in above 65 years of age group. The results are summarized in table 1.

Among these 260 patients analyzed, poor compliance was observed in n=60(23.07%) of the patients, while n=200(76.93%) of patients having good compliance as shown in table 2.

In order to find out any possible association between patient compliance with different age groups, univariate analysis was carried out revealing p-value and OR with 95% CI for age group 45-55years, 56-65 years and above 65 years is 0.24, 1.7(0.78-3.6), 0.84, 1.17(0.53-2.5) and 0.42, 1.7(0.54-5.3) respectively. Table 3 shows the respective association results.

No statistical association was observed between gender

and compliance of medication (p-value=0.96) however, female patient are more prone to non-compliance with OR, 95% CI 1.07(0.55-2.08) as mentioned in table 4.

**Table No.1: Age distribution among different patients**

Age	Frequency	Percentage
35-45 Years	52	20%
45-55 Years	104	40%
55-65 Years	78	30%
> 65 Years	26	10%
<b>Total</b>	<b>260</b>	<b>100%</b>

**Table No.2: Compliance observation in study population**

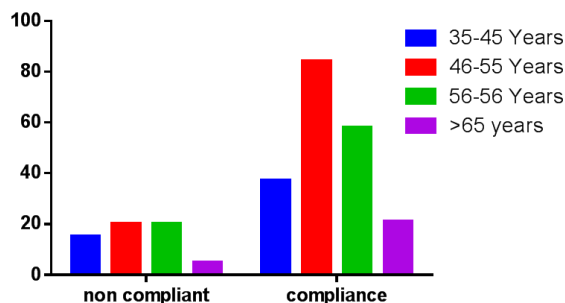
Poor compliance	Frequency	Percentage
Observed	60	23.07%
Not observed	200	76.93%
<b>Total</b>	<b>260</b>	<b>100%</b>

**Table No.3: Association of Compliance with different age groups**

Age group	Poor compliance	Good compliance	p-value	OR (95%CI)
35-45 Years	15	37	Reference	Reference
46-55 Years	20	84	0.24	1.7(0.78-3.6)
56-66 Years	20	58	0.84	1.17(0.53-2.5)
>65 years	5	21	0.42	1.7(0.54-5.3)

**Table No.4: Association of compliance with gender**

Poor compliance	Male	Female	p-value	OR (95%CI)
Observed	46	16	0.96	1.07 (0.55-2.08)
Not observed	136	44		
<b>Total</b>	<b>182</b>	<b>60</b>		



**Figure No.1: Patient compliance with different age groups**

## DISCUSSION

T2DM is a chronic metabolic disease, which is affecting almost every organ of the body. The number of patient is increasing day by day, but at the same time new drugs is continuously adding in the therapeutic armamentarium against diabetes. SGLT-2 inhibitors are

the new drugs, recently added to the treatment regimen against T2DM<sup>13, 14</sup>.

In our study 23.07% of patients presented with non/poor compliance when treated with SGLT-2 inhibitors with complain of polyuria while 76.93% patients do not complain about any side effects related to the stated drugs. The poor compliance was high in the age group of 46-55 years followed by age group >65 years and 56-65 years respectively. In a study conducted United States by Jennifer Cai, Victoria Divino et al, in 2107, where 23702 patients were evaluated for drug compliance, who were using different anti diabetes medication. Out of 23702 patients, 9633 were on SGLT-2 inhibitors. Poor compliance was observed to SGLT-2 inhibitors in these patients, which was slightly more for DAPA than CANA<sup>15</sup>.

SGLT-2 inhibitors facilitate the removal of glucose in urine by inhibiting sodium-glucose transporter 2 in glomeruli. These drugs cause a number of adverse effects, in which polyuria and UTI are the most commonly reported especially females are more prone to develop UTI<sup>12</sup> as compared to males and this is one of the reasons that females may shows noncompliance when treated with SGLT-2 inhibitors with OR, 95% CI 1.07(0.55-2.08).

Due to polyuria and UTI, strict compliance is difficult for most of the patients especially working group but patient counselling may be helpful to further reduce noncompliance because patient with hyperglycemia are exposed to micro and macro vascular complications thus drugs that enhances glucuresis are helpful to balance hyperglycemia and prevent the patients from long term micro-macro vascular complications<sup>3</sup>.

## CONCLUSION

SGLT-2 inhibitors are good choice to treat T2DM and manage hyperglycemia. Besides its adverse effects the drugs also has long term beneficial role in delaying macro vascular complications. The non-compliance reported in our study may be reduced, by proper counseling of the patients in other studies with large sample size.

### Author's Contribution:

Concept & Design of Study:	Jamaluddin, Manzoor khan
Drafting:	Nizamuddin
Data Analysis:	Amjad Mustafa, Waheed Iqbal
Revisiting Critically:	Manzoor Khan
Final Approval of version:	Shafaq Naz

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

- Papadakis MA, McPhee SJ, Rabow MW. Current medical diagnosis and treatment 2017:McGraw-Hill Education;2017.
- Tahrani AA, Barnett AH, Bailey CJ. SGLT inhibitors in management of diabetes. *The Lancet Diabetes Endocrinol* 2013;1(2):140-51.
- Kalra S. Sodium glucose co-transporter-2 (SGLT2) inhibitors: a review of their basic and clinical pharmacology. *Diabet Therap* 2014;5(2):355-66.
- Bays H. Sodium glucose co-transporter type 2 (SGLT2) inhibitors: targeting the kidney to improve glycemic control in diabetes mellitus. *Diabet Therap* 2013;4(2):195-220.
- Gomez-Peralta F, Abreu C, Lecube A, Bellido D, Soto A, Morales C, et al. Practical approach to initiating SGLT2 inhibitors in type 2 diabetes. *Diabet Therap* 2017;8(5):953-62.
- Briasoulis A, Al Dhaybi O, Bakris GL. SGLT2 inhibitors and mechanisms of hypertension. *Current Cardiology Reports* 2018;20(1):1.
- Singh JS, Fathi A, Vickneson K, Mordi I, Mohan M, Houston JG, et al. Research into the effect Of SGLT2 inhibition on left ventricular remodelling in patients with heart failure and diabetes mellitus (REFORM) trial rationale and design. *Cardiovascular Diabetol* 2016;15(1):97.
- Tamez-Perez HE, Delgadillo-Esteban E, Soni-Duque D, Hernández-Coria MI, Tamez-Peña AL. SGLT2 inhibitors as add on therapy in type 2 diabetes: a real world study. *J Diabet Metabolic Disorders* 2017;16(1):27.
- Dziuba J, Alperin P, Racketa J, Iloeje U, Goswami D, Hardy E, et al. Modeling effects of SGLT-2 inhibitor dapagliflozin treatment versus standard diabetes therapy on cardiovascular and microvascular outcomes. *Diabetes, Obesity and Metabolism* 2014;16(7):628-35.
- Li H, Shi F-H, Huang S-Y, Zhang S-G, Gu Z-C. Clinical adverse effects of sodium-glucose cotransporter 2 inhibitors: Protocol for a systematic review and meta-analysis. *Medicine* 2018;97(32).
- Liu J, Li L, Li S, Jia P, Deng K, Chen W, et al. Effects of SGLT2 inhibitors on UTIs and genital infections in type 2 diabetes mellitus: a systematic review and meta-analysis. *Scientific reports*. 2017; 7(1):2824.
- Kalra S, Baruah MP, Sahay R. Medication counselling with sodium glucose transporter 2 inhibitor therapy. *Ind J Endocrinol Metabolism* 2014;18(5):597.
- Scheen AJ. Pharmacodynamics, efficacy and safety of sodium-glucose co-transporter type 2 (SGLT2) inhibitors for the treatment of type 2 diabetes mellitus. *Drugs* 2015;75(1):33-59.
- Nauck MA. Update on developments with SGLT2 inhibitors in the management of type 2 diabetes. *Drug design, development and therapy* 2014; 8:1335.
- Jennifer Cai, Victoria Divino & Chakkarin Burudpakdee. Adherence and persistence in patients with type 2 diabetes mellitus newly initiating canagliflozin, dapagliflozin, dpp-4s, or glp-1s in the United States, *Current Medical Research and Opinion* 2017;33:7,1317-1328.

# Comparison of Ischemic and Hemorrhagic Strokes in Hypertensive Patients at Tertiary Care Hospital

Comparison of  
Ischemic and  
Hemorrhagic  
Strokes in  
Hypertensive

Shahzad Memon<sup>1</sup>, Hamid Ali Shaikh<sup>2</sup>, Kamal Ahmed<sup>4</sup>, Mujahid Ali Chandio<sup>3</sup>, Muhammad Zarar<sup>3</sup> and Arslan Badar Shaikh<sup>3</sup>

## ABSTRACT

**Objective:** To compare ischemic and hemorrhagic types of stroke in tertiary care hospital.

**Study Design:** Comparative study

**Place and Duration of Study:** This study was conducted at the Medical Department of PMC Hospital Nawabshah from August 2018 to January 2019.

**Materials and Methods:** This study included total 50 patients. All patients were admitted from Medical OPD and emergency department of PMCH Nawabshah. All the patients with clinical features of stroke were admitted. CT Scan was done to diagnose properly and treated accordingly.

**Results:** Out of total 50 patients, 32 (64%) were male and 18 (36%) were female. Age ranged from 31 to 90 years in males and females. Majority of patients presented from 61-70 years that were 19 (38%) of all. Ischemic stroke was common. It was 36 (72%) whereas hemorrhagic was in 14 (28%).

**Conclusion:** The incidence of ischemic stroke is common in accordance with age, sex and etiology as compared to hemorrhagic. Age presentation is common from 60 to 70 years.

**Key Words:** Stroke, Ischemic, Hemorrhagic, CT Scan

**Citation of articles:** Memon S, Shaikh HA, Ahmed K, Chandio MA, Zarar M, Shaikh AB. Comparison of Ischemic and Hemorrhagic Strokes in Hypertensive Patients at Tertiary Care Hospital. Med Forum 2019;30(5):59-62.

## INTRODUCTION

Cerebrovascular disease is the 3<sup>rd</sup> most common etiology of death in 3<sup>rd</sup> world. It is the 2<sup>nd</sup> most common cause of death throughout the globe. World Health Organization reports about 5 million people expires only in beginning of 21<sup>st</sup> century and 20% of these deaths occurred in south Asian region. Though there is decrease in incidence of stroke in developed countries but the incidence is still higher in south Asia and is continuously rising.<sup>1</sup>

In developing countries, the rate of death due to circulatory disorders is increased among patients suffering from stroke and ischemic heart disease.

<sup>1</sup>. Department of General Medicine, Pir Abdul Qadir Shah Jilani Institute, Gamabat.

<sup>2</sup>. Department of Neurosurgery / Medicine<sup>3</sup>, PUMHSW Nawabshah

<sup>4</sup>. Liaquat National Hospital and medical College Karachi.

Correspondence: Dr Shahzad Memon, Assistant Professor of General Medicine, Pir Abdul Qadir Shah Jilani Institute, Gamabat.

Contact No: 0333-7051582

Email: shahzadphysician@gmail.com

Received: February, 2019

Accepted: April, 2019

Printed: May, 2019

Among white people, the incidence rate is from 80% to 85% whereas 60-70% of Asian and blacks are affected by this disease.<sup>2</sup>

Stroke is the common complication of hypertension and may be due to cerebral hemorrhage or cerebral infarction. Carotid atheroma and transient cerebral ischemic attacks are common in hypertensive patients.<sup>3</sup> Hypertension is a major risk factor for ischemic and hemorrhagic strokes. Hypertension is found in 72-81% of patients with intra-cerebral hemorrhage. 80% of patients with diagnosis of acute stroke are hypertensive at the time of admission in hospital and 30% are classified as hypertensive on long term follow up.<sup>4</sup>

The risk of stroke increases above Blood Pressure levels of 115/75mmHg. This association is steep among adult population. 2/3<sup>rd</sup> of this burden occurs in middle aged persons aged between 45 to 69 years and 2/3<sup>rd</sup> occurs in developing countries.<sup>5</sup>

Acute stroke is characterized by the rapid appearance (usually over minutes) of a focal deficit of brain function, most commonly a hemiplegia with or without signs of focal higher cerebral dysfunction (such as aphasia), hemi sensory loss, and visual field defect or brainstem deficits. Weakness on one side of face or body, slurred speech, numbness on affected side, vision changes and balanced difficulties. Hemorrhagic stroke present with sudden headache associated with vomiting, neck stiffness and decreased consciousness.<sup>6,7</sup>

Computerized Tomography (C.T) is very sensitive and specific for hemorrhage with in first eight days of stroke only, in general, strategies in which most patients were scanned immediately cost least and achieved the most qualities as cost of providing C.T, ( even out of hours) was less than cost of inpatient care .<sup>8</sup>

Treatment includes medication, life style changes and least likely surgery. The medications used are aspirin, clopidogrel, heparin, warfarin, ACE inhibitors, beta blockers and anti diabetic medications.<sup>9</sup>

The rationale of our study is to compare the ischemic and hemorrhagic strokes according to age, sex, type of stroke and multiple variations in their presentations so that patients may be diagnosed easily and be advantageous to populace of Pakistan.

## MATERIALS AND METHODS

This is a comparative study of 50 patients admitted through Emergency/ medical Outpatient department (MOPD) in medical Department of Peoples Medical College Hospital Nawabshah This study was conducted from August 2018 to January 2019. This is tertiary care hospital receiving and treating the patients of not only but also other provinces of Pakistan.

All the patients admitted had aphasia, hemi-sensory loss and visual field defect. Physical examination was done to record the BP and pulse rate. Neurological examination was done including the examination of motor and sensory system, Glasgow coma scale (GCS), cranial nerves and higher mental functions. Examination of cardiovascular system was also done. Apart from the routine investigations, CT scan brain and ECG was also done to diagnose the disease. Chi-square test was used to check association between hypertension and type of acute stroke.

## RESULTS

A total of 50 stroke patients with history of hypertension were included in this study. Out of these 50 patients 32 (64%) were male and 18 (36%) were female.

Age ranged from 60 to 70 years. Mean age was 60.58, for male it was 61.3 and for females it was 59.2 (Table 1). The frequency of ischemic as well as hemorrhagic stroke was more in males as compared to females (Table 2). It was common in married than unmarried patients. New onset was common than recurrent and new onset was more common in patients suffering from ischemic than hemorrhagic. Crossed hemiplegia was less common as compared to uncrossed one among ischemic stroke patients. In our study, smoking was seen to be major risk factor. Other risk factors found were Diabetes Mellitus, IHD, Atrial

Fibrillation, and alcohol use. Other patients have no any risk factor but Hypertension.

Age ranged from 31 to 90 years in males and females. Majority of patients presented from 61-70 years that were 19 (38%) of all. 32 (64%) patients were male and 18 (36%) were female.

The rate of infarction was 36 (72%) as compared to hemorrhage that was 14 (28%). Incidence was higher in 6<sup>th</sup> and 7<sup>th</sup> decade of their life. It was higher in males as compared to females. 34 male were affected by this disease whereas only 16 female were suffered from both conditions.

**Table No. 1: Distribution of hypertensive stroke patients according to age groups**

Age groups	Male	Female	Total
31-40	01	01	02
41-50	5	03	8
51-60	8	5	13
61-70	12	7	19
71-80	5	01	6
81-90	01	01	02
Total	32(64%)	18(36%)	50

**Table No. 2: Cummulative distribution of hemorrhage and infarction in various age groups and sex**

Age groups	Sex	Infarction	Hemorrhage
31-40	Male	01	02
	Female	00	01
41-50	Male	04	02
	Female	02	01
51-60	Male	5	02
	Female	04	01
61-70	Male	8	03
	Female	6	01
71-80	Male	5	01
	Female	00	00
81-90	Male	01	00
	Female	00	00
Total		36 (72%)	14 (28%)

**Table No. 3: Relationship of sex with type of stroke**

Type	Sex		Total
	Male	Female	
Ischemic	24	12	36 (72%)
Hemorrhagic	8	6	14 (28%)
Total	32	18	50 (100%)

Ischemic and hemorrhagic types were common among male as compared to females. Ischemic was in 24 and 12 in male and females respectively. Hemorrhagic was found to among 8 males and 6 females. Overall, ischemic was common in both genders. It was 36 (72%) whereas hemorrhagic was in 14 (28%) (Table No.3).

## DISCUSSION

Stroke is the most common disorder in Pakistan. It is one of the common cause of increasing mortality and morbidity after IHD and Carcinoma. It is the clinical syndrome characterized by sudden onset of focal neurological signs lasting for more than 24 hours. This definition is also verified by WHO.<sup>10</sup>

Hypertension has been considered as a major risk factor for stroke and IHD. There is linear relationship between stroke and hypertension as said by Framingham study. This study entails that treating hypertension decreases the incidence of stroke. This implication has been well tested and compared in randomized trials of primary prevention of stroke.<sup>11</sup>

In studies conducted in Portugal, Poland and Taiwan, male female ratio was 1.2:1, 1.4:1 and 1.6:1 respectively. In our study male incidence is also increased as compared to females. Female ratio in our study is less because females have lesser smoking habit.<sup>12</sup>

The incidence of stroke was found to be highest among patients aged 61 to 70 in our study. Similar observations were reported by Al-Rajeh et al in Saudi Arabia.<sup>13</sup>

The mean age in our patients was 62.35% years. Slightly higher mean age (68 years) was reported by Fonesa et al, in Portugal. However amongst Mexican American population a relatively young mean age was found i.e. 58 years, which they attribute to high prevalence of Diabetes Mellitus in their population.<sup>14</sup>

Comparing the type of stroke in hypertensive patients our study showed an increase incidence of infarctive stroke of 36(72%) as compared to hemorrhagic stroke in 14( 28%). Different and similar observations are shown by many other populations probably depending upon the environmental, dietary and other social factors, for example: Japanese population showed an incidence of infarctive stroke to be 56%<sup>[131]</sup>. Brazilian population showed an incidence of 73% for cerebral infarction, 19% for cerebral hemorrhage and 8% for subarachnoid hemorrhage. American population showed an incidence of infarctive stroke to be 78%. Bamford et al have shown an incidence of 73% for infarctive stroke, 21% for hemorrhagic and 6% for subarachnoid hemorrhage in Great Britain.<sup>15</sup>

## CONCLUSION

It is concluded that the incidence of ischemic stroke is common among both genders as compared to hemorrhagic. Males are common victim of this disease and commonly come in medical emergency in their 6<sup>th</sup> and 7<sup>th</sup> decade of their life. Infarction is common as compared to hemorrhage.

### Author's Contribution:

Concept & Design of Study: Shahzad Memon

Drafting:	Hamid Ali Shaikh, Kamal Ahmed
Data Analysis:	Mujahid Ali Chandio, Muhammad Zarar, Arslan Badar Shaikh
Revisiting Critically:	Shahzad Memon, Kamal Ahmed
Final Approval of version:	Shahzad Memon

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. Mozaffarian D, Benjamin EJ, Go AS. Heart disease and stroke statistics-2016 update: a report from the American heart association. *Circulation* 2016;133(4):38–40.
2. Moran A, Forouzanfar M, Sampson U, Chugh S, Feigin V, Mensah G. The epidemiology of cardiovascular diseases in sub-Saharan Africa: the Global Burden of Diseases, Injuries and Risk Factors 2010 Study. *Progress in Cardiovascular Diseases* 2013;56(3):234–239.
3. United kingdom. State of the Nation Stroke statistics 2016, <https://www.stroke.org.uk>.
4. Tan KS, Navarro JC, Wong KS. Clinical profile, risk factors and aetiology of young ischaemic stroke patients in Asia: A prospective, multicentre, observational, hospital-based study in eight cities. *Neurol Asia* 2014;19(2):117–127.
5. Manorenj S, Inturi S, Jyotsna B, Savya V, Areli D, Reddy B. Prevalence, pattern, risk factors and outcome of stroke in women: a clinical study of 100 cases from a tertiary care center in South India. *Int J Research Med Sci* 2016;4(6):2388–2393.
6. Owolabi MO, Arulogun O, Melikam S, Adeoye AM, Akarolo-Anthony S, Akinyemi R, Arnett D, Tiwari H, Gebregziabher M, Jenkins C, Lackland D. The burden of stroke in Africa: a glance at the present and a glimpse into the future. *Cardiovascular J Africa* 2015;26(2 H3Africa Suppl):S27..
7. World Health Organization, “Non-communicable diseases (NCD) country profile of 2014 Geneva,” [http://apps.who.int/iris/bitstream/10665/128038/1/9789241507509\\_eng.pdf?ua=1](http://apps.who.int/iris/bitstream/10665/128038/1/9789241507509_eng.pdf?ua=1).
8. Gebremariam SA, Yang HS. Types, risk profiles, and outcomes of stroke patients in a tertiary teaching hospital in northern Ethiopia. *eNeurological Sci* 2016;3:41-7..
9. Wu CY, Wu HM, Lee JD, Weng HH. Stroke risk factors and subtypes in different age groups: a hospital-based study. *Neurol Ind* 2010;58(6):863.
10. Fekadu G, Chelkeba L, Melaku T, Tegene E. Pathological sub types and diagnostic protocols of

- stroke among adult patients admitted to jimma university medical center, South West Ethiopia. *J Neurol Neurophysiol* 2018;9(4):466.
11. World Health Organization, "The WHO step wise approach to stroke surveillance Geneva 2006," <http://www.who.int/chp/steps/Stroke/en/>.
  12. Jowi JO, Mativo PM. Pathological sub-types, risk factors and outcome of stroke at the Nairobi Hospital, Kenya. *East Afri Med J* 2008;85(12)..
  13. Kuriakose C, Shifafiya MN, Tharakan NS, Sattanathan K, Kumar RS. A prospective study of clinical profile of stroke in a tertiary care hospital. *Asian J Pharmaceutical and Clin Res* 2016;9(3): 1-4.
  14. Walker RW, Rolfe M, Kelly PJ, George MO, James OF. Mortality and recovery after stroke in the Gambia. *Stroke* 2003 Jul 1;34(7):1604-9.
  15. Tirschwell DL, Ton TG, Ly KA, Van Ngo Q, Vo TT, Pham CH, et al. A prospective cohort study of stroke characteristics, care, and mortality in a hospital stroke registry in Vietnam. *BMC Neurol* 2012;12(1):150.

# Comparison of Postoperative Outcomes of Open Versus Closed Hemorrhoidectomy at Tertiary Care Hospital

Postoperative  
Outcomes of  
Open Versus  
Closed  
Hemorrhoidectomy

Abdul Hakeem Jamali, Mashooq Ali Khowaja, Inayat Ali Zardari, Zulfqar Ali Imtiaz Memon, Altaf Hussain Ghumro and Imtiaz Ali Soomro

## ABSTRACT

**Objective:** The objective of our study is to compare the outcome of open hemorrhoidectomy with or without lateral internal sphincterotomy with regard to postoperative complications

**Study Design:** Comparative study

**Place and Duration of Study:** This study was conducted at the Surgical Department PMCH Nawabshah from January 2018 to January 2019.

**Materials and Methods:** All the patients were admitted through surgical OPD. Digital rectal examination along with proctoscopy was done to rule out other surgical ano-rectal pathologies. All the required investigations were done and open hemorrhoidectomy was done.

**Results:** This study was conducted on 100 patients. They were divided into two groups. Group A included 50 (50%) patients and Group B included 50 (50%). Group A underwent only open hemorrhoidectomy without LIS whereas Group B underwent LIS apart from open Hemorrhoidectomy. Postoperative pain was seen in 20% of patients in Group A whereas it was only 10% in Group B. Less hospital stay and early return to work was found in Group B patients.

**Conclusion:** It is concluded that the open hemorrhoidectomy with LIS is the better option as compared to without LIS keeping in view the outcome of both procedures.

**Key Words:** Proctoscopy, Open Hemorrhoidectomy, Postoperative Pain, Ano-Rectal

**Citation of articles:** Jamali AH, Khowaja MA, Zardari IA, Memon ZAI, Ghumro AH, Soomro IA. Comparison of Postoperative Outcomes of Open Versus Closed Hemorrhoidectomy at Tertiary Care Hospital. Med Forum 2019;30(5):63-65.

## INTRODUCTION

The word "Hemorrhoid" was first used in 1398, derived from old French "emoeeoides", from Latin "haemorrhoida", from greek αιμορροϊς (Haimorrhoids), "liable to discharge blood". It is divided into two words Haima meaning blood and rhoos means "stream, flow, and current".<sup>1</sup>

Hemorrhoids are simply defined as the abnormal changes in the anal cushion. These result in the rupture of the supporting connective tissue and later on the enlargement of the vascular plexus.

Haemorrhoids are the most common disease of all anal diseases usually affecting 1 in 4 of the population. In United Kingdom, more than 20,000 patients are operated for this disease.<sup>2</sup>

Department of Surgery, PUMHSW Nawabshah.

Correspondence: Dr. Mashooq Ali Khowaja, Associate Professor, Surgical Unit-III, PUMHSW Nawabshah.  
Contact No: 0300-2446047  
Email: altafkhadim@yahoo.com

Received: February, 2019  
Accepted: April, 2019  
Printed: May, 2019

According to Goligher classification, Hemorrhoids are classified into four grades. In Grade 1, hemorrhoids bleed but do not prolapse. In Grade 2, hemorrhoids bleed and also prolapse but reduce spontaneously. Grade 3 hemorrhoids bleed, prolapse and reduce manually. Diagnosis is done clinically.<sup>3</sup>

The treatment of haemorrhoids is divided into conservative and interventional. Conservative treatment includes change in diet and life style such increase in oral fluids, regular exercise, avoidance of straining and constipation inducing medications. The combinations of steroids, anesthetics, antiseptics and barrier creams help in relief of symptoms temporarily. In addition, venotonic therapies (Oral Flavonoid) have also enormous effects on bleeding, pruritis and discharge if any.<sup>4</sup>

Different Outpatient procedures are also performed. The most common among them is the use of Rubber Band Ligation but many studies have proved that it has recurrence rate of >30%. 4<sup>th</sup> grade present with persistent prolapse. Another OPD procedure is injection sclerotherapy. Others include infrared coagulation, bipolar, direct current and radiofrequency ablation therapy and also the combination therapy.<sup>5</sup>

Surgical therapies involve Haemorrhoidectomy. It is performed by two methods viz Open excision (Milligan-Morgan) and Closed (Ferguson). Recent



advances in open technique are diathermy, lasers and ultrasonic dissectors. Variations in Ferguson technique involve the Ligasure coagulator which is postulated to seal the tissue with minimal thermal spread with resultant reduced postoperative pain.<sup>6</sup>

All of these techniques have complications. These are pain, bleeding, urinary retention, infection, iatrogenic fissuring, stenosis and incontinence. Among all these, the dreadful complication is Postoperative pain. This is of two types viz rest pain and defecation pain. Exact cause of pain is still not determined but common theory is that it is due to spasm of Internal Anal Sphincter (IAS) because of insertion of anal pack, injury of nerve endings or the mucosal lining of the anal canal, suturing at the pedicle or below the dentate line, wound infection and the development of anal fissure.<sup>7</sup>

Lateral internal sphincterotomy is the commonly used adjunct treatment following open hemorrhoidectomy. Its supporters are of the opinion that it relieves patient from postoperative pain by abolishing spasm of the IAS.<sup>8</sup>

The rationale of study is to compare the outcomes of open hemorrhoidectomy with or without lateral internal sphincterotomy so that patients may be pain free postoperatively aimed at relieving patients from social isolation, economic burden and psychological trauma.

## MATERIALS AND METHODS

This is a comparative study of 100 patients admitted through Surgical Outpatient department (SOPD) in surgical Department of Peoples Medical College Hospital Nawabshah. This study was done from December 2017 to December 2018. PMC Hospital is a tertiary care hospital where patients are admitted not only from Sindh but also from other provinces of Pakistan. All the patients admitted had complain of bleeding per rectum, itching, something coming out of anus, painless defecation. On digital rectal examination, hemorrhoids were prolapsed and there was no any mass palpated in rectum. On proctoscopy, no any mass or polyp of rectum was found but only hemorrhoids at 3, 7, 11 o'clock were found that were prolapsed but not strangulated or thrombosed. All routine investigations were done apart from cardiac opinion and anesthesia fitness. All patients were operated on elective list. Open hemorrhoidectomy was done with or without lateral internal sphincterotomy.

## RESULTS

In this study, total 100 patients were included from all surgical wards of PMCH Nawabshah. They were divided into two groups. Group A included 50 (50%) patients who were operated for hemorrhoids with open hemorrhoidectomy without lateral internal sphincterotomy (LIS) and Group B included 50 (50%) who underwent open hemorrhoidectomy with LIS.

In Group A, 50 patients were operated and Group B also included 50 patients. They were assessed keeping in view the postoperative ratio of complications.

Among Group A, 20 (40%) patients complained of pain during defecation postoperatively. Only 3 (6%) complained of postoperative bleeding. 15 (30%) patients were catheterized on operative day due to retention of urine. 10 (20%) came on follow up with complain of stenosis. 2 (4%) came with stool incontinence and 2 (4%) with anal fissure. Table 1.

Among Group B patients, 5 (10%) complained of painful defecation after surgery. 4 (8%) developed bleeding postoperatively that was treated accordingly. 10 (20%) patients were catheterized on operative day due to retention of urine. 2 (4%) came with stenosis postoperatively and 2 (4%) developed stool incontinence and there was no any complication of anal fissure in this group postoperatively. Table 2.

**Table No.1: Group A**

S.No	Complications	No of patients	Percentage
1	Defecation pain	20	40%
2	Bleeding	3	6%
3	Urinary retention	15	30%
4	Stenosis	10	20%
5	Incontinence	2	4%
6	Anal fissure	2	4%

**Table No.2: Group B**

S.No	Complications	No of patients	percentage
1	Defecation pain	5	10%
2	Bleeding	4	8%
3	Urinary retention	10	20%
4	Stenosis	2	4%
5	Incontinence	2	4%
6	Anal fissure	0	0%

## DISCUSSION

During screening colonoscopy, higher incidence of hemorrhoids is found up to 40% and 44.7% are symptomatic which require to undergo surgical procedures. Excisional hemorrhoidectomy is the best choice in these cases with 2% medium term recurrence and 10% long term recurrence. However, it has also demerit of postoperative pain due to different reasons. One of these is the spasm of lateral internal sphincter. Some surgeons use lateral internal sphincterotomy to decrease postoperative pain. But still this debate is controversial.<sup>9</sup>

Currently, majority are of the opinion that spasm of lateral sphincter is the cause of postoperative pain.<sup>10</sup> In our study it is also observed that patients of Group A who did not undergo LIS developed more pain as compared to Group B patients.

Lewis et al reported the incidence of fecal incontinence up to 17% in those patients who underwent LIS. Khubchand et al reported the fecal incontinence

incidence upto 22% but in our study it 4% only and it was transient later on relived with conservative therapy. Some studies have used nitroglycerine and botulinum toxin for transient relaxation of Internal Anal Sphincter (IAS) but these drugs are effective temporarily. In our study, LIS has proved to be effective for long term.<sup>11</sup>

One study showed that 14% of patients were reported to develop urinary retention and this study showed no difference for urinary retention to both type of patients who underwent LIS or not.<sup>12</sup> Same was observed in our study. Group A and Group B patients developed somewhat equal ratio of urinary retention from 30% to 40%. There was no any difference found among both groups. So it is said that effect of LIS is lacking in Urinary retention.

One international study shows the similar incidence of postoperative bleeding in all patients who were operated for LIS or not.<sup>13</sup> Same is found in our study. It was from 6% to 8% postoperatively that was treated conservatively and no any patient needed intervention.

3 studies showed the decrease in hospital stay of patients with LIS as compared to other group.<sup>14</sup> Same was found in our study. Hospital stay of Group B was minimum and they returned early to their jobs because of rapid relief from postoperative pain.

## CONCLUSION

Our study concluded that the open hemorrhoidectomy with Lateral internal Sphincterotomy is the better procedure because of decreased postoperative pain, minimum hospital stay and early mobilization of the patients.

### Author's Contribution:

Concept & Design of Study: Abdul Hakeem Jamali  
Drafting: Mashooq Ali Khowaja,  
Inayat Ali Zardari

Data Analysis: Zulfaqar Ali Imtiaz  
Memon, Altaf Hussain  
Ghumro, Imtiaz Ali  
Soomro

Revisiting Critically: Abdul Hakeem Jamali,  
Mashooq Ali Khowaja,  
Inayat Ali Zardari

Final Approval of version: Abdul Hakeem Jamali

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

- Hollingshead JR, Phillips RK. Hemorrhoids: modern diagnosis and treatment. *Postgrad Med J* 2016;92:4–8.
- Das D, Choudhury U, Lim Z. Effectiveness of internal sphincterotomy in reducing post open hemorrhoidectomy pain: a randomized comparative clinical study. *Int J Collab Res Intern Med Public Health* 2013;5:428.
- Taha SA. Routine internal sphincterotomy with hemorrhoidectomy for third and fourth degree hemorrhoids greatly improves the outcome. *IJGE* 2013;1:48–51.
- Raza M, Khan A, Kamran R. Hemorrhoidectomy with and without lateral internal sphincterotomy. *J Rawalpindi Med Coll* 2013;17:189–91.
- Lu M, Shi GY, Wang GQ. Milligan-Morgan hemorrhoidectomy with anal cushion suspension and partial internal sphincter resection for circumferential mixed hemorrhoids. *World J Gastroenterol* 2013;19:5011–5.
- Joshi GP, Neugebauer EA. Evidence-based management of pain after haemorrhoidectomy surgery. *Br J Surg* 2010;97:1155–68.
- Orr PM, Shank BC, Black AC. The role of pain classification systems in pain management. *Crit Care Nurs Clin North Am* 2017;29:407–18.
- Bonakdar RA. Integrative pain management. *Med Clin North Am* 2017;101:987–1004.
- Ahmad N, Aziz M. Closed lateral Internal Sphincterotomy under local anesthesia in OPD in the treatment of chronic Anal Fissure. *Annals King Edward Med Univ* 2004;10(1).
- Abbas T, Maqsood R, Bajwa MA, Akhtar MT. Is stapled hemorrhoidectomy a safe procedure for third and fourth grade hemorrhoids. *Pak Armed Forces Med J* 2019 Feb 28;69(1):92–6..
- Rathore, M. M., & Shukr, I. (2010). Outcome of surgical haemorrhoidectomy by open and closed techniques. *Pak Armed Forces Med J* 60(3), 402–4.
- Rathore MM, Shukr I. Outcome of surgical haemorrhoidectomy by open and closed techniques. *Pak Armed Forces Med J* 2010;60(3):402–8.
- Sammour T, Barazanchi AW, Hill AG. Evidence-based management of pain after excisional haemorrhoidectomy surgery: a PROSPECT review update. *World J Surg* 2017;41(2):603–14..
- Ala S, Eshghi F, Enayatifard R, Fazel P, Rezaei B, Hadianamrei R. Efficacy of cholestyramine ointment in reduction of postoperative pain and pain during defecation after open hemorrhoidectomy: results of a prospective, single-center, randomized, double-blind, placebo-controlled trial. *World J Surg* 2013;37(3):657–62.

# Frequency of Pre Diabetes in Patients with Positive Family History at Tertiary Care Hospital

Muhammad Zarar, Shahzad Memon, Arslan Badar Shaikh, Mujahid Ali Chandio, Anwar Ali Jamali and Ruqayya Farhad

## ABSTRACT

**Objective:** To find out the frequency of pre-diabetes in patients with positive family history at People's Medical College Hospital Nawabshah.

**Study Design:** Cross sectional study

**Place and Duration of Study:** This study was conducted at the Medical Department and Medical OPD of People's Medical College Hospital Nawabshah from January 2018 to January 2019.

**Materials and Methods:** A total of 70 patients having one or more than one risk factors like history of diabetes mellitus, obesity, hypertension, low HDL and hypertriglyceridemia were included in this study. Blood samples were taken for overnight 8 hours fasting blood glucose estimation. If it was impaired, per oral 75 grams of glucose was given to them and blood samples after two hours for glucose tolerance test.

**Results:** A total of 70 patients were included in this study. There were 40(57.14%) males and 30(42.86%) females as presented in figure 5. Age ranged from 30 to 45 years. 15 (21.42%) patients aged from 30 to 35 years. 20 (28.57%) patients were of 36 to 40 years and 35(50%) patients age was from 41 to 45. Rate of pre diabetes was seen to be higher among those who had family history of D.M. 40 (57.14%) patients had positive family history. Next risk factor was hypertension (B.P > 140/90 mmHg) seen in 15(21.42%) patients. Hypertriglyceridemia was in 10 (14.28%) patients and hypercholesterolemia was in 5 (7.14%) patients

**Conclusion:** The most common risk factor for developing Diabetes Mellitus is positive family history of Diabetes Mellitus then next is the hypertension and last one is the cholesterol level or obesity.

**Key Words:** Pre-diabetes, Type 2 diabetes, Hypertriglyceridemia, Hypercholesterolemia

**Citation of articles:** Zarar M, Memon S, Shaikh AB, Chandio MA, Jamali AA, Farhad R. Frequency of Pre Diabetes in Patients with Positive Family History at Tertiary Care Hospital. Med Forum 2019;30(5):66-68.

## INTRODUCTION

Pre diabetes is defined as the state in which glycaemic parameters are at or above the normal level but below the diabetic threshold including the impaired fasting glucose and impaired glucose tolerance.<sup>1</sup> These persons usually develop type 2 diabetes within a decade. International Diabetic Federation has estimated the rise in diabetes up to 552 million by 2030 A.D which predicts that 3 persons will develop diabetes within ten seconds and 10 million per year.<sup>2</sup> It is proved that 183 million people even don't know about their disease of Diabetes Mellitus (D.M). In South Asia, 120.9 million people will develop D.M by 2030.<sup>2</sup>

Department of Medicine, PUMHSW Nawabshah.

Correspondence: Dr Muhammad Zarar, Senior Registrar Medicine, PUMHSW Nawabshah.

Contact No: 0333-7024058

Email: zarrarahmed@yahoo.com

Received: February, 2019

Accepted: April, 2019

Printed: May, 2019

Many studies including study of Butler show that obese people with impaired fasting glucose (IFG) had deficiency of Beta cell of pancreas. Prediabetes usually converts into diabetes within a few years.<sup>3</sup> This was proved by study of Nichols findings which showed 1.3% newly diagnosed patients developed Diabetes Mellitus at 41.4 months whereas previously diagnosed patients developed this disease at 29 months.<sup>4</sup> Recent diabetes prevention prospective study in China showed that incidence of diabetes in prediabetics was 90%.<sup>5</sup> Pakistan is sixth of Top Ten countries having Diabetes Mellitus. It is expected to be 4<sup>th</sup> with 15 million people suffering from DM by the year 2025.<sup>6,7</sup> People with pre diabetics have not only increased risk of D.M but also are vulnerable to develop cardiovascular diseases. Some studies show that free fatty acids and insulin resistance with prediabetics promote coronary artery atherosclerosis.<sup>8,9</sup> The rationale of our study is to find out the rate of pre diabetes among population in order to make it necessary to do screening with risk factor, early detection of pre diabetes and its management with modification of life style, diet, regular exercise and prevention of obesity.

## MATERIALS AND METHODS

This is a comparative study of 70 patients admitted through Emergency/ Medical Outpatient department (MOPD) in medical Department of Peoples Medical College Hospital Nawabshah This study was conducted from January 2018 to January 2019. This is tertiary care hospital receiving and treating the patients of not only but also other provinces of Pakistan.

All the patients admitted had positive family history of Diabetes mellitus and hypertension as considered high risk to them. Both genders were included in study. Age ranged from 30 to 45 years. All diagnosed patients of type 1 and type 2 D.M were excluded from the study.

First degree healthy relatives of patients with known risk factors for diabetes mellitus were admitted from Medical wards and MOPD of People's Medical College Hospital. A detailed medical history regarding first degree relative with known risk factors either one or more than one for diabetes like family history, hypertension, hypercholesterolemia and obesity was taken. Blood samples were taken for overnight 8 hours fasting blood glucose, if it is impaired then 75 grams of glucose was given them orally and blood samples after two hours for glucose tolerance test. These samples were collected in test tubes containing no preservative and transported within half hour to People's Medical College Hospital Laboratory.

Frequency, proportion and percentage were computed for qualitative variables like sex, family history, prediabetes in first degree relatives. Mean and standard deviation were computed for quantitative variables like age, BMI, blood pressure, HDL level and triglyceride level. Stratification was done to control effect modifiers like age, gender, history of first degree diabetes, obesity, hypertension, low HDL and Hypertriglyceridemia to observe an outcome.

## RESULTS

A total of 70 patients were included in this study. There were 40(57.14%) males and 30(42.86%) females as presented in figure 5. Age ranged from 30 to 45 years. 15 ( 21.42%) patients aged from 30 to 35 years. 20 (28.57%) patients were of 36 to 40 years and 35(50%) patients age was from 41 to 45 as is shown in table 1 below.

Both genders were included in this study. 40(57.14%) males and 30 (42.86%) females were studied according to risk factors for D.M.

Rate of pre diabetes was seen to be higher among those who had family history of D.M. 40 (57.14%) patients had positive family history. Next risk factor was hypertension (B.P > 140/90 mmHg) seen in 15(21.42%) patients. Hypertriglyceridemia was in 10 (14.28%) patients and hypercholesterolemia was in 5 (7.14%) patients as is shown in table 2.

**Table No.1: Age Distribution**

S.No	Age	No of patients	Percentage
1	30 -35	15	21.42%
2	36-40	20	28.58%
3	41-45	35	50%
total		70	100%

**Table No.2: Risk factor**

S.No	Risk factor	No of patients	Percentage
1	D.M	40	57.14%
2	HTN	15	21.42%
3	Hypertriglyceridemia	10	14.28%
4	Hypercholesterolemia	5	7.14%
Total		70	100%

## DISCUSSION

D.M is rampant in the globe nowadays particularly type 2 irrespective of sex difference. Its risk enhances as age enters into its 4<sup>th</sup> decade but can occur at any age mostly due to change in life style, diet, physical activity and obesity.<sup>10</sup> In our study the average age was 38.57±5.03 years. National Diabetes Prevalence survey of Pakistan showed prevalence upto 11% whereas another survey report of New Castle Heart Project on adults aged 25 years showed prevalence of pre diabetes among 23.4% in South Asia.<sup>10</sup> NHANES-III showed that in overweight adults aged above 45 years, 45.9% had abnormal metabolism of glucose. Out of these, 12.5% reported Diabetes by self, 10.8% were not diagnosed for diabetes earlier and 22.6% had prediabetes. It is also observed that most of increase in diabetes prevalence occur in developing countries with the rate of 170% increase and by the year 2025 about 75% of all persons with diabetes will be living in third world countries. In our study, rate of prediabetes due to obesity is from 7.14% to 14.28%.<sup>12</sup>

According to survey conducted in China in 2010, the prevalence of prediabetics was estimated to be greater than 57% in old persons. Incidence was higher in rural population as compared to rural. But in our study, incidence is higher in middle aged people but not in old ones.<sup>13</sup>

In NHANESIII prevalence of prediabetes was high (44.3%) in person with positive family history of diabetes. same was observed in our study. The rate of prediabetes with positive family history was 57.14%.<sup>14</sup> In our study, systolic and diastolic blood pressure increased from normal to prediabetes to undiagnosed diabetes. Masoumeh Sadeghi et al and A. Basit also showed similar association of blood pressure to prediabetes and diabetes.<sup>15</sup>

In Shaikh et al study, HDL cholesterol level decreased from normal in prediabetes to undiagnosed diabetes

while the triglyceride level increased. Type 2 diabetics often have elevated triglyceride and depressed HDL cholesterol. But in our study, increased triglycerides were found in 10 (14.28%) and hypercholesterolemia was found in 5 (7.14%). Akiko S Hosler reported prevalence of prediabetes in high risk group including Age  $\geq 45$  years=11.3%, BMI  $\geq 25.0$  kg/m<sup>2</sup>=8.0% and Family history=9.6%. Joshi SR et al reported association of diabetes and hypertension which were 18.4%<sup>9</sup>. In our study, patients with positive family history were 57.14%.<sup>16</sup>

## CONCLUSION

It is concluded that the most common risk factor for developing Diabetes Mellitus is positive family history of Diabetes Mellitus then next is the hypertension and last one is the cholesterol level or obesity.

### Author's Contribution:

Concept & Design of Study: Muhammad Zarar  
Drafting: Shahzad Memon, Arslan Badar Shaikh

Data Analysis: Mujahid Ali Chandio,  
Anwar Ali Jamali,  
Ruqayya Farhad

Revisiting Critically: Muhammad Zarar,  
Shahzad Memon

Final Approval of version: Muhammad Zarar

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 2011; 34:S62-9.
2. One in ten will have diabetes by 2030. international Diabetes Federation: Diabetes atlas. Press Release. 5th ed. [updated 2011 Nov. 14].
3. Siu SC, Wong KW, Lee KF, Lo YY, Wong CK, Chan AK, et al. Prevalence of undiagnosed diabetes mellitus and cardiovascular risk factors in Hong Kong professional drivers. *Diabetes Res Clin Pract* 2012;96(1):60-7.
4. Zafar J, Bhatti F, Akhtar N, Rasheed U, Bashir R, Humayun S, et al. Prevalence and risk factors for diabetes mellitus in a selected urban population of a city in Punjab. *JPMA* 2011;61:40-7.
5. Mijajlović MD, Aleksić VM, Šternić NM, Mirković MM, Bornstein NM. Role of prediabetes in stroke. *Neuropsychiatric disease and treatment* 2017;13:259-263.
6. Kurihara O, Takano M, Yamamoto M, Shirakabe A, Kimata N, Inami T, et al. Impact of prediabetic status on coronary atherosclerosis: a multivessel angioscopic study. *Diabetes Care* 2013 Mar 1;36(3):729-33..
7. Huang Y, Cai X, Mai W, Li M, Hu Y. Association between prediabetes and risk of cardiovascular disease and all cause mortality: systematic review and meta-analysis. *BMJ* 2016;355:i5953..
8. Huang Y, Cai X, Chen P, Mai W, Tang H, Huang Y, Hu Y. Associations of prediabetes with all-cause and cardiovascular mortality: a meta-analysis. *Annals Med* 2014;46(8):684-92..
9. Wang C, Lang J, Xuan L, Li X, Zhang L. The effect of health literacy and self-management efficacy on the health-related quality of life of hypertensive patients in a western rural area of China: a cross-sectional study. *Int J Equity in Health* 2017;16(1):58..
10. Díaz-Redondo A, Giraldez-García C, Carrillo L, Serrano R, García-Soidán FJ, Artola S, et al. Modifiable risk factors associated with prediabetes in men and women: a cross-sectional analysis of the cohort study in primary health care on the evolution of patients with prediabetes (PREDAPS-Study). *BMC Family Pract* 2015;16(1):5-10.
11. Qin L, Xu H. A cross-sectional study of the effect of health literacy on diabetes prevention and control among elderly individuals with prediabetes in rural China. *BMJ Open*. 2016;6(5):e011077..
12. Zhang B, Zhai FY, Du SF, Popkin BM. The China Health and Nutrition Survey, 1989–2011. *Obesity Reviews* 2014;15:2-7.
13. Hu Z, Gao F, Qin L, Yang Y, Xu H. A Case-Control Study on Risk Factors and Their Interactions with Prediabetes among the Elderly in Rural Communities of Yiyang City, Hunan Province. *J Diabet Res* 2019.
14. Wagner R, Thorand B, Osterhoff MA, Müller G, Böhm A, Meisinger C, et al. Family history of diabetes is associated with higher risk for prediabetes: a multicentre analysis from the German Center for Diabetes Research. *Diabetologia* 2013;56(10):2176-80..
15. Schillinger D, Grumbach K, Piette J, Wang F, Osmond D, Daher C, et al. Association of health literacy with diabetes outcomes. *JAMA* 2002; 288(4):475-82.
16. Yamashita T, Kart CS. Is diabetes-specific health literacy associated with diabetes-related outcomes in older adults? *J Diabetes* 2011;3(2):138-46.

# Effect of Cause of Death on Postmortem Cerebrospinal Fluid Electrolytes ( $K^+$ , $Na^+$ and $Cl^-$ ) Concentration

Riasat Ali<sup>1</sup>, Nasreen Akhtar<sup>2</sup>, Mansoor Mirza<sup>1</sup>, Syed Mudassir Hussain<sup>1</sup>, Saman Ambreen<sup>3</sup> and Syeda Maira Hussain<sup>1</sup>

## ABSTRACT

**Objective:** To find out the effect of cause of death on postmortem Sodium, Potassium and Chloride levels in cerebrospinal fluid.

**Study Design:** Observational study

**Place and Duration of Study:** This study was conducted at the Forensic Medicine Department, King Edward Medical University (KEMU), Lahore for a period of 6 months from December 2013 to June 2014.

**Materials and Methods:** Medicolegal autopsy cases were included in which the exact cause and time of death were known. A total number of consecutive 106 samples were collected. Unknown and putrefied dead bodies, Poisoning cases and Cases with head injuries were not included. Study was completed in 6 months.

**Results:** The  $K^+$ ,  $Na^+$  and  $Cl^-$  levels are significantly affected by certain causes of death.

**Conclusion:** Biochemistry of Cerebrospinal Fluid alone may not be very useful in postmortem interval estimation.

**Key Words:** Postmortem interval, Cerebrospinal fluid, Potassium, Sodium, Chloride, Cause of death

**Citation of articles:** Ali R, Akhtar N, Mirza M, Hussain SM, Ambreen S, Hussain SM. Effect of Cause of Death on Postmortem Cerebrospinal Fluid Electrolytes ( $K^+$ ,  $Na^+$  and  $Cl^-$ ) Concentration. Med Forum 2019; 30(5):69-72.

## INTRODUCTION

The accurate estimation of the time of death is a critical investigational problem for the authorized medical officer while conducting medicolegal autopsy.<sup>1</sup> Several physical changes start in the dead body after death, known to our ancestors since ancient times and still continue to be used as the main parameters for the estimation of time since death such as cooling of the dead body, development of rigor mortis, development of lividity, etc.<sup>2,3</sup> Moreover, many chemical changes also start in the various body fluids after death. These body fluids are whole blood, serum, Cerebrospinal Fluid, aqueous humor, synovial fluid, and vitreous humor.<sup>4,5</sup>

Postmortem Cerebrospinal fluid electrolyte (Sodium, Potassium and Chloride) levels change with the passage

of time and are useful for the estimation of time since death. The focus of this study is to determine the effect of cause of death on postmortem Cerebrospinal Fluidsodium, potassium and chloride ion concentration as these electrolytes are used to determine the time since death.<sup>2</sup>

## MATERIALS AND METHODS

This observational study was conducted at the Department of Forensic Medicine and Toxicology, KEMU, Lahore and completed in 6 months. Medicolegal autopsies conducted. Only those cases were included in which the exact time of death was given by the attending physician who issued Death Certificate, by the law enforcement agencies or near relatives.

**Inclusion Criteria;** Cases where the exact time of death was provided by the police, the attending physician or near relatives.

**Exclusion Criteria;** Unknown and putrefied dead bodies, poisoning cases and cases with head injuries

**Sample size:** A total number of consecutive 106 samples fulfilling the above mentioned inclusion criteria were taken from the cases brought to the mortuary.

**Collection of cerebrospinal fluid:** These samples were collected by opening the cranial cavity first, from Rt. or Lt. lateral ventricle of the brain by using Liver biopsy needle attached with 20 ml syringe and inserted in the posterior and dependent part of the lateral ventricle of brain up to 1.5 cm depth and as much of the

<sup>1</sup>. Department of Forensic Medicine & Toxicology, King Edward Medical University, Lahore.

<sup>2</sup>. Department of Forensic Medicine & Toxicology, Al Aleem Medical College, Lahore.

<sup>3</sup>. Department of ENT, Benazir Bhutto Hospital, Rawalpindi.

Correspondence: Dr. Riasat Ali. Assistant Professor of Forensic Medicine & Toxicology, King Edward Medical University, Lahore.

Contact No: 0300-9649147

Email: dr.riasat423@gmail.com

Received: February, 2019

Accepted: April, 2019

Printed: May, 2019

Cerebrospinal Fluid was aspirated as possible.<sup>6,7</sup> Samples were immediately transferred to the pathology lab, centrifuged and analyzed for sodium, potassium and chloride ions by Auto analyzer. On average, approximately 5-6 ml of Cerebrospinal Fluid was obtained from each subject. Only clear, transparent samples not containing any free tissue fragments were used for study. A detailed Proforma was used for each case to fill relevant information. The analysis of the samples was carried out in the laboratory of the Pathology Department, King Edward Medical University, Lahore.

## RESULTS

The data analysis was done by using SPSS v-21 (SPSS-Inc, Chicago, USA). Regression and correlation analysis was applied. P-value  $\leq 0.05$  was considered as statistically significant. Mean, SD, frequencies and percentages were calculated. Finally, t-test was used to determine if any two data sets are significantly different or not.<sup>8-12</sup> In this study data of 106 cases was obtained. The mean PMI in hours was  $12.43 \pm 4.44$  with range of 5 to 23.45 hours. The mean potassium was  $6.06 \pm 1.99$  with range of 3.1 to 11.5 mEq/L, and mean sodium was  $124.2 \pm 6.36$  with range of 108 to 138 mEq/L. The mean age was  $32.5 \pm 9.69$  with range of 12 to 61 years. Data analysis showed that the majority of cases were males 79.25% (84 cases) and females were only 20.75% (22 cases). Gender distribution of the 106 cases used in this study. The average age of male cases was 33.81 years and female average age was 27.50 years.

**Table No.1: Different causes of death in the studied cases**

Cause of Death	No of Cases	%tage of Cases
Firearm Injury	80	75.47%
Blunt Weapon Injury	5	4.72%
Asphyxial Death	17	16.04%
Sharp Edge Weapon Injury	4	3.78%

The Table 1 shows that Firearm Injuries are the predominant (75.47%) cause of death in the present study. Then Asphyxia (16.04%), followed by Blunt Weapon Injury (4.72%), and Sharp Edge Weapon Injury (3.75%).

Generally the potassium level is not significantly dependent on the cause of death. But there is a significant effect on the potassium ( $K^+$ ) levels when making a comparison of death due to firearm injuries verses asphyxia and firearm injuries verses blunt weapon injuries. Statistical analysis revealed that  $K^+$  level is slightly higher in the cases reported with death due to firearm related injuries. Whereas,  $K^+$  level is slightly lower in the cases reported with death due to asphyxia.

**Table No.2: Effects on potassium levels due to different causes of death**

Statistical Analysis for $K^+$ Levels			
Comparison	t – value	p – value	Significance
Firearm injury and Asphyxia cases	3.41	$P < 0.05$	Significant
Firearm injury and Sharp edge weapon injury cases	0.49	$p > 0.05$	NS
Firearm injury and Blunt weapon injury cases	1.8	$P < 0.05$	Significant
Asphyxia and Sharp edge weapon injury cases	1.47	$p > 0.05$	NS
Asphyxia and Blunt weapon injury cases	0.42	$p > 0.05$	NS
Sharp edge weapon injury and Blunt weapon injury cases	1.21	$p > 0.05$	NS

**Table No.3: Effects on sodium levels due to different causes of death**

Statistical Analysis for Sodium ( $Na^+$ ) Levels			
Comparison	t – value	p – value	Significance
Firearm injury and Asphyxia cases	1.2	$p > 0.05$	NS
Firearm and Sharp edge weapon injury cases	0.05	$p > 0.05$	NS
Firearm injury and Blunt weapon injury cases	2.0	$P < 0.05$	Significant
Asphyxia and Sharp edge weapon injury cases	0.911	$p > 0.05$	NS
Asphyxia and Blunt weapon injury cases	0.56	$p > 0.05$	NS
Sharp edge weapon injury and Blunt weapon injury	1.47	$p > 0.05$	NS

Similarly, t-test was applied to evaluate the effect of different causes of death on sodium ( $Na^+$ ) levels. It is shown in Table 03 that there is a significant effect on the sodium levels when making a comparison of death cases due to the firearm injuries verses blunt weapon injuries.  $Na^+$  level is slightly higher in the cases reported with death due to blunt weapon injuries.

Finally, the t-test was applied again to evaluate the effect on Chloride ( $Cl^-$ ) levels due to different causes of death. The results in table 04 indicate that generally the chloride level is also not dependent on the cause of death. There is only a significant effect on the Chloride levels when making a comparison of death cases due to the sharp edge weapon injuries against the firearm

injuries and asphyxia and  $\text{Cl}^-$  level is slightly higher in the sharp edge weapon cases.

**Table No.4: Effects on chloride levels due to different causes of death**

Statistical Analysis for Chloride ( $\text{Cl}^-$ ) Levels			
Comparison	t value	p value	Significance
Firearm injury and Asphyxia cases	0.67	$p>0.05$	NS
Firearm injury and Sharp edge weapon injury	1.73	$P<0.05$	Significant
Firearm and Blunt weapon injury cases	0.7	$p>0.05$	NS
Asphyxia and Sharp edge weapon injury cases	1.84	$P<0.05$	Significant
Asphyxia and Blunt weapon injury cases	0.17	$p>0.05$	NS
Sharp edge weapon and Blunt weapon injuries cases	1.63	$p>0.05$	NS

## DISCUSSION

Cerebrospinal fluid is an inert, isolated and well protected body fluid and it can be used to estimate the postmortem interval. The Cerebrospinal Fluid electrolytes (sodium and potassium) are valuable biochemical markers in postmortem interval estimation.<sup>2</sup>

In this study the samples were collected with great care. The cerebrospinal fluid was drawn gently and the researcher tried to obtain as much fluid as possible. It is important to collect the Cerebrospinal Fluid as much as possible to get accurate levels for all the salutes.<sup>6,7</sup> This technique of sampling is helpful in avoiding wrong results as literature highlighted that certain factors such as sampling techniques and analytical apparatus may lead to wrong potassium level.<sup>7,13-15</sup> In the present study careful sampling was done to avoid the tissue contamination. Only crystal transparent samples free from tissue debris were included in the study. Ordinary Regression Equations were devised using the data of 106 samples. Gamero et al. studied the precision of estimating the time since death comparing different equations and determined their degree of accuracy.<sup>13</sup>

In this research, there were four different causes of death. Firearm Injuries were the major cause of death followed by Asphyxia, Blunt Weapon Injury, and Sharp Edge Weapon Injury. The statistical analysis indicates that generally the potassium level is not significantly

dependent on the cause of death. Results indicate that the  $\text{K}^+$  level is slightly higher in the cases reported with death due to firearm related injuries. Whereas,  $\text{K}^+$  level is slightly lower in the cases reported with death due to asphyxia. Similarly,  $\text{Na}^+$  level is slightly higher in the cases reported with death due to blunt weapon injuries and  $\text{Cl}^-$  level is slightly higher in the death cases due to the sharp edge weapon injuries.

## CONCLUSION

This study showed that the postmortem cerebrospinal  $\text{K}^+$ ,  $\text{Na}^+$  and  $\text{Cl}^-$  levels are significantly affected by certain causes of death. Biochemistry of Cerebrospinal Fluid alone may not be very useful in postmortem interval estimation.

### Author's Contribution:

Concept & Design of Study: Riasat Ali  
 Drafting: Nasreen Akhtar, Mansoor Mirza  
 Data Analysis: Syed Mudassir Hussain, Saman Ambreen, Syeda Maira Hussain  
 Revisiting Critically: Riasat Ali, Nasreen Akhtar  
 Final Approval of version: Riasat Ali

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. Saukko P, Knight B. Knight's Forensic Pathology. 3<sup>rd</sup> ed. London, United Kingdom: Edward Arnold (Publishers) Ltd; 2004.p.216-20
2. Yadav J, Deshpande A, Arora A, Athawal BK, Dubey BP. Estimation of time since death from CSF electrolyte concentration in Bhopal region of central India. Legal Medicine 2007;9(6):309-13.
3. Awan NR. Principles and Practice of Forensic Medicine and Toxicology. 2<sup>nd</sup> ed. Lahore, Pakistan: Zubair Pakistan; 2018.
4. Saugstad OD, Olaisen B. Postmortem hypoxanthine levels in the vitreous humour, an introductory report. F Sci Int 1978;12:33-6.
5. Tumram NK, Bardale RV, Dongre AP. Postmortem analysis of synovial fluid and vitreous humour for determination of death interval: A comparative study. F Sci Int 2011;204(1):186-90.
6. Lie JT. Changes of potassium concentration in the vitreous humor after death. J Med Sci 1967; 254:136-42.
7. Coe JJ, Apple FS. Variations in vitreous humor chemical values as a result of instrumentation. J F Sci 1985;30:828-35.



8. Zimmerman DW. Teacher's Corner: A Note on Interpretation of the Paired-Samples t Test. *J Educ Behavioral Statistics* 1997;22(3):349-60.
9. Mankiewicz R. *The Story of Mathematics*. Princeton, New Jersey, USA: Princeton University Press; 2004.
10. Madea B, Henssge C, Hanig W, Gerbracht A. References for determining the time of death by potassium in vitreous humor. *F Sci Int* 1989; 40(3):231-43.
11. Foerch JS, Forman DT, Vye MV. Measurement of potassium in vitreous humor as an indicator of postmortem interval. *Am J Clin Pathol* 1979; 72:651-52.
12. Gamero LJJ, Romero JL, Ramos HM, Arufe M, Vizcaya M. Precision of estimating time of death by vitreous potassium - comparison of various equations. *F Sci Int* 1992;56(2):137-45.
13. N Akhtar, R Ali, AR Malik, A Asghar, K Aziz. *Pak J Med Health Sci* 2015;9(1), 88-92.

# Laparoscopic Cholecystectomy With or Without Drain

Laparoscopic  
Cholecystectomy With  
or Without Drain

Abdul Manan, Ashar Ahmad Khan, Irfan Ahmad, Muhammad Usman, Tania Mahar and  
Muhammad Afzal Sajid

## ABSTRACT

**Objective:** To assess the efficacy of drain in laparoscopic cholecystectomy.

**Study Design:** Randomized control trial study

**Place and Duration of Study:** This study was conducted at the Department of Surgery, Nishtar Medical University/Hospital, Multan from January 2018 to December 2018.

**Materials and Methods:** A total 226 patients of both genders undergoing surgical treatment for gall stone disease were included. Patient's ages were ranging from 20 to 60 years. All the patients were randomly allocated into two groups; Group A (with drain placement) and Group B (without drain placement) and each comprised 113 patients. Sign and symptoms were recorded. Complications were noted post-operatively and on 3 months follow-up. Mortality rate was also examined.

**Results:** There were 70 (61.95%) females and 43 (38.05%) males in group-A while in group-B, 83 (73.45%) were females and 30 (26.55%) were males. All the patients underwent laparoscopic cholecystectomy. Postoperative complications were more in patients who underwent laparoscopic cholecystectomy without drain as compared to those with drain.

**Conclusion:** The rate of complications was higher in patients who underwent cholecystectomy without drain.

**Key Words:** Gall stone disease, Drain Placement, without drain, Complication, Mortality

**Citation of articles:** Manan A, Khan AA, Ahmad I, Usman M, Mahar T, Sajid MA. Laparoscopic Cholecystectomy With or Without Drain. Med Forum 2019;30(5):73-76.

## INTRODUCTION

Gall stone disease is one of the commonest problems being faced on the surgical floor. Since the advent of ultrasound it is diagnosed more often and there is stress over the surgeons to make protocols for whom surgery should be offered as well as to avoid unnecessary surgery.<sup>1</sup> Gall stone disease is generally classified into asymptomatic, symptomatic and complicated. Surgery is indicated in relation to symptoms and to safe-guard against life threatening complications. Acute cholecystitis is an inflammation of gall bladder. It can cause severe peritonitis and death unless treated properly. Among 95% of the patients it is calculous-cholecystitis, while in 5% of the patients it is acalculouscholecystitis. Male to female ratio is 1:3.<sup>2</sup> Presenting complains are pain, nausea, vomiting and fever. Murphy's sign is positive in 40% of the patients. About 85% of the patients have elevated white blood cells count.

Department of Surgical Unit 4, Nishtar Medical University, Multan.

Correspondence: Dr. Abdul Manan, Assistant Professor, Surgical Unit 4, Nishtar Medical University, Multan.

Contact No: 0300-6301942

Email: drmanan2001@yahoo.com

Received: January, 2019

Accepted: March, 2019

Printed: May, 2019

X-ray abdomen is rarely helpful. Technetium iminodiacetic acid scan is most specific test. Ultrasound abdomen can accurately detect gallstones. Complications like pericholecystic abscess, cholecystoenteric fistula, perforation, empyema, and gallstone ileus may be present. The mortality rate due to complications is 20%. Cholecystectomy should be done as soon as possible when the patient becomes fit for surgery. The appropriate treatment for acute cholecystitis is cholecystectomy. The mortality and morbidity rate after surgery remains the same whether it is performed early or six weeks after the resolution of acute phase. Cholecystectomy, irrigation and drainage of abscess, evacuation of bile are the definitive treatments for the complications of acute cholecystitis. Fistula is treated by cholecystectomy and closure of defect in intestine.<sup>3,4</sup>

Acute calculous cholecystitis, acute postoperative cholecystitis, acute post-traumatic cholecystitis occur after burns, trauma, operations, childbirth, multiple transfusions, bacterial sepsis and debilitating diseases. The female to male ratio is 1:1.<sup>5</sup> However the incidence of gangrene and perforation remains the high. The etiology is unknown or may be multifactorial like sepsis, stasis, and ischemia. The clinical features are pain, tenderness, and fever.<sup>5,6</sup> Practice of cholecystectomy is now shifted almost to laparoscopic approach but open cholecystectomy remains the main stay in complicated disease.<sup>7,8</sup> After surgery placement of drains merits as per disease status and operative course and quality which is safety as well as one cause

of morbidity. After elective cholecystectomy, drains are not placed unless and until bile leaks.<sup>9,10</sup> No study has been conducted previously in our hospital to evaluate the usefulness of drains in such procedures for gall stone disease. So, we plan to do study to compare the postoperative results in laparoscopic cholecystectomy with and without the drain in our setup.

## MATERIALS AND METHODS

This observational study was conducted at department of General Surgery, Nishtar Medical University/ Hospital, Multan over a period one year from 1<sup>st</sup> of January to 31<sup>st</sup> December, 2018. In this study total 226 patients of both genders with ages 20 to 60 years presented with gall stone disease were included. Patient's detailed medical history including age, sex, residency were examined after taking informed written consent from all the patients. Patients with other abdominal disorders, previous history of gall stone disease and those who were not interested to participate were excluded from the study. All the patients had underwent laparoscopic cholecystectomy. Patients were randomly divided into two groups by using Draws technique. Group-A consist of 113 patients (Cholecystectomy with drain) and Group-B consist of 113 patients (cholecystectomy without drain placement). Sign and symptoms were recorded. Post-operative complications were examined in both groups. Follow-up was done for 3 months post-operatively. Mortality rate was also examined. All the statistical data was analyzed by SPSS 19.

## RESULTS

Out of 113 patients, 70 (61.95%) were females and 43 (38.05%) were males in group-A, while 83 (73.45%) were females and 30 (26.55%) were males in group-B. In Group-A, 42 (37.17%) patients were between 20 to 35 years, 46 (40.71%) patients were 36 to 50 years and 27 (23.89%) were above 50 years of age. In Group B, 45 (39.82%) patients were between 20 to 35 years, 47 (41.59%) were between 36 to 50 years and 21 (18.58%) were above 50 years of age. According to the residency status in Group-A 72 (63.72%) patients had rural while 41 (36.28%) patients had urban background and in Group-B, 65 (57.52%) with rural and 48 (42.48%) had urban background. Cholecystectomy with CBD exploration done in 7 patients (3 Group A, 4 Group B), Hypertension found in 28 patients (16 Group A, 12 Group B). Jaundice in 8 (3 in Group A and 5 Group B), Diabetes mellitus found in 30 (14 Group A, 16 Group B). (Table 1)

Symptoms were recorded in Group-A and B such as porcelain gall bladder, hemolytic disorder, polyp, symptomatic gall stone disorder, with micro vascular disorder, empyema gall bladder, post ERCP stone extraction, pancreatitis history, perforation and traumatic gall bladder in 2 and 5, 5 and 1, 4 and 15, 20

and 35, 25 and 29, 27 and 2, 7 and 12, 5 and 4, 6 and 5, 13 and 5 patients respectively. Table 2

According to the complications, surgical site infection found in 12 (10.62%) patients in Group B and 1 (0.88%) patients in Group A, septicemia in 10 patients (2 Group A, 8 Group B), sub hepatic fluid collection found in 15 patients (Group A 1, Group B 14), hematoma in 6 patients (2 Group A, 4 Group B), injury to gut found in 3 patients (Group a 1, Group B 2), bile duct injury found in 5 patients (Group A 1, Group B 4), post-operative jaundice found in 6 patients (2 in Group A, 4 in Group B), biliary stricture found in 3 patients (Group A 1 and Group B 2). There was 1 death recorded and patient belongs to without drain placement group.

**Table No.1: Demographic information of the patients**

Variable	Group A (n=113)	Group B (n=113)
<b>Sex</b>		
Female	70 (61.95%)	83 (73.45%)
Male	43 (38.05%)	30 (26.55%)
<b>Age (years)</b>		
20 – 35	42 (37.17%)	45 (39.82%)
36 – 50	46 (40.71%)	47 (41.59%)
>50	27 (23.89%)	21 (18.58%)
<b>Residency</b>		
Rural	72 (63.72%)	65 (57.52%)
Urban	41 (36.28%)	48 (42.48%)
<b>Co-morbidities</b>		
CBD exploration	3 (2.65%)	4 (3.54%)
Hypertension	16 (14.16%)	12 (10.62%)
Jaundice	3 (2.65%)	5 (4.42%)
Diabetes mellitus	14 (12.39%)	16 (14.16%)

**Table No.2: Symptoms associated to gall stone disease**

Symptom	Group A (n=113)	Group B (n=113)
Porcelain gall bladder	2 (1.77%)	5 (4.24%)
Hemolytic disorder	5 (4.24%)	1 (0.88%)
Polyp	4 (3.54%)	15 (13.27%)
Symptomatic gall stone disorder	20 (17.70%)	35 (30.97%)
Microvascular disorder	25 (22.12%)	29 (25.66%)
Empyema gall bladder	27 (23.89%)	2 (1.77%)
Post ERCP stone extraction	7 (6.19%)	12 (10.62%)
Pancreatitis history	5 (4.24%)	4 (3.54%)
Perforation	16 (14.16%)	5 (4.42%)
Traumatic gall bladder	13 (11.50%)	5 (4.42%)

**Table No.3: Post-operative complications found in all the patients**

Complications	Group A (n=113)	Group B (n=113)
SSI	1 (0.88%)	12 (10.62%)
Septicemia	2 (1.77%)	8 (7.08%)
Gastro hepatic fluid	1 (0.88%)	14 (12.39%)
Hematoma	2 (1.77%)	4 (3.54%)
Injury to gut	1 (0.88%)	2 (1.77%)
Bile duct injury	1 (0.88%)	4 (3.54%)
Post-operative jaundice	2 (1.77%)	4 (3.54%)
Billiary stricture	1 (0.88%)	2 (1.77%)

P-value = 0.035

## DISCUSSION

Gall stone disease is the most common disorder found all over the world and surgical treatment for this disorder is the most frequent performing procedure in surgical departments.<sup>11</sup> In our study the overall female patients population was high 67.70% as compared to male patients 32.30%. These results shows similarity to some previous study conducted regarding cholecystectomy in which female patients population was high as compared to males 60 to 75%.<sup>12,13</sup>

In present study, we found that 38.50% patients were ages between 20 to 35 years and 41.15% patients were of ages 36 to 50 years. A study conducted by Abad-ur-Rehman et al<sup>14</sup> reported the mean age of patients was 37.34 years (Range 15 to 68 years). According to the residency status in Group-A 72 (63.72%) patients had rural residency while 41 (36.28%) had urban residency and in Group-B, 65 (57.52%) patients with rural residence and 48 (42.48%) patients had urban residency. Cholecystectomy with CBD exploration done in 7 (3 Group A, 4 Group B), Hypertension was found in 28 patients (16 Group A, 12 Group B), Jaundice in 8 (3 in Group A and 5 Group B) and Diabetes mellitus in 30 (14 Group A, 16 Group B). A study conducted by Abusedra et al<sup>15</sup> shows a little difference to our study regarding comorbidities.

In our study, symptoms were recorded in Group A and B such as porcelain gall bladder, hemolytic disorder, polyp, symptomatic gall stone disorder, with microvascular disorder, empyema gall bladder, post ERCP stone extraction, pancreatitis history, perforation and traumatic gall bladder in 2 and 5, 5 and 1, 4 and 15, 20 and 35, 25 and 29, 27 and 2, 7 and 12, 5 and 4, 6 and 5, 13 and 5 patients respectively. In our study, surgical site infection was found in 12 (10.62%) patients in Group B and in 1 (0.88%) patient in Group A, septicemia in 10 patients (2 Group A, 8 Group B), sub hepatic fluid collection found in 15 patients (Group A =1, Group B= 14), hematoma in 6 patients (2 Group A,

4 Group B), injury to gut found in 3 patients (Group A= 1, Group B =2), bile duct injury found in 5 patients (Group A 1, Group B 4), post-operative jaundice found in 6 patients (2 in Group A, 4 in Group B), biliary stricture found in 3 patients (Group A =1 and Group B =2). These results showed that the rate of complications was high in Group B without drain placement than the drain placement group. Results of our studies shows similarity to some other studies in which those patients who underwent cholecystectomy with drain placement had a low rate of complications than the patients underwent surgical treatment without drain placement.<sup>16-19</sup> Placement of drain is also related to many complications like gut perforation, infection and bleeding. In our study, we found wound infection in 3 patients postoperatively. In our study the overall mortality rate was 0.88% and that patient belongs to without drain placement group. These results were similar to another study in which mortality rate was 0.75% and belongs to without drain placement group.<sup>20</sup>

## CONCLUSION

The morbidity is higher among the patients in which drains were not placed after cholecystectomy as compared to those in which drains were placed because complications were either missed or detected late.

### Author's Contribution:

Concept & Design of Study: Abdul Manan  
 Drafting: Ashar Ahmad Khan, Irfan Ahmad  
 Data Analysis: Muhammad Usman, Tania Mahar, Muhammad Afzal Sajid  
 Revisiting Critically: Abdul Manan, Ashar Ahmad Khan  
 Final Approval of version: Abdul Manan

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. Dikshit V, Gupta R, Kothari P, Gupta A, Kamble R, Kesan K. Conservative management of type 2 gallbladder perforation in a child. *WJCC* 2015; 16;3(7):671.
2. Gunasekaran G, Naik D, Gupta A, Bhandari V, Kuppusamy M, Kumar G, Chishi NS. Gallbladder perforation: a single center experience of 32 cases. *Korean J Hepatobiliary-Pancreat Surg* 2015; 19(1):6-10.
3. American Society of Anesthesiology (ASA) physical status classification system ASA last approved; 2014.
4. Date RS, Thrumurthy SG, Whiteside S, Umer MA, Pursnani KG, Ward JB, et al. Gallbladder

- perforation: case series and systematic review. *Int J Surg* 2012;10(2):63–8.
5. Lo HC, Wang YC, Su LT. Can early laparoscopic cholecystectomy be the optimal management of cholecystitis with gallbladder perforation? a single institute experience of 74 cases. *Surg Endosc* 2012;26:3301–6.
  6. Derici H, Kamer E, Kara C, Ünalp HR, Tansug̃ T, Bozdağ̃ AD, Nazli O. Gallbladder perforation: clinical presentation, predisposing factors, and surgical outcomes of 46 patients. *Turk J Gastroenterol* 2011; 22(5): 505–12.
  7. Bedirli A, Sakrak O, Sözüer EM, Kerek M, Güler I. Factors effecting the complications in the natural history of acute cholecystitis. *Hepatogastroenterol* 2001; 48: 1275–8.
  8. Alvi AR, Ajmal S, Saleem T. Acute free perforation of gall bladder encountered at initial presentation in a 51 years old man: a case report. *Cases J* 2009;2:166.
  9. Huang CC, Lo HC, Tzeng YM, Huang HH, Chen JD, Kao WF, et al. Percutaneous transhepatic gall bladder drainage: a better initial therapeutic choice for patients with gall bladder perforation in the emergency department. *Emerg Med J* 2007;24 (12):836–40.
  10. Lin HC, Chen TS. Gallbladder perforation in cholecystitis with liver abscess formation and septic thrombophlebitis of portal vein mimicking presentation of liver malignancy. *Adv Digest Med* 2014; 1(3):95–9.
  11. Abusedera MA, El-Badry AM. Percutaneous treatment of large pyogenic liver abscess. *Egypt J Radiol Nucl Med* 2014;45(1):109–15.
  12. Date RS, Thrumurthy SG, Whiteside S, Umer MA, Pursnani KG, Ward JB, et al. Gallbladder perforation: Case series and systematic review. *Int J Surg* 2012;(10)63–68.
  13. Karimian F, Aminian A, Mirsharifi R, Mehrkhani F. Surgical options in the management of cystic duct avulsion during laparoscopic cholecystectomy. *Patient Safety Surg* 2008, 2:17
  14. Rehman A, Sarwar AR, Sajjad A. Morbidity in surgery for gall stone disease: comparison between drain placement and nonplacement. *PJMHS* 2011; 12(1):
  15. Picchio M, Angelis FD, Zazza S, Filippo AD, Mancini R, Pattaro G, et al. Drain after elective laparoscopic cholecystectomy. A randomized multicentre controlled trial. *Surg Endosc* 2012; 26:2817–22
  16. Lucarelli P, Picchio M, Martellucci J, Angelis FD, Filippo AD, Stipa F, et al. Drain after laparoscopic cholecystectomy for acute calculous cholecystitis: a pilot randomized study. *Ind J Surg* 2015
  17. Nagpal A, Goyal S, Abbey L, Singh A. Drainage in cholecystectomy: required or not? a comparative randomized study in Northern Indian subjects. *World J Laparoscop Surg* 2012;5:63–66.
  18. Ishikawa K, Matsumata T, Kishihara F, Fukuyama Y, Masuda H, Kitano S. Laparoscopic cholecystectomy with and without abdominal prophylactic drainage. *Digestive Endoscop* 2011;23:153–6.
  19. Rath PK, Shaikh AR, Kella N, Behan RB. Laparoscopic cholecystectomy without the use of Drain in Selected Cases JLUMHS. 2016;15:35–41.
  20. Halim A, Ahmad I, Iqbal J, Khan Z. Role of drain in laparoscopic cholecystectomy. *J Med Sci (Peshawar)* 2011;19: 49–53.

# Prevalence of Anemia Among Women of Reproductive Age Presenting at Teaching Hospital Gujrat

Zahid Azam Chaudry<sup>1</sup>, Ammara Khan<sup>2</sup> and Nawal Moeen<sup>1</sup>

## ABSTRACT

**Objective:** To resolve the prevalence of anemia with associated factors in women of childbearing age of Gujrat.

**Study Design:** Cross sectional study

**Place and Duration of Study:** This study was conducted at the Government Aziz Bhatti Shaheed Teaching Hospital (ABSTH), Gujrat from March 2018 to August 2018.

**Materials and Methods:** 150 women of 16-50 years of age. *Sampling Technique:* Random Sampling. Women presenting at OPD of Medicine & Gynecology Department of ABSTH, Gujrat were questioned via a structured questionnaire to determine associated factors after taking informed consent. Laboratory report of blood tested for Hemoglobin (Hb) within last 3 months were recorded, if not they were tested for Hb from Pathology Department of Teaching Hospital. *Analysis:* Microsoft Excel.

**Results:** In childbearing age (16-50 years) of women anemia was found to be 56%, which meant that 84 of the 150 women suffered from anemia. 26% of the anemic women had severe anemia, while 41% had moderate anemia. The highest prevalence of anemia was among women of 30-43 years age group. Most of the women who were suffering from anemia had unsatisfactory dietary habits and poor socioeconomic status.

**Conclusion:** Anemia is highly prevalent in reproductive age group women of Gujrat, Pakistan presenting at public sector hospitals. Associated with lower socio-economic status, poor dietary intake and lack of both education & health education.

**Key Words:** Iron Deficiency, Socioeconomic status, Anemia, Reproductive Age, Dietary Habits

**Citation of articles:** Chaudry ZA, Khan A, Moeen N. Prevalence of Anemia Among Women of Reproductive Age Presenting at Teaching Hospital Gujrat. Med Forum 2019;30(5):77-80.

## INTRODUCTION

Anemia is a condition where the red blood cells are less than the normal count or the hemoglobin level is low. Anemia undermines the capability of blood to transport oxygen. People with anemia have the symptoms fatigue, tiredness, pale and may develop shortness of breath and have palpitations. Anemia is a global health concern and the population under influence is around 1.62 billion which accounts to 24.8% of the world population. However the population under highest influence of anemia are non-pregnant women (468.4 million, 95% CI: 446.2–490.6). In the Eastern Mediterranean Region of WHO anemia in non pregnant women is 32.4%.

<sup>1</sup>. Department of Community Medicine / Pharmacology & Therapeutics<sup>2</sup>, Nawaz Sharif Medical College, University of Gujrat, Gujrat.

Correspondence: Dr. Zahid Azam Chaudry, Assistant Professor, Community Medicine, Nawaz Sharif Medical College, University of Gujrat, Gujrat.

Contact No: 0345-4361987

Email: zahid\_azam@yahoo.com

Received: December, 2018

Accepted: March, 2019

Printed: May, 2019

In Pakistan Anemia is characterized as a public health issue at a higher end for preschool children and at a moderate level for non pregnant women of reproductive age.<sup>1</sup> Anemia among women in their child bearing age in Pakistan is around 54% with a variation of 50-70% in different parts of the country.<sup>2</sup>

Many factors contribute to anemia which include genetics, infectious diseases, nutrition, multiparity, frequent labor, abortions, but iron deficiency accounts for 75% of anemia in women.<sup>3-5</sup> Iron deficiency needs to be addressed by young women considering their physical growth, menstruation cycles, pregnancy and fetal growth life stages.<sup>6,7</sup> Mothers having deficient iron supplies are at high risk of having children who are also deficient in iron.<sup>8,9</sup> Insufficient consumption of foods rich in iron and low bioavailability of iron taken is the primary cause of iron deficiency in pregnancy.<sup>1</sup> In Developing countries multiparity, low socioeconomic status, low education and lack of awareness are also contributory factors to iron deficiency.<sup>10</sup>

In pregnancy anemia is a known risk which can endanger the life of mother and fetus. Anemia is linked with high rates of pre-eclampsia (31.2%), maternal sepsis and pre-term labor (28.2%).<sup>3,11</sup> Anemia can be classified into three types in pregnancy as severe anemia where hemoglobin levels are lower than 7.0 g/dL. The other two types are mild anemia where

hemoglobin levels are between 7.0-9.9 g/dL and 10.0 to 11.0 g/dL respectively.<sup>12, 13</sup>

In 2005, a study was conducted in Ethiopia to study the correlates of anemia which showed that rural residence, poor hygienic conditions, poor education and economic situation as well as multiparity were key predisposing factors.<sup>14</sup> Similar studies conducted in Tanzania, Tabas, Argentina and Lebanon also showed that the major risk factors as well as correlates are common to all developing countries.<sup>15-19</sup> In the urban areas of Pakistan anemia in pregnant women has been reported in the range of 29-50%. Studies conducted in some cities of Pakistan; Karachi, Lahore and Multan had reported anemia due to iron deficiency as 64%, 73% and 76% respectively.<sup>20-22</sup>

Clinical measurements are subjective and the chances of error are more as compared to measuring hemoglobin concentration which is a predictable indicator when measuring anemia in the population. Hemoglobin (Hb) levels are proxy indicator for iron deficiency. Measuring Hb is inexpensive and easy.<sup>1</sup> According to WHO the recommended Hemoglobin level, for non-pregnant women (age 15 and over) is 12 gm/dL and for males (15 years and over) it is 13 gm/dL. Anemia is much frequent in reproductive period of women and especially during pregnancy.<sup>23</sup>

In the developing countries like Pakistan, anemia because of iron deficiency during pregnancy is a revealed dilemma.<sup>24</sup> Anemia and associated factors in childbearing age women presenting at teaching public sector hospital of district Gujrat Punjab Pakistan remains a less explored dimension.

## MATERIALS AND METHODS

**Study Design:** Cross-sectional

**Study Area:** Public Sector Teaching Hospital (Aziz Bhatti Shaheed Teaching Hospital) Gujrat

**Study Period:** March 2018 till August 2018

**Study Population:** 150 Women between the ages 16yrs – 50yrs

**Sampling Technique:** Random sampling **Data**

**Collection Tools:** Structured questionnaire including; Sociodemographic Data (age, education, income, marital status), Diet, Gynecological & Obstetric history, current or history of chronic illness. The questionnaire was pilot tested before the start of the study

**Inclusion Criteria:** Women of ages 16 to 50 years presenting in OPD of Medical or Gynecology ward of Aziz Bhatti teaching hospital and consenting to be a part of the study.

**Exclusion Criteria:** pregnant women and women breast feeding at the time of the study.

**Data Analysis:** Data analysis was done on Microsoft Excel. Informed consent and maintenance of confidentiality was insured at the time of study.

## RESULTS

From 150 women selected randomly who fulfilled the inclusion and exclusion criteria it was found that 92% of the women presenting to the public tertiary care hospital were from lower socioeconomic class, 70% were from rural area, 40% were educated and only 6.6 % women fulfilled the satisfactory level of nutrition intake while 60% women had a poor nutritional status.

**Table No.1: Demographic, Educational, Nutritional and Socioeconomic Classification of Participants in numbers and percentages.**

Characteristics	Group	Number	%age
Residence	Urban	55	30
	Rural	95	70
Educational Status	Educated	60	40
	Uneducated	90	60
Nutritional Status	Satisfactory	10	6.6
	Unsatisfactory	50	33.3
	Poor	90	60
Socioeconomic Status	Upper	00	00
	Middle	12	08
	Lower	138	92

From 150 women 84 (56%) were anemic and 27 % of women were just above the required level of Hemoglobin and were at risk of becoming anemic during pregnancy or any illness or nutritional deficiency.

**Table No.2: Percentage of anemic, non anemic and at risk women.**

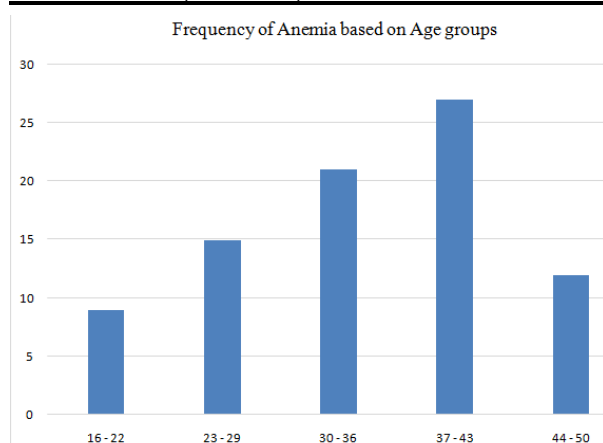
	Number of women	Percentage
Anemic	84	56%
At Risk	40	27%
Normal	26	17%

Amongst the 84 anemic women the following was the distribution of anemia based on Hemoglobin levels ranging from mild to severe anemia. Most of the women 34(41%) of the 84 iron deficient women had moderate anemia.

**Table No.3: Percentage of Anemic women by Hemoglobin levels.**

Hemoglobin concentration with levels of Anemia	No. of deficient women	Percentage
9.0 – 11.0 g/dL Mild	28	33%
7.0 – 9.0 g/ dL Moderate	34	41%
Below 7.0 g/dL Severe	22	26%

It was also found that amongst the anemic women majority of the females were between 30-40 years of age.



**Figure No.1: Number of Anemic women in various age Groups**

## DISCUSSION

Anemia is a concern for the world as around 25 percent of world population is suffering from it. The major bulk of the affected population is found in the developing and under developed countries. The associated factors of anemia across these countries are common mostly poor socioeconomic status, nutrition and education. Based on the various studies anemia has serious health hazards especially during pregnancy and for the newborn. Developing countries like Pakistan are still off the guards to find a way to overcome such deficiencies. Anemia in Pakistan on an average is around 50-70% across urban and rural area and all socioeconomic groups.

The prevalence of anemia and associated factors in Gujrat were explored in order to understand the recent status. As the study was done in women presenting to public sector hospital more than 90% of these women were from low socioeconomic status and majority 70 % from rural areas. Almost 60 % of these women were uneducated or having education less than primary education (5<sup>th</sup> grade). Amongst the selected women only 6% knew about and followed a balanced diet in their meals.

As far as anemia in these reproductive age women was concerned more than half (56%) of the women were anemic and 26% of the anemic were severely anemic (below 7gm/dl) with majority being moderately anemic. Most of the women who were anemic were between 30 -45 years of age.

Keeping in view above results it can be inferred that anemia is still a major health issue of Pakistan. The high percentage of anemia in women having access to a tertiary care hospital of a major district having better educational opportunities and health facilities in the province of Punjab having the highest budget.

Studies conducted in Korangi, Karachi, Faisalabad, Bahawalpur also depicted most of anemic women to be from poor educational and economic background. From the studies it is elicited that etiologies remain same over

the decades. The situation in areas with limited access and poor health facilities and education across various provinces of Pakistan may be even worse which need to be explored.

## CONCLUSION

The prevalence of anemia in women of childbearing ages is still high in women belonging to rural areas and socioeconomically deprived fractions seeking health care from public hospitals. They are more likely to endanger themselves and newborn during prospective pregnancies leading to high MMR, Still births & IMR. Emphasis on health education, dietary requirements of women, provision of nutritional supplements and treatment for any illness is mandatory for a healthy mother & children.

### Author's Contribution:

Concept & Design of Study:	Zahid Azam Chaudry
Drafting:	Nawal Moeen
Data Analysis:	Ammara Khan
Revisiting Critically:	Zahid Azam Chaudry, Nawal Moeen
Final Approval of version:	Zahid Azam Chaudry

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. De Benoist B, Cogswell M, Egli I, McLean E. Worldwide prevalence of anaemia; WHO Global Database of anaemia 1993-2005.
2. WHO A. Guide for Programme Managers. Geneva: World Health Organization. Iron Deficiency Anemia. Assessment, Prevention and Control. 2001.
3. Sharma JB. Nutritional anaemia during pregnancy in third world countries. Progress in obstetrics and Gynaecol 2003;15:103-22.
4. Balarajan Y, Ramakrishnan U, Özaltin E, Shankar AH, Subramanian SV. Anaemia in low-income and middle-income countries. The Lancet 2011; 378(9809):2123-35.
5. Masukume G, Khashan AS, Kenny LC, Baker PN, Nelson G, Scope Consortium. Risk factors and birth outcomes of anaemia in early pregnancy in a nulliparous cohort. PLoS One 2015;10(4): e0122729.
6. Méndez RE, Pacheco B, Noriega HV, Quihui L, Morales G, Valencia ME. Prevalence of iron deficiency and iron deficiency anemia in pregnant adolescents from northwest Mexico, 2007-2008. Archivos latinoamericanos de Nutricion 2009; 59(2):147-51.
7. Ansari T, Ali L, Aziz T, Ara J, Liaquat N, Tahir H. Nutritional iron deficiency in women of child



- bearing age—what to do? J Ayub Medical College Abbottabad 2009;21(3):17-20.
8. Wagener IE, Bergmann RL, Kamtsiuris P, Eisenreich B, Andres B, Eckert C, Dudenhausen JW, Bergmann KE. Prevalence and risk factors of iron deficiency in young mothers. Gesundheitswesen (Bundesverband der Ärzte des Öffentlichen Gesundheitsdienstes (Germany) 2000; 62(3):176-8.
  9. Kitai E, Kaplan B, Raick Y, Cohen Y, Neri A, Friedman J. Community screening to reveal iron deficiency in healthy menstruating women in Israeli suburban. Eur J Obstet Gynecol Reproductive Biol 1996;67(1):21-5.
  10. Shams S, Ahmad Z, Wadood A. Prevalence of Iron Deficiency Anemia in Pregnant Women of District Mardan. Pakistan. J Preg Child Health 2017; 4(356):2.
  11. Buzyan LO. Mild anemia as a protective factor against pregnancy loss. Int J Risk Safety in Med 2015;27(s1):S7-8.
  12. Salhan S, Tripathi V, Singh R, Gaikwad HS. Evaluation of hematological parameters in partial exchange and packed cell transfusion in treatment of severe anemia in pregnancy. Anemia 2012;2012.
  13. Barooti E, Rezazadehkermani M, Sadeghirad B, Motaghipisheh S, Tayeri S, Arabi M, et al. Prevalence of iron deficiency anemia among Iranian pregnant women; a systematic review and meta-analysis. J Reproduc Infertil 2010;11(1):17.
  14. Raghuram V, Anil M, Jayaram S. Prevalence of Anaemia amongst women in the reproductive age group in a rural area in south India. Int J Biol Med Res 2012;3(2):1482-4.
  15. Kaur S, Deshmukh PR, Garg BS. Epidemiological correlates of nutritional anemia in adolescent girls of rural Wardha. Ind J Community Med 2006; 31(4):255-8.
  16. Sadeghian M, Fatourehchi A, Lesanpezheshki M, Ahmadnezhad E. Prevalence of anemia and correlated factors in the reproductive age women in rural areas of Tabas. J Family Reproduct Health 2013;7(3):139.
  17. Goetz LG, Valeggia C. The ecology of anemia: Anemia prevalence and correlated factors in adult indigenous women in Argentina. Am J Human Biol 2017;29(3):e22947.
  18. Asmar MK, Zablith CG, Daou R, Yéretzian JS, Daoud H, Rady A, et al. Prevalence of anemia and associated factors in women of childbearing age in rural Lebanon. J Public Health 2018;26(1):39-49.
  19. Karim SA, Khurshid M, Memon AM, Jafarey SN. Anaemia in pregnancy-its cause in the underprivileged class of Karachi. J Pak Med Assoc 1994;44:90.
  20. Sohail R, Zainab S, Zaman F. Prevalence of anemia in obstetrical population. Annal King Edward Med Univ 2004;10(2).
  21. Awan MM, Akbar MA, Khan MI. A study of anemia in pregnant women of railway colony, Multan. Pak J Med Res 2004;43(1):11-4.
  22. Chansung K. Prevalence of iron deficiency anemia in reproductive age group non pregnant women in underdeveloped area of Amphoe Banfang, Khon Kaen, Thailand. J Clin Epidemiol 1996;49:S20.
  23. Mohyiddin MA. National health survey of health profile of peoples of Pakistan. Islamabad: Pak Medical Research Council and Federal Bureau of Statistics 1995;27-44.
  24. Ullah I, Zahid M, Khan MI, Shah M. Prevalence of Anemia in Pregnant Women in District Karak Khyberpakhtunkhwa, Pakistan. Int J Biosci 2013; 3:77-83.

# Prognosis of Childhood Tetanus (Age Group 1-12 Years) in Cases Presented in DHQ Teaching Hospital DGK

Mukhtar Ahmad, Asma Akbar, Ayaz Ali, Sara Ilyas Khan and Sidra Choudhary

## ABSTRACT

**Objective:** To evaluate the prognosis of non neonatal tetanus in children.

**Study Design:** Prospective observational study

**Place and Duration of Study:** This study was conducted at the Department of Pediatrics Medicine, DHQ Teaching Hospital, Dera Ghazi Khan from January 2018 to January 2019.

**Materials and Methods:** A total of 80 children, aged 1-12 years, diagnosed with tetanus, admitted to pediatrics department, were enrolled in this study. Diagnosis was confirmed by clinical evaluation by minimum of 2 independent pediatricians. Courses of illness along with effects of management during hospital stay and on followup visits were recorded in all patients by collecting data from patients or their parents / guardians.

**Results:** Out of a total of 80 children, there were 43 (53.8%) male and 37 (46.2%) female. Mean hospital stay was noted to be 16.3 days with a standard deviation of 3.6 days. Mean incubation period was 6.5 days with a standard deviation of 1.7 days. Mortality was reported in 2 (2.5%) children, while serious complications were observed in 8 (10.0%). Aspiration pneumonia was the commonest complication, found in 6 (7.5%). We noted 60 (75.0%) children to be unvaccinated.

**Conclusion:** Prognosis was better in our setting in comparison to most of the other studies. Case fatality rate was 2.5% while most of the children (75.0%) presented with tetanus were unvaccinated.

**Key Words:** Tetanus, prognosis, incubation period, unvaccinated

**Citation of articles:** Ahmad M, Akbar A, Ali A, Khan SI, Choudhary S. Prognosis of Childhood Tetanus (Age Group 1-12 Years) in Cases Presented in DHQ Teaching Hospital DGK. Med Forum 2019;30(5):81-83.

## INTRODUCTION

Tetanus is serious, spastic paralyzing illness caused by neurotoxin "tetanospasmin" produced by clostridium tetani, a gram positive spore forming obligate aerobic bacillus. Tetanospasmin is second most poisonous substance known after botulinum.<sup>1</sup> Tetanus is preventable and both active and passive immunizations are available.<sup>2</sup> Although number of affected people and case fatality rate decreased worldwide after introduction of vaccination in to routine vaccination program in 1940s, but in our country it is still a common illness to encounter.

Case-fatality rates from tetanus vary from 20% to 70% depending on treatment, age and general health of the patient.<sup>3</sup> Many advances have been made since in its prevention and management but It is still a common

disease in developing countries like Pakistan.<sup>5</sup> It mainly involve younger children due to lack of immunization and poor management of open wounds.<sup>4</sup> Its prevention is cost effective than treatment, especially for resource limited countries like Pakistan. There is special interest shown worldwide to reduce the mother and neonatal tetanus, non-neonatal tetanus is relatively ignored and studied less.<sup>6,7</sup> Although it is major health concern in areas like subcontinent, not much data is available for tetanus beyond neonatal periods, as quoted from Manish Narang "the exact incidence of neonatal tetanus in India is unknown".<sup>8</sup> Mortality, as described in PICU based study done in Civil hospital Karachi was 26%.<sup>2</sup> Prognosis of cases with tetanus depends upon multiple factors e.g. age, incubation period, route of injury, complications, and delays in treatment or prophylaxis. This study was aimed to study the prognosis of non-neonatal tetanus in age group 1-12 years admitted to Teaching hospital Dera Ghazi Khan.

## MATERIALS AND METHODS

This was a prospective observational study, conducted at the department of pediatrics medicine, DHQ Teaching Hospital, Dera Ghazi Khan, from 1<sup>st</sup> January 2018 to 1<sup>st</sup> January 2019. A total of 80 children, aged 1-12 years, diagnosed with tetanus, admitted to pediatrics department, were enrolled in this study.

Department of Paediatrics Medicine, D.G.Khan Medical College and Teaching Hospital, Dera Ghazi Khan.

Correspondence: Dr. Mukhtar Ahmad, Associate Professor and Head of Paediatrics Medicine Department, D.G.Khan Medical College and Teaching Hospital, Dera Ghazi Khan.  
Contact No: 0332-6459999  
Email: drmkagmc@gmail.com

Received: February, 2019

Accepted: April, 2019

Printed: May, 2019

Diagnosis was confirmed by clinical evaluation by minimum of 2 independent pediatricians. Case definition was based on the clinical criteria highlighted by the presence of lock jaw, hypertonia, seizures on stimulation and tussardonicus. Children with other causes of seizures and hypertonia like meningoencephalitis, cerebrovascular accident (CVA), electrolyte imbalance, and epilepsy were ruled out on clinical and laboratory investigation where necessary. Courses of illness along with effects of management during hospital stay and on follow up visits were recorded in all patients on a predesigned proforma, by collecting data from patients, parents or their guardians. All the data was entered and analyzed by using SPSS version 20.

## RESULTS

Out of a total of 80 children, there were 43 (53.8%) male and 37 (46.2%) female. Most of the children, 31 (38.8%) were between the age of 1 to 5 years, 30 (37.5%) between 5.1 to 6 years while 19 (23.7%) above 10.

Mean hospital stay was noted to be 16.3 days with a standard deviation of 3.6 days. Mean incubation period was 6.5 days with a standard deviation of 1.7 days.

Focus of infection was unknown in 54 (67.5%) children, thorn prick in 5 (7.1%), road traffic accidents (RTA) in 8 (10.0%), ear infection in 4 (5.0%), fall and open wound in 4 (5.0%), minor skin abrasion in 3 (3.8%) and knife cut in 2 (2.5%).

Serious complications were observed in 8 (10.0%). Aspiration pneumonia was the commonest complication, found in 6 (7.5%), apnoea in 1 (1.25%) and ventilator support was required in 1 (1.25%).

We noted 60 (75.0%) children to be unvaccinated, 13 (16.3%) had vaccination status as unknown while only 7 (8.7%) were vaccinated but no booster dose was done in these children.

**Table No.1: Distribution of Children in terms of Age Groups and Gender**

Gender	Age Groups			P Value
	1-5 (n=31)	5-10 (n=30)	10-12 (n=19)	
Male	15 (48.4%)	14 (46.7%)	14 (73.7%)	0.135
Female	16 (51.6%)	16 (53.3%)	5 (26.3%)	

Tablet phenobarbital 3mg/kg/day, tablet valium 0.8mg/kg/day or tablet rivotril 1.5mg/kg/day were used as anticonvulsants. In 11 (13.8%), continuous infusion midazolam (2 microgram/kg/min) was given. In terms of antibiotics, Injection ceftriaxone as 75 mg/kg/day, injection benzyl penicillin (4 lac units/kg/day) were used initially. In 5 (7.1%) patients, antibiotics were changed to injection Meropenum and injection amikacin and in one (1.25%) injection vancomycin was administered.

Tablet Baclofen 10mg/kg/day was given to 3 (3.8%) patients.

Mortality was reported in 2 (2.5%) children. Seventy Five (93.75%) children were fully cured and got discharged. No neurological sequelae were observed at the time of discharge.

**Table No.2: Data of Two Expired Children**

Age (years)	4	8
Gender	1 male	1 female
Incubation period	Unknown	7 days
Vaccination status	Unvaccinated	Unvaccinated
Hospital stay (days)	2	1
Source	Unknown	Ear infection

## DISCUSSION

Although, vaccination initiatives are seen to produce significant triumph around the world but still, many challenges are in front achieving absolute success in a country like Pakistan. Control of spasm along with improvement in cardiovascular stability, proper wound debridement, anti-toxins, antibiotics and other necessary supportive care are the corner stones for the treatment of tetanus.<sup>9</sup>

We noted more males as compared to females in the current study. Overall male predominance in our society could be the reasons for this as male get more attention in terms of healthcare facilities. In a 2 year study conducted at PICU from Karachi showed that 52% children with tetanus were male which is pretty similar to what we found in our study.<sup>2</sup>

In the present study, 39% children were between the age of 1 to 5 years. Similar findings have been seen in another local study where they found majority (57%) cases between 2 to 6 years of age.<sup>2</sup> A study conducted in Mumbai, India<sup>10</sup> found similar results in terms of most common age group among children with tetanus.

In our study, otogenic route was seen in all children from 1 to 5 years of age which is pretty similar to other finding from Karachi.<sup>2</sup> Dirty fingers are most commonly used in to ears in this age group that could be a reason for this finding.<sup>10</sup>

We noted 60 (75.0%) children to be unvaccinated, 13 (16.3%) had vaccination status as unknown while only 7 (8.7%) were vaccinated but no booster dose was done in any of the children. Tetanus is totally preventable if proper and timely immunization is done.<sup>11</sup> A 5 dose regimen of tetanustoxoid gives sufficient immunity. The shocking finding in our study were that in this 21st century, a disease which is easily preventable and recommendation of immunization dosing and schedules are clear, large number of population is still affected due to lack of vaccination. The cost of treatment is far more than prevention in a country like ours.

Mortality was reported in 2 (2.5%) children in our study while 94% children were fully cured and got discharged whereas no neurological sequelae were observed at the time of discharge. Local data from Karachi<sup>2</sup> reported a much higher mortality rate as 26% so we observed that prognosis of non-neonatal tetanus was good in our settings as most of the children discharged and on follow-up no residual disease was discovered.

Globally, lots of advancement has been made in the past few decades to reduce the morbidity and mortality related to tetanus.<sup>13</sup> However, it is still causing major health issues in developing countries like Pakistan.<sup>14,15</sup> Lack of proper immunization coverage for the prevention of maternal as well neonatal / non neonatal tetanus is contributing towards the burden of this disease in our country while boosting collective efforts for universal vaccination in the developed countries have brought lots of success.<sup>16-18</sup> Restrictions to proper financial and human resource are the major reason why a totally preventable disease like tetanus is still haunting us. Proper strategy to vaccinate all and awareness about the overall disease and its preventive aspects can surely bring fruits regarding tetanus and its manifestations in our country.<sup>19,20</sup>

## CONCLUSION

Prognosis was better in our setting in comparison to most of the other studies. Case fatality rate was 2.5% while most of the children (75.0%) presented with tetanus were unvaccinated.

### Author's Contribution:

Concept & Design of Study: Mukhtar Ahmad  
 Drafting: Asma Akbar, Ayaz Ali  
 Data Analysis: Sara Ilyas Khan, Sidra Choudhary  
 Revisiting Critically: Mukhtar Ahmad, Asma Akbar  
 Final Approval of version: Mukhtar Ahmad

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. Brook I. Tetanus in children. *Pediatr Emergency Care* 2004;20:48-51.
2. Naseem F, Mahar IA, Arif F. Two years' study of Tetanus cases in a Paediatric Intensive Care Unit. *Pak J Med Sci* 2016;32(3):641-5.
3. Lan LG, Kong KO, Chew PH. A ten year retrospective study of tetanus at a general hospital in Malaysia. *Singapore Med J* 2001;42(8):346-50.
4. Sutiono AB, Qiantoria A, Suwa H, Ohta T. Characteristic tetanus infection in disaster affected areas: case study of the Yogyakarta earthquake in Indonesia. *BMC Res Notes* 2009;2:34.
5. Khurram M, Mahmood N. Tetanus in post 2005 Pakistan earthquake scenario. *J Coll Physicians Surg Pak* 2007;17:577-8.
6. Aceh epidemiology group. Outbreak of tetanus cases following the tsunami in Aceh province, Indonesia *Glob Public Health* 2006;1(2):173-7.
7. Campbell J. Tetanus: a major killer still at large. *Afri Health* 2000;22(4):8-10.
8. Narang M, Khurana A, Gomber S, Choudhary N. Epidemiological trends of tetanus from East Delhi, India: a hospital-based study. *J Infect Public Health* 2014;7(2):121-4.
9. Yen LM, Thwaites CL. Tetanus. *The Lancet* J 2019;393(10181):1657-68.
10. Tullu M.S, Deshmukh CT, Kamat JR. Experience of pediatric tetanus cases from Mumbai. *Indian Pediatr* 2000;37:765-71.
11. CDC. Tetanus surveillance. United states, 2001-2009. *MMWR* 2011;60:365-96.
12. Pakistan demographic health survey 2016-2017.
13. Kyu HH, Mumford JE, Stanaway JD, Barber RM, Hancock JR, Vos T, et al. Mortality from tetanus between 1990 and 2015: findings from the global burden of disease study 2015. *BMC Public Health* 2017;17:179.
14. Lambo JA, Nagulesapillai T. Neonatal tetanus elimination in Pakistan: progress and challenges. *Int J Infect Dis* 2012;16(12):e833-42.
15. Khan AA, Zahidie A, Rabbani F. Interventions to reduce neonatal mortality from neonatal tetanus in low and middle income countries-a systematic review. *BMC Public Health* 2013;13(1):1.
16. Singh A, Pallikadavath S, Ogollah R, et al. Maternal tetanus toxoid vaccination and neonatal mortality in rural north India. *PLoS One* 2012;7(11):e48891.
17. Williams WW, Lu P, O'Halloran A, et al. Surveillance of Vaccination Coverage Among Adult Populations - United States, 2014. *MMWR Surveill Summ* 2016;65(No. SS-1):1-36.
18. Wu LA, Kanitz E, Crumly J, D'Ancona F, Strikas RA. Adult immunization policies in advanced economies: vaccination recommendations, financing, and vaccination coverage. *Int J Public Health* 2013;58(6):865-74.
19. Roper MH, Vandelaer JH, Gasse FL. Maternal and neonatal tetanus. *Lancet* 2007;370(9603):1947-59.
20. Marulappa VG, Manjunath R, Mahesh Babu N, et al. A Ten Year Retrospective Study on Adult Tetanus at the Epidemic Disease (ED) Hospital, Mysore in Southern India: A Review of 512 Cases. *J Clin Diagn Res* 2012;6(8):1377-80.

# Analysis of Liver Histology and Severity of Metabolic Syndrome in Patients Suffering from Non-alcoholic Fatty Liver Disease

Metabolic Syndrome  
in Patients with  
Non-alcoholic Fatty  
Liver Disease

Kashif Aziz Ahmad<sup>1</sup>, Akmal Khurshid Bhatti<sup>2</sup>, Zara Tahir<sup>2</sup>, Tahir Mahmood Butt<sup>2</sup> and Imran Idris Butt<sup>2</sup>

## ABSTRACT

**Objective:** To analyze liver histology and severity of metabolic syndrome in patients suffering from nonalcoholic fatty liver disease.

**Study Design:** Comparative study.

**Place and Duration of Study:** This study was conducted at the Idris Teaching Hospital of Sialkot Medical College, Sialkot and Lahore General Hospital, Lahore from January 2018 to December 2018

**Materials and Methods:** This is a comparative analysis in which we explored specific relationships between hepatic histology and markers of the metabolic syndrome. There were total 50 patients included in this study. The diagnosis was based on the histological presence of macrovesicular steatosis, with or without lobular inflammation, hepatocellular degeneration, or fibrosis.

**Results:** In this study the data was collected from 50 patients with biopsy-proven NAFLD, a relationship between the severity of the metabolic syndrome and NAFLD was observed. While measures of adiposity correlated with hepatic steatosis, hepatic inflammation and fibrosis were associated with the presence and severity of the metabolic syndrome. This finding has clinical implications, since hepatic ultrasound and serum transaminases have limited utility in predicting hepatic inflammation and fibrosis and there is current reliance on liver biopsies to confirm the diagnosis and indicate prognosis.

**Conclusion:** It is concluded that NAFLD is associated with a high prevalence of obesity. There was a trend towards an association between NASH and metabolic syndrome, in addition patients with NAFLD with MetS were more likely to have severe steatosis and portal inflammation on liver biopsy.

**Key Words:** Liver, Metabolic, Syndrome, Obesity, Disease

**Citation of articles:** Ahmad KA, Bhatti AK, Tahir Z, Butt TM, Butt II. Analysis of Liver Histology and Severity of Metabolic Syndrome in Patients Suffering from Non-alcoholic Fatty Liver Disease. Med Forum 2019;30(5):84-87.

## INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is the most common liver disease since its prevalence is estimated to be 20-30% in general population of Western countries. NAFLD occurs as a histological spectrum of disease and includes the subtypes of simple steatosis and nonalcoholic steatohepatitis (NASH)<sup>1</sup>. It was thought to be a benign condition but is now increasingly recognized as a major cause of liver-related morbidity and mortality<sup>2</sup>.

<sup>1</sup>. Department of Medicine, Lahore General Hospital, Lahore.

<sup>2</sup>. Department of Community Medicine, Sialkot Medical College, Sialkot.

Correspondence: Dr. Kashif Aziz Ahmad, Assistant Professor, Medical Unit-3, Lahore General Hospital, PGMI, Ameer-ud-Din Medical College Lahore  
Contact No: 0321-4577127  
Email: drkashifaziz@yahoo.com

Received: January, 2019

Accepted: April, 2019

Printed: May, 2019

The metabolic syndrome is a clustering of risk factors that greatly increases an individual's probability for developing atherosclerotic cardiovascular disease (ASCVD), type 2 diabetes mellitus and chronic kidney disease<sup>3</sup>. The predominant underlying risk factors appear to be abdominal obesity, atherogenic-dyslipidaemia, hypertension, elevated plasma glucose, a prothrombotic state, and a proinflammatory state<sup>4</sup>.

Nonalcoholic fatty liver disease (NAFLD) is now considered a hepatic component of metabolic syndrome (MS) because of the close association between the two conditions. Prevalence of metabolic risk factors including diabetes mellitus, obesity, etc. is rapidly increasing which is consequently increasing the prevalence of NAFLD in Asia<sup>5</sup>. Patients with NAFLD are at risk not only for the liver-related morbidity and mortality but also for the increased cardiovascular disease risk and increased incidence of diabetes mellitus on long-term follow-up<sup>6</sup>.

NAFLD is strongly associated with obesity, metabolic syndrome (MetS), and cardiovascular risk factors and is more common in obese patients. Nonetheless, a smaller, but significant, proportion of patients develop NAFLD despite having a relatively normal body mass index

(BMI)<sup>7</sup>. This condition is often referred to as lean or non-obese NAFLD. Traditionally considered a condition unique in Asia, NAFLD has also been found in 10% of lean Americans in the National Health and Nutrition Examination Survey III<sup>8</sup>. The severity, factors associated with advanced disease, and prognosis of non-obese NAFLD are not well understood. A recent international study reported that non-obese NAFLD patients might have more-severe histological necro-inflammation and higher mortality than obese patients. Other smaller studies reported mixed results on the disease severity<sup>9</sup>.

## MATERIALS AND METHODS

This study was conducted at Idris Teaching Hospital, Sialkot Medical College, Sialkot and Lahore General Hospital, Lahore from January 2018 to December 2018. The data was collected from Idris Teaching Hospital, Sialkot Medical College, Sialkot and pathological work was done at Pathology Department of Lahore General Hospital, Lahore. This is a comparison analysis in which we explored specific relationships between hepatic histology and markers of the metabolic syndrome. There were 50 patients that were included in this study. The diagnosis was based on the histological presence of macrovesicular steatosis, with or without lobular inflammation, hepatocellular degeneration, or fibrosis.

All subjects were negative for viral hepatitis, anti-nuclear antibody, anti-smooth muscle antibody, and anti-mitochondrial antibody and had normal iron and copper studies. Nine male subjects and eight female subjects had preexisting type 2 diabetes. Out of these five managed their diabetes with diet alone, and 12 were taking metformin. Each subject and their respective control was given a score of 1 for each feature of the metabolic syndrome, for a maximum score of 5, with a score of  $\geq 3$  being diagnostic of the metabolic syndrome. Informed consent of each patient was considered before the start of study. The permission of Ethical Committee was also considered.

**Biochemical Analysis:** A pathologist blinded to subject details scored liver biopsies, allotting a score from 0 to 4 for inflammation, steatosis, and fibrosis as previously described. For additional fibrosis assessment, all biopsies were stained with Masson's Trichrome, percent fibrosis was calculated in triplicate by microscopy and image analysis and data were expressed as mean percentages.

**Statistical Analysis:** The data of the different baseline variable was analyzed on SPSS 11 packages. Data of 50 patients was expressed as mean and SD Significance was set at 0.05.

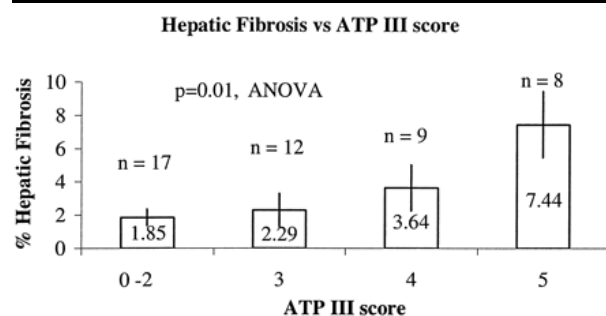
## RESULTS

In this study the data was collected from 50 patients with biopsy-proven NAFLD, a relationship between the

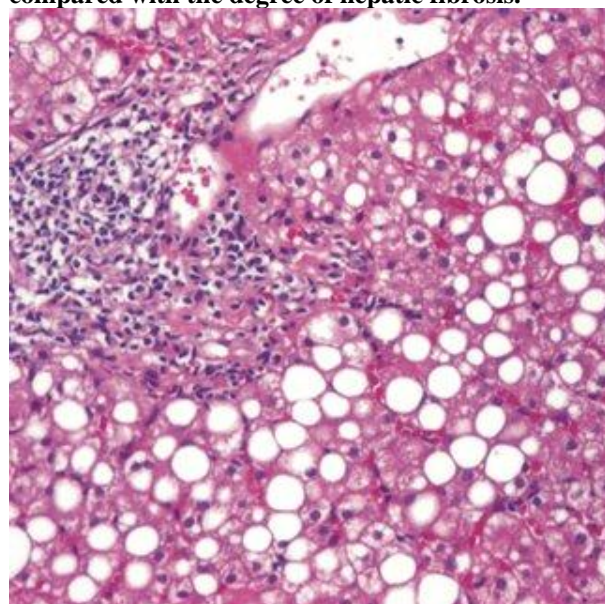
severity of the metabolic syndrome and NAFLD was observed. The mean age of selected patients were  $42.44 \pm 9.24$  years and men accounted for 63.0%. The mean BMI of patients was  $26.90 \pm 3.45$ . All the demographic values of selected patients are explained in table 01. While measures of adiposity correlated with hepatic steatosis, hepatic inflammation and fibrosis were associated with the presence and severity of the metabolic syndrome. This finding has clinical implications, since hepatic ultrasound and serum transaminases have limited utility in predicting hepatic inflammation and fibrosis and there is current reliance on liver biopsies to confirm the diagnosis and indicate prognosis. We suggest that features of the metabolic syndrome would potentially be a better guide in determining which patients should be considered for biopsy and/or potential specific therapy. We collected all the laboratory values of selected patients.

**Table No.1: Laboratory values differences between NAFLD participants with and without metabolic syndrome.**

Laboratory values	Mean $\pm$ SD	p Value*
Age (years)	42.44 $\pm$ 9.24	$\leq 0.078$
Male (%)	67.7	0.004
BMI	26.90 $\pm$ 3.45	$\leq 0.001$
Triglycerides (mg/dL)	185.1 $\pm$ 103.6	<0.001
Cholesterol, total (mg/dL)	196.8 $\pm$ 42.3	0.86
Cholesterol, HDL (mg/dL)	41.2 $\pm$ 10.2	<0.001
Cholesterol, LDL (mg/dL)	121.2 $\pm$ 35.3	0.66
Cholesterol, HDL/LDL	37.0 $\pm$ 15.6	<0.001
Fasting glucose (mg/dL)	96.6 $\pm$ 14.6	<0.001
Fasting insulin ( $\mu$ U/mL)	27.2 $\pm$ 31.4	<0.001
Fasting C peptide (mg/dL)	4.6 $\pm$ 1.6	<0.001
HOMA-IR (mg/dL $\times$ $\mu$ U/mL/405)	6.5 $\pm$ 7.4	<0.001
HbA1c (%)	5.6 $\pm$ 0.5	0.04
Alanine aminotransferase (U/L)	77.6 $\pm$ 47.9	0.47
Aspartate aminotransferase (U/L)	53.6 $\pm$ 34.4	0.69
Alkaline phosphatase (U/L)	85.1 $\pm$ 32.8	0.43
$\gamma$ -Glutamyltransferase (U/L)	60.3 $\pm$ 39.6	0.15
Albumin (g/dL)	4.17 $\pm$ 0.39	0.04
Serum iron ( $\mu$ g/dL)	90.5 $\pm$ 31.1	0.006
Serum ferritin (ng/mL)	236.3 $\pm$ 265.4	0.27
Transferrin saturation (%)	25.6 $\pm$ 10.4	0.008
Albumin (g/dL)	4.17 $\pm$ 0.39	0.04



**Figure No.1: Features of the metabolic syndrome compared with the degree of hepatic fibrosis.**



**Figure No.2: Histological analysis of liver suffering from NAFLD.**

## DISCUSSION

In this cross-sectional study of 50 patients with biopsy-proven NAFLD, a relationship between the severity of the metabolic syndrome and NAFLD was observed. While measures of adiposity correlated with hepatic steatosis, hepatic inflammation and fibrosis were associated with the presence and severity of the metabolic syndrome<sup>10</sup>. This finding has clinical implications, since hepatic ultrasound and serum transaminases have limited utility in predicting hepatic inflammation and fibrosis, and there is current reliance on liver biopsies to confirm the diagnosis and indicate prognosis<sup>11</sup>. We suggest that features of the metabolic syndrome would potentially be a better guide in determining which patients should be considered for biopsy and/or potential specific therapy<sup>12</sup>. Recent studies have pointed that NAFLD, in its whole spectrum ranging from pure fatty liver to non-alcoholic steatohepatitis (NASH), might represent another feature of MS<sup>13</sup>. Pathophysiologic considerations, clinical associations, and laboratory investigations support that insulin resistance and hyperinsulinaemia have a central role in pathogenesis of both MS and non-alcoholic fatty

liver. Studies concluded that NAFLD, in the presence of normoglycaemia and normal or moderately increased body weight, is characterized by clinical and laboratory data similar to those found in diabetes and obesity such as impaired insulin sensitivity and abnormalities in lipid metabolism<sup>14</sup>. Ninety percent of individuals with NAFLD have at least one risk factor of MS, and 33% have all the features of MS. Study concluded that liver fat content is significantly increased in subjects with the MS as compared with those without the syndrome, independently of age, gender, and body mass index<sup>15</sup>. In 304 NAFLD patients without diabetes mellitus the prevalence of metabolic syndrome increased from 18% in normal weight individuals to 67% in obese individuals<sup>16</sup>. The presence of multiple metabolic disorders such as diabetes mellitus, obesity, dyslipidaemia<sup>17</sup> and hypertension is associated with a potentially progressive, severe liver disease<sup>18</sup>. Obesity is found in 30-100% of subjects with NAFLD<sup>19</sup>. In obese persons steatosis is 4.6 fold higher than in normal weight persons<sup>20</sup>.

## CONCLUSION

It is concluded that NAFLD is associated with a high prevalence of obesity and MetS. There was a trend towards an association between NASH and MetS; in addition, patients with NAFLD with MetS were more likely to have severe steatosis and portal inflammation on liver biopsy.

**Acknowledgment;** Dr. Muhammad Tariq Rehmani, Associate Professor, Pathology Department, Lahore General Hospital, Lahore.

### Author's Contribution:

Concept & Design of Study:	Kashif Aziz Ahmad
Drafting:	Kashif Aziz Ahmad, Akmal Khurshid Bhatti, Tahir Mahmood Butt
Data Analysis:	Tahir Mahmood Butt, Zara Tahir
Revisiting Critically:	Kashif Aziz Ahmad, Akmal Khurshid Bhatti
Final Approval of version:	Imran Idris Butt

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

- Huang HL, Lin WY, Lee LT, et al. Metabolic syndrome is related to nonalcoholic steatohepatitis in severely obese subjects. *Obes Surg* 2007; 17:1457-63.
- Taniguchi CM, Emanuelli B, Kahn CR. Critical nodes in signalling pathways: insights into insulin action. *Nat Rev Mol Cell Biol* 2006; 7:85-96.
- Donnelly KL, Smith CI, Schwarzenberg SJ, Jessurun J, Boldt MD, Parks EJ. Sources of fatty

- acids stored in liver and secreted via lipoproteins in patients with nonalcoholic fatty liver disease. *J Clin Invest* 2005;115:1343–1351.
4. Sanyal AJ. Mechanisms of Disease: pathogenesis of nonalcoholic fatty liver disease. *Nat Clin Pract Gastroenterol Hepatol* 2005;2:46–53.
  5. Qureshi K, Abrams GA. Metabolic liver disease of obesity and role of adipose tissue in the pathogenesis of nonalcoholic fatty liver disease. *World J Gastroenterol* 2007;13:3540–3553.
  6. Sanyal AJ, Campbell-Sargent C, Mirshahi F, et al. Nonalcoholic steatohepatitis: association of insulin resistance and mitochondrial abnormalities. *Gastroenterol* 2001; 120:1183–1192.
  7. Paterson JM, Morton NM, Fievet C, Kenyon CJ, Holmes MC, Staels B. Metabolic syndrome without obesity: hepatic over expression of 11- $\beta$ -hydroxysteroid dehydrogenase type 1 in transgenic mice. *Proc Natl Acad Sci* 2004;101:7088–7093.
  8. Wei Y, Rector RS, Thyfault JP, Ibdah JA. Nonalcoholic fatty liver disease and mitochondrial dysfunction. *World J Gastroenterol* 2008;14: 193–199.
  9. Schattenberg JM, Wang Y, Singh R, Rigoli RM, Czaja MJ. Hepatocyte CYP2E1 overexpression and steatohepatitis lead to impaired hepatic insulin signaling. *J Biol Chem* 2005; 280:9887–9894.
  10. Bugianesi E, Manzini P, D'Antico S, et al. Relative contribution of iron burden, HFE mutations, and insulin resistance to fibrosis in nonalcoholic fatty liver. *Hepatology* 2004;39:179–187.
  11. Li Z, Yang S, Lin H, et al. Probiotics and antibodies to TNF inhibit inflammatory activity and improve nonalcoholic fatty liver disease. *Hepatology* 2003; 37:343–350.
  12. Duseja A, Sharma B, Kumar A. Nonalcoholic fatty liver in a developing country is responsible for significant liver disease. *Hepatology* 2010;52: 2248–2249.
  13. Marrero JA, Fontana RJ, Su GL. NAFLD may be a common underlying liver disease in patients with hepatocellular carcinoma in the United States. *Hepatology* 2002;36:1349–1354.
  14. Song HY, Lee HK, Lee JS. Risk factors of cryptogenic hepatocellular carcinoma in patients with low body mass index or without metabolic syndrome. *Korean J Int Med* 2012;27:47–52.
  15. McKimmie RL, Daniel KR, Carr JJ. Hepatic steatosis and subclinical cardiovascular disease in a cohort enriched for type 2 diabetes: the Diabetes Heart Study. *Am J Gastroenterol* 2008; 103:3029–3035.
  16. Volzke H, Robinson DM, Kleine V. Hepatic steatosis is associated with an increased risk of carotid atherosclerosis. *World J Gastroenterol* 2005; 11:1848–1853.
  17. Brea A, Mosquera D, Martín E. Nonalcoholic fatty liver disease is associated with carotid atherosclerosis: a case-control study. *Arterioscler Thromb Biol* 2005; 25:1045–1050.
  18. Shibata M, Kihara Y, Taguchi M. Nonalcoholic fatty liver disease is a risk factor for type 2 diabetes in middle-aged Japanese men. *Diabetes Care* 2007;30:2940–2944.
  19. World Health Organization, Department of Non-communicable Disease Surveillance; Geneva: 1999. Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications: Report of a WHO Consultation 1999.
  20. Balkau B, Charles MA. Comment on the provisional report from the WHO consultation. European Group for the Study of Insulin Resistance (EGIR) *Diabet Med* 1999;16:442–443.



# The Impact on Teaching Strategies on BDS Students Learning and Academic Improvement at Faryal Dental College

Impact on  
Teaching  
Strategies on  
BDS Students

Maryam Masood<sup>1</sup>, Sana Akram<sup>2</sup>, Hira Asghar<sup>3</sup>, Rumana Aqeel<sup>4</sup>, Ayesha Riaz<sup>1</sup> and Muhammad Omer Aslam<sup>1</sup>

## ABSTRACT

**Objective:** To examine the preferences about different teaching strategies of dental students in our institute.

**Study Design:** Descriptive study

**Place and Duration of Study:** This study was conducted at the Faryal Dental College Lahore from November 2018 to April 2019.

**Materials and Methods:** Total one hundred and twenty undergraduate dental students of both genders were included in this study. A self developed questionnaire was distributed to all the students. Student's preferences for different teaching methodologies were recorded. Analyze the views and preferences between all the students.

**Results:** There were 70 (58.33%) males while 41.67% were females. 85% students reported that the lectures schedule should be announced in advance. 85% of students preferred morning lectures and 15% students preferred afternoon lectures. 96 (80%) students preferred power point lectures method. Most of the student reported that they should have received lecture handouts and study materials before the session and practical work at the end of session.

**Conclusion:** Majority of students preferred power point presentation of lectures. Teachers should have to take students opinion before starting the course, this activity will be helpful to develop a good teaching environment and would have a positive impact on student performance.

**Key Words:** Dental students, Teaching Methods, Preferences, Views

**Citation of articles:** Masood M, Akram S, Asghar H, Aqeel R, Riaz Am Aslam MO. The Impact on Teaching Strategies on BDS Students Learning and Academic Improvement at Faryal Dental College. Med Forum 2019;30(5):88-91.

## INTRODUCTION

Worldwide, Teaching environment and teaching strategies plays an important role in improving the student's performance. Now a day it is big challenge for dental teachers to provide a positive teaching environment for enhancing student satisfaction level.<sup>1</sup> Students of dental colleges or dental students want to get education according to their experiences, personality and style and this miscellany preference presents a big challenge for teachers to provide a good teaching environment so that students performance could be increased. Student performance and level of satisfaction improve when the teaching environment is according to their preferences and views.<sup>2</sup> Teachers should adopt the different teaching strategies because it

will be effective for student performance.<sup>3</sup> Effective teaching is critical for student learning, especially in professional-fields such as dentistry. Teaching-effectiveness can be defined as the extent to which the teaching activity fulfills its intended purpose, function and goal.<sup>4</sup> For improving the teaching faculty and teaching environment routine evaluation of teaching strategies is very essential.<sup>5</sup> Since from the 19<sup>th</sup> century many of teaching modalities applied to improve the student performance. Lecture system is very essential for education especially in health care education.<sup>6,7</sup> As per teaching faculty, there are many advantages of lectures and one of the greatest advantage is the ability to share information with a large number of students.<sup>8</sup> Lectures will continue to be the main teaching strategy of choice for delivering the basic-curriculum to as many students as will fit in a lecture theater because of the economic constraint s on institutions, staff, facilities and students.<sup>9</sup>

Many of studies regarding teaching strategies documented that the educators must have to change their teaching modalities according to student preferences and style of learning. It developed a positive interest to the students for getting the education. Multiple studies have been conducted for the preferences and views of dental students towards teaching modalities to improve the student

<sup>1</sup>. Department of Orthodontics / Operative<sup>2</sup> / Dental Material<sup>3</sup> / Oral Pathology<sup>4</sup>, Faryal Dental College, M2 Lahore.

Correspondence: Maryam Masood, Senior Registrar  
Orthodontics, Faryal Dental College, M2 Lahore.  
Contact No: 03317036880  
Email: mariamharoon12@gmail.com

Received: April, 2019  
Accepted: April, 2019  
Printed: May, 2019

performance, impact of dental education on their stress level, teaching effectiveness in classrooms and clinics.<sup>10-12</sup>

## MATERIALS AND METHODS

This descriptive study was conducted at Faryal Dental College Lahore and the duration of this study was 6 months, Nov 2018 to April 2019. In this study total 120 dental students of both genders were included. A self developed questionnaire was distributed to all the students with written aim of study and consent. Not interested students were excluded from the study. Questionnaire consist of 3 parts, first part contains demographical data, 2<sup>nd</sup> part contains student preference for lectures time length, timing of lectures, teaching methods, timing of lectures announcement. The 3<sup>rd</sup> part contains the questions about the lectures and clinical sessions (preference of materials' provision before the session, having an interactive session, and having handouts and clinical demonstration after the lecture). Compare the views and preferences between male and females. Data was analyzed by SPSS 20.0. Chi-square test was applied. P-value <0.05 was considered as significant.

## RESULTS

From all the students 70 (58.33%) were male while 41.67% were females. 60 (50%) of all the students reported that lectures length should be for 40 minutes, 35 (29.17%) students preferred lecture length >40 minute and 25 (20.83%) students preferred <40 minutes. 102 (85%) students preferred morning lectures, 18 (15%) students preferred afternoon lectures (p-value <0.05) [Table 1]. Ninety six (80%) students preferred power point lectures method, 14 (11.67%) preferred online courses, 10 (8.33%) preferred chalkboard lectures method, the difference was statistically significant p-value <0.05 (Table 2).

**Table No.1: Students preference about length and timing of lectures**

Variable	No.	%
<b>Gender</b>		
Male	70	58.33
Female	50	41.67
<b>Lecture Length</b>		
<40 minutes	25	20.83
40 minutes	60	50
>40 minutes	35	29.17
<b>Lecture Timing</b>		
Morning	102	85
Afternoon	18	15

P-value <0.05

One hundred and two (85%) students agreed, 13 (10.83%) reported neutral and 5 (4.17%) student was disagreed about the lectures schedule should be

announced in advance (P-value <0.05 (Table 3). Eighty four (70%) students agreed that they should have received study material before lectures while 28 (23.33%) reported neutral and 8 (6.67%) reported disagreed (Table 4)

105 (87.5%) students preferred that they should have lectures handouts while 10 (8.33%) students opinion was neutral and 5 (4.17%) students reported disagreed. 108 (90%) students were agreed to have practical demonstration after lectures while 10 (8.33%) were neutral and only 2 (1.67%) were disagreed. (Table 5)

**Table No.2: Preference of students for teaching method**

Variable	No.	%
Powerpoint	96	80.0
Chalkboard	10	8.33
Online	14	11.67

P-value <0.05

**Table No.3: % figure 2: Student preference about the lecture schedule announcement**

Variable	No.	%
Agreed	102	85
Neutral	13	10.83
Disagree	5	4.17

P-value <0.05

**Table No.4: Provision of study material before lecture**

Variable	No.	%
Agreed	84	70
Neutral	28	23.33
Disagree	8	6.67

**Table No.5: Students opinion about lectures handouts and practical demonstration after lectures**

Variable	No.	%
<b>Should have Lecture Handouts</b>		
Agreed	105	87.5
Neutral	10	8.33
Disagree	5	4.17
<b>Practical Work After Lectures</b>		
Agreed	108	90
Neutral	10	8.33
Disagree	2	1.67

P-value <0.05

## DISCUSSION

Teaching strategies plays an important role to develop a positive environment between teachers and students also effective for student's performances.<sup>13</sup> The present study was conducted aimed to analyze the students preferences towards teaching strategies so that it could be helpful to develop a positive teaching environment. In this study 120 students were included in which 70 (58.33%) were male while 41.67% were females. These results showed similarity to some other studies in which

male student population was high as compared to female students<sup>14,15</sup> but some international studies showed different in which females student was high in numbers as compared to female.<sup>16</sup>

In our study the questionnaire demonstrated that majority of the students preferred morning time classes 85% and there was no significant difference between male and female p-value >0.05 while 15% student shows interest in afternoon lectures and in these students mostly were males with p-value <0.05. These results was similar to the some other studies conducted regarding teaching strategies in which majority of students preferred morning classes.<sup>17</sup> In present study we found that 96 (80%) students preferred power point lectures method, 14 (11.67%) preferred online courses, 10 (8.33%) preferred chalkboard lectures method, the difference was statistically significant p-value <0.05. A study they reported that majority of students preferred powerpoint lectures presentation.

In our study, 102 (85%) students agreed, 13 (10.83%) reported neutral and 5 (4.17%) student was disagreed about the lectures schedule should be announced in advance. Many of studies illustrated that schedule of lectures should be announced in advance is very helpful for the students in preparation of lectures and class.<sup>18,19</sup> We found that 84 (70%) students agreed that they should have received study material before lectures. A study<sup>20</sup> reported active learning as a process that encourages students to interact with the material being presented. Another study demonstrated prepared slides before lecture is helpful for student to maintain the performance.<sup>21</sup> In our study, 105 (87.5%) students preferred that they should have lectures handouts while 10 (8.33%) students opinion was neutral and 5 (4.17%) students reported disagreed. 108 (90%) students were agreed to have practical demonstration after lectures while 10 (8.33%) were neutral and only 2 (1.67%) were disagreed. Previous researches reported that the distribution of handouts before lecture is very effective for student concentration during lecture instead of working on taking notes. This strategy is very effective and produce a positive impact on student academic performance.<sup>20,21</sup>

## CONCLUSION

It is concluded that majority of students preferred power point presentation of lectures. Teachers should have to take students opinion before starting the course, this activity will be helpful to develop a good teaching environment and would have a positive impact on student performance.

### Author's Contribution:

Concept & Design of Study: Maryam Masood  
 Drafting: Sana Akram, Hira Asghar  
 Data Analysis: Rumana Aqeel, Ayesha

Riaz, Muhammad Omer  
 Aslam  
 Maryam Masood, Sana  
 Akram

Revisiting Critically:

Final Approval of version: Maryam Masood

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. Fang AL. Utilization of learning styles in dental curriculum development, The New York State Dent J 2002; 68( 8): 34–8.
2. Lujan HL Dicarlo SE. First-year medical students prefer multiple learning styles. Adv Physiol Edu 2006; 30(1): 13–6.
3. Murphy RJ, Gray SA, Straja SR, Bogert MC, Student learning preferences and teaching implications. J Dent Edu 2004;68(8): 859–66.
4. Jahangiri L, Mucciolo TW, Choi M, Spielman AI. Assessment of teaching effectiveness in U.S. dental schools and the value of triangulation. J Dent Edu 2008;72(6): 707–18.
5. Endorf M, McNeff M. The adult learner: five types. Adult Learning 1991; 2(7): 20–5.
6. DaRosa DA, Kolm P, Follmer HC, Pemberton LB, Pearce WH, Leapman S. Evaluating the effectiveness of the lecture versus independent study. Evaluation Program Planning 1991;14(3): 141–6.
7. Novak JC. Active learning in continuing professional education: the challenge of leadership. New Directions Adult Continuing Edu 1992; 1994(56):63–81.
8. Lake DA. Student performance and perceptions of a lecture-based course compared with the same course utilizing group discussion. Phys Therap 2001; 81(3): 896–902.
9. Perrin R, Laing G. The lecture: a teaching strategy through the looking glass. J Business Edu Scholarship Teaching 2014; 8(1): 67.
10. Berk NW, Close JM, Weyant RJ. Do student perceptions of their dental curriculum change over time? J Dent Edu 1998; 62(11): 934–7.
11. Henzi D, Davis E, Jasinevicius R, Hendricson W, Cintron L, Isaacs M. Appraisal of the dental school learning environment: the students' view. J Dent Edu 2005; 69(10): 1137–47.
12. Clark DM, Oyen OJ, Feil P. The use of specific dental school-taught restorative techniques by practicing clinicians. J Dent Edu 2001; 65(8): 760–65.
13. Ebrahimpourtaher A. Methodological preferences of engineering students in relation to EFL: Focus on gender. Procedia-Social Behav Sci 2013; 70: 841–52.

14. Mokhtari H. A quantitative survey on the influence of students' epistemic beliefs on their general information seeking behavior. *J Acad Librarianship* 2014; 40(3/4): 259-63.
15. Graham S, Liu X, Bartlett B, Ng C, Harris RK, Aitken A, et al. Reading for writing: a meta-analysis of the impact of reading interventions on writing. *Rev Educ Res* 2018;88:243–84.
16. Gore A, Chavan P, Kadam Y, Dhumale G. Application of biostatistics in research by teaching faculty and final-year postgraduate students in colleges of modern medicine: A cross-sectional study. *Int J Appl Basic Med Res* [Internet] 2012;2(1):11.
17. Weissgerber TL, Garovic VD, Milin-Lazovic JS, Winham SJ, Obradovic Z, Trzeciakowski JP, et al. Reinventing Biostatistics Education for Basic Scientists. *PLoS Biol* 2016;14(4).
18. Milic NM, Masic S, Milin-Lazovic J, Trajkovic G, Bukumiric Z, Savic M, et al. The importance of medical students' attitudes regarding cognitive competence for teaching applied statistics: Multi-site study and meta-analysis. *PLoS One* 2016; 11(10).
19. Fielding S, Poobalan A, Prescott GJ, Marais D, Aucott L. Views of medical students: what, when and how do they want statistics taught? *Scott Med J* 2015;60(4):164–9.
20. Milic NM, Trajkovic GZ, Bukumiric ZM, Cirkovic A, Nikolic IM, Milin JS, et al. Improving education in medical statistics: Implementing a blended learning model in the existing curriculum. *PLoS One* 2016;11(2).
21. Rubio Hurtado MJ, Ruiz-Bueno A, Martínez-Olmo F. Students' perceptions of the usefulness of learning activities for the development of competencies. *Rev Investig Educ* 2016;34(1): 221–40.

# Frequency of Cerebrospinal Fluid Leakage in Patients with Caries Spine Treated with Cage Fixation Procedure with Anterior Approach

Mumtaz Ahmed<sup>1</sup>, Muhammad Feroz Nawaz<sup>1</sup>, Habib Ullah<sup>2</sup> and Faisal Ali<sup>1</sup>

## ABSTRACT

**Objective:** To determine the frequency of cerebrospinal fluid leakage in patients with caries spine treated with cage fixation procedure with anterior approach.

**Study Design:** Descriptive study

**Place and Duration of Study:** This study was conducted at the Department of Neurosurgery Bahawal Victoria Hospital, Bahawalpur from November 2014 to May 2015.

**Materials and Methods:** A total of 157 patients with proven tuberculosis and having significant kyphosis ( $>40^\circ$  of segmental kyphosis) and instability (anteroposterior translation;  $>40^\circ$  of segmental kyphosis), 30 to 60 years of age were included. Patients with h/o previous operation and those who were not willing to participate excluded from the study. All patients were followed for 1 month for presence or absence of CSF leakage (yes/no) and final outcome was noted.

**Results:** There were 102 (64.97%) males while 35.03% patients were females with mean age of  $48.07 \pm 8.35$  years (30-60 years). Cerebrospinal fluid leakage was found in 13 (8.28%) patients, whereas no CSF leakage in 144 (91.72%) patients.

**Conclusion:** The cage fixation procedure with anterior approach is safe and effective with low rate of cerebrospinal fluid leakage.

**Key Words:** Pott's disease, Surgery, Anterior approach, Cerebrospinal fluid, Leakage

**Citation of articles:** Ahmed M, Nawaz MF, Habibullah, Ali F. Frequency of Cerebrospinal Fluid Leakage in Patients With Caries Spine Treated With Cage Fixation Procedure With Anterior Approach. Med Forum 2019;30(5):92-95.

## INTRODUCTION

Worldwide, Pott's disease (tuberculous spondylitis) considered as one of the oldest diseases.<sup>1</sup> Spinal tuberculosis is the frequent type of skeletal tuberculosis and approximately rated 50% of tuberculosis cases.<sup>2</sup> In 1779, first advanced case of spinal TB was reported by Percival Pott.<sup>3</sup> In TB patients there is just  $<1\%$  of spinal involvement but in developing and developed countries the prevalence of tuberculosis is increasing day by day due to multiple causes and this situation accounts to increase the rate of spinal TB.<sup>4</sup> The most influenced part of spine are lower thoracic and upper lumbar vertebrae.<sup>5</sup>

<sup>1</sup>. Department of Neurosurgery, Quaid-e-Azam Medical College/Bahawal Victoria Hospital Bahawalpur.

<sup>1</sup>. Department of Neurosurgery, Sahiwal Medical College/DHQ Teaching Hospital, Sahiwal.

Correspondence: Dr. Habib Ullah, Senior Registrar,  
Department of Neurosurgery, Quaid-e-Azam Medical  
College/Bahawal Victoria Hospital Bahawalpur.  
Contact No: 0312-3131213  
Email: drhabibullahkhan@live.com

Received: September, 2018  
Accepted: February, 2019  
Printed: May, 2019

In scientific language this malignant disorder is known as tuberculous spondylitis and mostly found in thoracic part of the spine.<sup>5,6</sup>

The previous studies reported that the pott's disease is resulted due to proliferate of TB from other sites and then the infection proliferate from two adjacent vertebrae.<sup>7</sup> This malignant infection causes bone extinction and development of abscess, which could induce untreatable neurologic deficit and devastating situation in the case of diagnosis delays. Indeed, for avoiding the severity of the related complications, the early diagnosis is the main priority for the management of spinal tuberculosis. Early and accurate diagnosis and proper treatment will be effective and it can help to decrease the spinal TB rate.<sup>8</sup>

The symptoms of spinal TB are backache and neckache, radicular pain in arms and legs, weakness in both upper and lower limbs and spinal deformity with sphinteric involvement and bedsores.<sup>9</sup> Studies described that early and effective treatment methodologies is helpful in the prevention of long term neurological deficits.<sup>10</sup> Due to unawareness, many of patients presented late and it caused severe neurological disorders.<sup>11</sup> Surgical treatment for severe spinal instability or progressive neurological symptoms with evidence of cord compression and deformation is considered.<sup>7</sup> After meticulous debridement of all

infected tissue, the anterior column defect is then reconstructed with bone graft or titanium cages can also be used to reconstruct these defects.<sup>12-14</sup> Cerebrospinal fluid leakage associated with cage fixation of caries spine has been reported in 9.1% patients.<sup>15</sup>

## MATERIALS AND METHODS

This descriptive, case series study was carried out at Department of Neurosurgery, Bahawal Victoria Hospital, Bahawalpur from 15<sup>th</sup> November 2014 to 14<sup>th</sup> May 2015. A total of 157 patients with proven tuberculosis and having significant kyphosis ( $>40^\circ$  of segmental kyphosis) and instability (anteroposterior translation;  $>40^\circ$  of segmental kyphosis), 30 to 60 years of age were included. Patients with h/o previous operation and those who were not willing to participate excluded from the study. The patients were explaining all the risks or complications of the procedure to the patients and patients underwent cage fixation of caries spine through anterolateral approach. All patients were given same injectible antibiotics pre-operatively and for 5 days post-operatively. All patients were followed for 1 month for presence or absence of CSF leakage (Yes/No) and final outcome was noted. The data was analyzed using SPSS-20.

## RESULTS

There were 102 (64.97%) males while 35.03% patients were females with mean age of  $48.07 \pm 8.35$  years (30-60 years). CSF leakage was found in 13 (8.28%) patients, whereas no CSF leakage in 144 (91.72%) patients (Table 1).

**Table No.1: Demographic information of the patients (n=157)**

Variable	No.	%
<b>Age (years)</b>		
30-40	35	22.29
41-50	58	36.94
51-60	64	40.76
<b>Gender</b>		
Male	102	64.97
Female	55	35.03
<b>Duration of symptoms (years)</b>		
$\leq 3$	94	59.87
$> 3$	63	40.13
<b>CSF</b>		
Yes	13	8.28
No	144	91.72

**Table No.2: Comparison of CSF leakage with age groups**

Age (years)	CSF Leakage		p-value
	Yes	No	
30-40	2 (5.71%)	33 (94.29%)	0.813
41-50	5 (8.62%)	53 (91.38%)	
51-60	6 (9.38%)	58 (90.62%)	

When the CSF leakage compared with age, gender and duration of disease, it was found no significant difference statistically (Tables 2-4).

**Table No.3: Comparison CSF leakage with gender**

Gender	CSF Leakage		p-value
	Yes	No	
Male	8 (7.84%)	94 (92.16%)	0.787
Female	5 (9.09%)	50 (90.91%)	

**Table No.4: Comparison of CSF leakage with duration of disease**

Duration of disease (years)	CSF Leakage		P value
	Yes	No	
$\leq 3$ years	5 (5.32%)	89 (94.68%)	0.100
$> 3$ years	8 (12.70%)	55 (87.30%)	

## DISCUSSION

Spinal TB is usually insidious in onset; rarely it may present acutely. The symptoms are backache and neck-ache, radicular pain in arms and legs, weakness in both upper and lower limbs and spinal deformity with sphinteric involvement and bedsores. Sciatica mimicking symptoms have also been reported. Surgical treatment for severe spinal instability or progressive neurological symptoms with evidence of cord compression and deformation is considered.<sup>16-18</sup>

Surgeon's used both techniques anterior or posterior for surgical treatment of spinal disorders and described that these methods showed significant outcomes regarding prevention of long term neurological deficit.<sup>19</sup> Meticulous debridement of all infected tissue, the anterior column defect is then reconstructed with bone graft or titanium cages can also be used to reconstruct the defects.<sup>14</sup>

The age range was 30 to 60 years with mean age of  $48.07 \pm 8.35$  years, 102 (64.97%) were males and 55 (35.03%) were females. These results shows similarity to some other studies in which males patients was high in numbers as compared to females with age ranges 40 to 65 years.<sup>20</sup> in the present study and CSF leakage was found in 13 (8.28%) patients, whereas no CSF leakage in 144 (91.72%) patients in the present study. While Hsu et al<sup>15</sup> reported that cerebrospinal fluid leakage associated with cage fixation of caries spine has been reported in 9.1% patients.

Ali et al<sup>10</sup> believes that canal decompression and correction of spinal deformity is best achieved through anterior decompression and grafting technique. Out of 36 cases, excellent results were achieved in 27 cases within first 2 months. All these patients achieved power of 4/5 according to Medical Research Council grading and were walking without support independently after 6 months. Sphinteric improvement was seen in 29 cases in first 4 months. The early management for spinal TB

is the use of ATT drug. This type of management is suitable for cases that are in the early course of disease, without myelopathy and without demonstrable radiological instability or cord compression. Even then, such patients should be closely observed with repeated imaging to look for delayed instability. Anti-tubercular drugs with immobilization and external orthosis is a must in the initial stage of treatment.<sup>22</sup>

Anterior surgery on the spine represents a less commonly utilized but important adjunct in the armamentarium of the spine surgeon. The anterior approach provides excellent exposure of the thoracic and lumbar spine.<sup>23</sup> Through a single-stage approach, direct visualization for spine decompression and stabilization is possible. Anterior approaches to structured insufficiency of the anterior and middle column and to anterior decompression of the neural structures are based on solid theoretical concepts with favorable clinical results.<sup>24</sup> Spinal reconstruction in cases of tumor, infection or trauma will continue, under certain circumstances, to be routine indications for anterior surgery of the thoracic and lumbar spine.<sup>25,26</sup>

Advocates of the traditional anterior approach<sup>27</sup> cite the ability to directly access the disease pathology and perform decompression, less muscle dissection and the ability to place a large graft under compressive load for fusion. Spinal instability is likely to increase after surgical decompression in the immediate postoperative period. The bone graft does not give initial stability and graft related complications occur more often when the span of the graft exceeds a two-disc space.<sup>28</sup> Many of previous studies regarding caries spine illustrated cage fixation method with anterior approach had a better outcomes with no procedural complications and the rate of cerebrospinal fluid leakage was low.<sup>29-30</sup>

## CONCLUSION

There is low frequency of cerebrospinal fluid leakage after cage fixation with anterior approach in caries spine patients. So, we recommend that anterior approach for cage fixation should be used primary approach in carries spine patients in order to reduce their morbidity.

### Author's Contribution:

Concept & Design of Study:	Mumtaz Ahmed
Drafting:	Muhammad Feroz Nawaz
Data Analysis:	Habib Ullah, Faisal Ali
Revisiting Critically:	Mumtaz Ahmed, Muhammad Feroz Nawaz
Final Approval of version:	Mumtaz Ahmed

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. Bynum H. Spitting blood. The history of tuberculosis. Oxford: Oxford University Press; 2012. 6-10.
2. Khalequzzaman S, Hoque HW. Tuberculosis of Spine Magnetic Resonance Imaging (MRI) Evaluation of 42 Cases. *Med Today* 2012;24(2): 59-62.
3. Sai-Kiran NA, Vaishya S, Kale SS, Sharma BS, Mahapatra AK. Surgical results in patients with tuberculosis of the spine and severe lower-extremity motor deficits: a retrospective study of 48 patients. *J Neurosurg Spine* 2007;6:320-26.
4. Rasouli MR, Mirkoohi M, Vaccaro AR, Yarandi KK, Rahimi-Movaghar V. Spinal Tuberculosis: diagnosis and management. *Asian Spine J* 2012; 6(4):294-308.
5. Ali M, Khan HM, Khanzada K, Usman M, Hussain R, Rehman ZU. Level of spinal involvement in patients operated for spinal tuberculosis. *J Postgrad Med Inst* 2012;26(4):439-43.
6. Moon MS, Kim SS, Lee BJ, Moon JL. Spinal tuberculosis in children: Retrospective analysis of 124 patients. *Ind J Orthop* 2012;46(2):150-8.
7. Pola E, Rossi B, Nasto LA, Colangelo D, Logroscino CA. Surgical treatment of tuberculous spondylodiscitis. *Eur Rev Med Pharmacol Sci* 2012;16(Suppl 2):79-85.
8. Abbas A, Rizvi SRH, Mahesri M, Salahuddin HRA. Conservative Management of Spinal Tuberculosis: initial series from Pakistan. *Asian Spine J* 2013;7(2):73-80.
9. Ansari S, Amanullah MF, Ahmad K, Rauniyar RK. Pott's Spine: diagnostic imaging modalities and technology advancements. *N Am J Med Sci* 2013; 5(7):404-11.
10. Ali M, Khwanzada K, Ayub S, Khan H. Anterior spinal decompression and bone grafting in densely paraplegics due to tuberculosis. *Pan Arab J Neurosurg* 2010;14(1):63-7.
11. Park DW, Sohn JW, Kim EH. Outcome and management of spinal tuberculosis according to the severity of disease: a retripective study of 137 adult patients at Korean teaching Hospital. *Spine* 2007;32(4):E103-5.
12. Garg B, Kandwal P, Nagaraja UB, Goswami A, Jayaswal A. Anterior versus posterior procedure for surgical treatment of thoracolumbar tuberculosis: a retrospective analysis. *Ind J Orthop* 2012; 46(2):165-70.
13. Sundararaj GD, Amritanand A, Venkatesh K, Arockiaraj J. The use of Titanium Mesh Cages in the reconstruction of anterior column defects in active spinal infection: can we rest the crest? *Asian Spine J* 2011;5(3):155-61.

14. Khan Z, Sharafat S, Ali M, Azam F, Khanzada K, Siddique M, et al. Role of anterior decompression with internal fixation in dorsal spine tuberculosis. *Pak J Neurolog Sci* 2013;8(2):1-6.
15. Hsu LC, Cheng CL, Leong JC. Pott's paraplegia of late onset. The cause of compression and results after anterior decompression. *J Bone Joint Surg Br* 1988;70(4):534-8.
16. Jain AK, Dhammi IK. Tuberculosis of the spine: a review. *Clin Orthop Relat Res* 2007;460:39-49.
17. National Collaborating Centre for Chronic Conditions. TB (partial update) clinical guideline DRAFT (November 2010). Tuberculosis: clinical diagnosis and management of tuberculosis, and measures for its prevention and control. London: Royal College of Physicians, 2006 [assessed on 2011 Apr 16]. (<http://guidance.nice.org.uk/nicemedia/live/12193/51951/51951.pdf>)
18. Carey ME. Infections of the spine and spinal cord. In: Youmans JR, editor. *Neurological Surgery*. 4<sup>th</sup> ed. Philadelphia PA: WB Saunders;1996.p. 3270-304.
19. World Health Organization. HIV/TB Facts 2011 [assessed on 2011 Jun 11]. [http://www.who.int/hiv/topics/tb/hiv\\_tb\\_factsheet\\_june\\_2011.pdf](http://www.who.int/hiv/topics/tb/hiv_tb_factsheet_june_2011.pdf)
20. Gautam MP, Karki P, Rijal S, Singh R. Pott's spine and Pott's paraplegia. *J Nep Med Assoc* 2005; 44(159):106-15.
21. Grammatico L, Baron S, Rusch E, Lepage B, Surer N, Desenclos JC, et al. Epidemiology of vertebral osteomyelitis (VO) in France: analysis of hospital-discharge data 2002-2003. *Epidemiol Infect* 2008; 136(5):653-60.
22. Shridher K. Tuberculosis of the spine. In: Ramaurthin B, Jaudon PN, editors. *Textbook of Neurosurgery*. 2<sup>nd</sup> ed. New Delhi, Churchill Livingstone;1996.p.496-513.
23. Dunn HK. Anterior stabilization of thoracolumbar injuries. *Clin Orthop Relat Res* 1984;(189):116-24.
24. Kaneda K, Abumi K, Fujiya M. Burst fractures with neurologic deficits of the thoracolumbar-lumbar spine: results of anterior decompression and stabilization with anterior instrumentation. *Spine* 1984;9(8):788-95.
25. Esses SI, Botsford DJ, Kostuik JP. Evaluation of surgical treatment for burst fractures. *Spine* 1990; 15(7):667-73.
26. Haas N, Blauth M, Tschern H. Anterior plating in thoracolumbar spine injuries: indication, technique, and results. *Spine* 1991;16(3 Suppl):S100-11.
27. Jain AK, Dhammi IK, Prashad B, Sinha S, Mishra P. Simultaneous anterior decompression and posterior instrumentation of the tuberculous spine using an anterolateral extrapleural approach. *J Bone Joint Surg Br* 2008;90:1477-81.
28. Chen WJ, Wu CC, Jung CH, Chen LH, Niu CC, Lai PL. Combined anterior and posterior surgeries in the treatment of spinal tuberculous spondylitis. *Clin Orthop Relat Res* 2002;398:50-9.
29. Oga M, Arizono T, Takasita M, Sugioka Y. Evaluation of the risk of instrumentation as a foreign body in spinal tuberculosis: Clinical and biologic study. *Spine (Phila Pa 1976)* 1993; 18:1890-4.
30. Ozdemir HM, Us AK, Ogün T. The role of anterior spinal instrumentation and allograft fibula for the treatment of pott disease. *Spine (Phila Pa 1976)* 2003;28:474-9.



# Prevalence of Pathologic Tooth Migration in Patients with Periodontitis

Fareedullah Shan, Muhammad Naeem and Raham Zaman

Pathologic Tooth Migration in Patients with Periodontitis

## ABSTRACT

**Objective:** The aim of this study was to determine the prevalence of pathologic tooth migration in patients with periodontitis.

**Study Design:** Descriptive / cross sectional study

**Place and Duration of Study:** This study was conducted at the Bacha Khan Medical Complex, Dental Department, Mardan from January 2018 to September 2018.

**Materials and Methods:** This study was conducted on 102 patients. Patients having age from 10 to 70 years, both genders, having chronic or aggressive periodontitis, no medical conditions affecting periodontium were included. Patients with smoking, oral breathing, bruxism, and gingivitis were excluded. Both chronic and aggressive Periodontitis was diagnosed on the basis of clinical examination according to the 1999 American academy of periodontology classification. Data were analyzed by SPP version 20. Descriptive statistics were computed. Chi-square test was applied to compare the frequency of pathologic tooth migration (PTM) among genders, age groups, educational levels and type of periodontitis.  $P < 0.05$  was considered significant.

**Results:** The males ( $n=70$ , 68.6%) were more than females ( $n=32$ , 31.4%). The mean age was  $37.58 \pm 13.34$  years. Of whole sample ( $n=102$ ), the patients affected by chronic localized periodontitis were in highest number ( $n=72$ , 70.59%) followed by chronic generalized periodontitis ( $n=20$ , 19.61%). The least frequency was found for aggressive periodontitis ( $n=10$ , 9.8%). The prevalence of pathologic tooth migration was 32.4% ( $n=33$ ). The most common features of PTM was 'flaring and spacing' ( $n=22$ , 21.6%), followed by 'flaring, spacing and rotation' ( $n=8$ , 7.8%) and least was 'flaring, spacing, rotation and extrusion' ( $n=4$ , 3.9%).

**Conclusion:** Our findings showed that prevalence of pathologic tooth migration was 32.4% in patients having periodontitis. PTM was more in aggressive periodontitis and in old ages.

**Key Words:** Pathologic tooth migration, periodontitis, aggressive periodontitis

**Citation of articles:** Shan F, Naeem M, Zaman R. Prevalence of Pathologic Tooth Migration in Patients with Periodontitis. Med Forum 2019;30(5):96-99.

## INTRODUCTION

The definition of migrated tooth is "the dentition movement into abnormal positions relative to the basal bone of the alveolar process and the adjacent and antagonistic teeth due to loss of nearby or opposing teeth, interferences of occlusion, abnormal habits, or dystrophic and inflammatory disease of the attaching and supporting structures of the teeth."<sup>1</sup> Pathologic tooth migration (PTM) is defined as occurrence of displacement of tooth when the disruption of balance due to periodontal disease among the factors that maintain the physiologic tooth position.<sup>2</sup> Pathologic tooth migration is a disease of periodontal origin that has esthetic effects.<sup>3</sup>

Department of Dental Section Bacha Khan Medical College, Mardan.

Correspondence: Fareedullah Shan, Assistant professor and Head of department of Periodontology, Dental Section Bacha Khan Medical College, Mardan.

Contact No: 0300-5722188

Email: muhammadsjeff@gmail.com

Received: January, 2019

Accepted: April, 2019

Printed: May, 2019

The equilibrium responsible for tooth position may be disrupted by several causative factors. These factors are periodontal detachment, inflamed tissue exerting pressure, occlusal forces, noxious habits e.g. tongue thrust and teeth grinding, hypodontia without replacement, gingival hyperplasia, and iatrogenic.<sup>4</sup> Nevertheless, the literature found that damage of dental supporting tissue is the most significant cause in pathogenesis of pathologic migration. Periodontal pathologies in the maxillary anterior area can affect one or more teeth.<sup>5</sup> Periodontal problems and its outcome such as spacing, pathological tooth migration, flaring in labial direction, or tooth loss usually results in functional and aesthetic issue, either in isolation or with restorative needs.<sup>6</sup> The features of advanced periodontitis are severe loss of attachment, decreased support of alveolar bone, increased mobility of teeth, and recession of gingivae.<sup>7</sup>

In 1997 by Towfighi et al.<sup>8</sup> Published a study on the prevalence on PTM for the first time. Their study included only patients with moderate to severe periodontitis. They reported that the features of pathologic migration were spacing, extrusion, rotation, labial flaring, and migration into edentulous saddles. PTM prevalence was 30.03%. Another study conducted on Indian population to determine the

prevalence of pathologic tooth migration and reported 11.4% prevalence.

There is lack of literature on pathologic tooth migration in our country. The periodontal susceptibility may vary in different populations due to level of education and oral hygiene maintenance, genetic and environmental factors. So the aim of this study was to determine the prevalence of pathologic tooth migration in patients with periodontitis.

## MATERIALS AND METHODS

This cross sectional descriptive study was conducted on patients reporting to Bacha Khan Medical Complex, Dental Department, Mardan from January 2018 to September 2018. A total of 102 participants were selected by non-probability consecutive sampling technique. A detailed explanation of the aim and procedure of the study was given. An informed consent was taken from participants/guardians.

Patients having age from 10 to 70 years, both genders, having chronic or aggressive periodontitis, no medical conditions affecting periodontal health like diabetes etc were included. Patients with characteristic or factors of smoking, oral breathing, bruxism, and patients who were simply suffering from gingivitis (without periodontitis) were excluded.

Both chronic and aggressive Periodontitis was diagnosed in the participants on the basis of clinical examination according to the 1999 American academy of periodontology classification.<sup>9</sup> Clinical attachment loss was measured as the distance between the cement-enamel junction (CEJ) and the base of the pocket. Clinical attachment loss at 6 points of each tooth was calibrated using periodontal probe by hand (mesio-facial, mid-facial, disto-facial, mesio-lingual, mid-lingual, and disto-lingual). All measurements were performed by a periodontist.

Data were entered and analyzed by SPP version 20. Mean and standard deviations were calculated for quantitative variables like age. Frequencies and percentages were calculated for qualitative variable like gender, type of Periodontitis (Chronic or Aggressive), pathologic tooth migration, and feature of pathologic tooth migration (flaring, spacing, rotation, and extrusion). Chi-square test was applied to compare the frequency of PTM among genders, age groups, educational levels and type of periodontitis.  $P < 0.05$  was considered significant.

## RESULTS

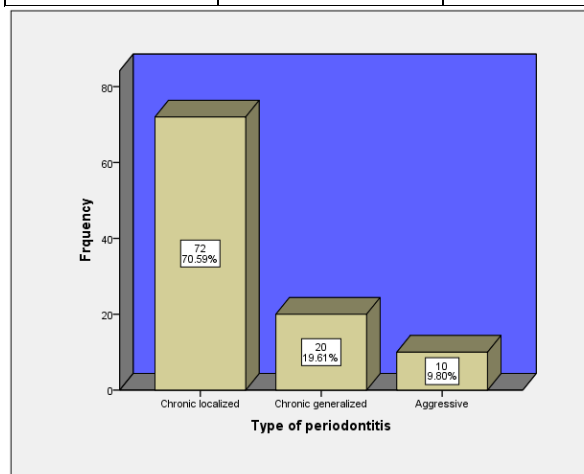
Total participant were 102. The males ( $n=70$ , 68.6%) were more than females ( $n=32$ , 31.4%). The mean age was  $37.58 \pm 13.34$  years. The age range was from 16 to 60 years.

Most of the participants were illiterate ( $n=32$ , 31.4%) followed by matric level of education ( $n=24$ , 23.5%). The details are shown in the table 1. Of whole sample

( $n=102$ ), the patients affected by chronic localized periodontitis were in highest number ( $n=72$ , 70.59%) followed by chronic generalized periodontitis ( $n=20$ , 19.61%). The least frequency was found for aggressive periodontitis ( $n=10$ , 9.8%). (Fig 1). Among the patients affected by periodontitis the frequency of pathologic tooth migration was 33 (32.4%). The detailed frequency for pathologic tooth migration is given in table 2. The most common features of PTM was 'flaring and spacing' ( $n=22$ , 21.6%), followed by 'flaring, spacing and rotation' ( $n=8$ , 7.8%) and least was 'flaring, spacing, rotation and extrusion' ( $n=4$ , 3.9%). (Table 3) All cases of aggressive periodontitis had pathologic tooth migration (PTM). Chronic generalized periodontitis cases ( $n=14$ , 70%) were more affected by PTM than chronic localized periodontitis ( $n=9$ , 12.5%). These difference were statistically significant ( $P < 0.05$ ). (Table 4) The highest frequency of pathologic tooth migration was found in patients having secondary level of education (63.6%) followed by middle (57.1%). The details are given in the Table 5. Effect of gender on the prevalence of pathologic tooth migration was not statistically significant ( $P > 0.05$ ). The detailed statistics are depicted in table 6. In old ages the frequency of pathologic tooth migration was more than younger ages. These results were statistically significant ( $P < 0.05$ ). Details are given in table 7.

**Table No.1: Frequency of educational level of the participants**

Educational level	Frequency	Percent
Illiterate	32	31.4
Matric	24	23.5
Secondary	11	10.8
Bachelor	16	15.7
Master and above	12	11.8
Middle	7	6.9
Total	102	100



**Figure No.1: Distribution of chronic and aggressive periodontitis**

**Table No.2: Frequency of pathologic tooth migration**

Pathologic tooth migration	Frequency	Percent
Yes	33	32.4
No	69	67.6
Total	102	100

**Table No.3: Frequency of various features of pathologic tooth migration**

Features of PTM*	Frequency	Percent
Nil	68	66.7
Flaring and spacing	22	21.6
Flaring, spacing and rotation	8	7.8
Flaring, spacing, rotation and extrusion	4	3.9
Total	102	100

\* Pathologic tooth migration

**Table No.4: Frequency of pathologic tooth migration stratified by type of periodontitis**

Type of periodontitis	Pathologic tooth migration				P- value*
	Yes		No		
	n	%	N	%	
Chronic localized	9	12.50	63	87.50	0.000
Chronic generalized	14	70.0	6	30.0	
Aggressive	10	100.0	0.0	0.0	

\*chi square test, P&lt;0.05 is significant

**Table No.5: Frequency of pathologic tooth migration stratified by educational level**

Educational level	Pathologic tooth migration				P-value <sup>*</sup>
	Yes		No		
	N	%	N	%	
Illiterate	7	21.9	25	78.1	0.002
Primary	0	0	0	0	
Matric	12	50	12	50	
Secondary	7	63.6	4	36.4	
Bachelor	3	18.8	13	81.2	
Master and above	0.00	0.00	12	100	
Middle	4	57.1	3	42.9	

\*chi square test, P&lt;0.05 is significant

**Table No.6: Frequency of pathologic tooth migration stratified by genders**

Gender	Pathologic tooth migration				P-value *
	Yes		No		
	N	%	n	%	
Male	19	27.10	51	72.90	0.096
Female	14	43.80	18	56.20	

\*chi square test, P&lt;0.05 is significant

**Table No.7: Frequency of pathologic tooth migration stratified by age groups**

Age group	Pathologic tooth migration				P-value*
	Yes		No		
	N	%	n	%	
20-10	4	25.00	12	75.00	0.016
21-30	4	18.20	18	81.80	
31-40	6	21.40	22	78.60	
41-50	10	45.50	12	54.50	
51-60	9	64.30	5	35.70	

\*chi square test, P&lt;0.05 is significant

## DISCUSSION

This study was aimed to determine the prevalence of pathologic tooth migration in patients affected by periodontitis. Two factors affect tooth position; healthy normal height of periodontium, and the exerting forces on dentition. In case of imbalance among these factors lead to loss of maintenance of physiological tooth position and as a consequence the pathologic tooth migration.<sup>10</sup> Previous literature showed that the PTM prevalence in patients affected by periodontitis is 30.03–55.8%.<sup>8</sup> disruption of balance for tooth position can happened by several factors such as loss of periodontal attachment, pressure from inflamed tissue, occlusal factors, un-replaced missing posterior teeth, ectopic attachment of frenum, and oral habits such as tongue thrust, digit sucking, playing with wind instruments.<sup>11</sup>

In this study the males were than females. This may due to lack of awareness and less education among females than males and hence less presentation for dental care. In contrast to our study, the females were more than males in Indian research by Moka et al.<sup>12</sup> This difference in gender ratio may be due to level of awareness and education in females.

Our findings showed that most of the participants were illiterate and had low level of education. We selected only those patients affected by periodontitis, so their periodontal loss may due to lack of awareness for oral hygiene because of low literacy among these participants. Education have prime role in maintenance of oral health.<sup>13</sup>

Our results found that most common periodontitis was chronic localized followed by chronic generalized and least one was aggressive periodontitis. Previous study showed that generalized periodontitis is higher in frequency than localized.<sup>14</sup> However, their study was on elderly population and on general population. On other hand the current study included only patients affected by periodontitis.

The current results showed that the prevalence of pathologic tooth migration was 32.4%. This shows that every third patients affected by periodontitis have PTM. Khorshidi et al.<sup>3</sup> in a cross-sectional epidemiological study determined the prevalence of pathologic tooth

migration among patients with periodontitis and reported that pathologic migration prevalence was 11.4%. This difference in results may due to sample size, educational level of the participants, genetic and environmental variation. Towfighi et al.<sup>8</sup> conducted a research on pathologic migration of anterior teeth in patients with moderate to severe periodontitis and found the prevalence of PTM to 30.03%. These results are in consistent with the current findings.

The features of PTM in our study were flaring, spacing, rotation and extrusion. Flaring and spacing was the most common feature of PTM. Similar results were found by others.<sup>8</sup>

The present study found that the frequency of PTM was more in aggressive periodontitis as compared to chronic periodontitis. In aggressive periodontitis the attachment loss is more aggressive and hence more loss of "stabilizing effect" of periodontal ligament. To our knowledge no such comparison is available in literature.

Our results found that low literacy was not associated with increased frequency of pathologic tooth migration. It may be due the fact we selected all participants having periodontitis; education have a role in maintenance of oral hygiene only. Gender was not a contributory factor for pathologic tooth migration in our study. Khorshidi et al.<sup>3</sup> also found a similar frequency of pathologic tooth migration in both genders.

In our study the age was a significant factor for pathologic tooth migration. The reason for this may that in old ages there is more severe periodontitis and hence more pathologic tooth migration. Khorshidi et al.<sup>3</sup> reported that PTM is more in severe periodontitis as compared to mild and moderate.

## CONCLUSION

Our findings showed that prevalence of pathologic tooth migration was 32.4% in patients having periodontitis. PTM was more in aggressive periodontitis and in old ages.

### Author's Contribution:

Concept & Design of Study: Fareedullah Shan  
 Drafting: Muhammad Naeem  
 Data Analysis: Raham Zaman  
 Revisiting Critically: Fareedullah Shan,  
 Muhammad Naeem  
 Final Approval of version: Fareedullah Shan

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. Oh SL. An interdisciplinary treatment to manage pathologic tooth migration: A clinical report. *J Prosth Dent* 2011;106(3):153-8.
2. Carranza FA. Periodontal response to external forces. In: Newman MG, Takei HH, Klokkevold PR, Carranza FA, editors. *Carranza's Clinical Periodontology*. 12th ed. St. Louis: Saunders Elsevier; 2015.p.300-8. .
3. Khorshidi H, Moaddeli MR, Golkari A, Heidari H, Raoofi S. The prevalence of pathologic tooth migration with respect to the severity of periodontitis. *J Int Soc Prev Comm Dent* 2016; 6(Suppl 2):S122.
4. Rathod SR, Kolte AP, Chintawar S. The dynamic relationship between pathological migrating teeth and periodontal disease. *J Int Soc Periodontol* 2013;17(6):762-4.
5. Livada R, Shiloah J, Hottel TL. Non-Orthodontic, Non-Restorative Closure of Acquired Diastemata. *J Tennes Dent Assoc* 2015;95(2):34-6; quiz 7-8.
6. Ngom PI, Diagne F, Benoist HM, Thiam F. Intraarch and interarch relationships of the anterior teeth and periodontal conditions. *Angle Orthod* 2006;76(2):236-42.
7. Helm S, Petersen PE. Causal relation between malocclusion and periodontal health. *Acta Odontol Scand* 1989;47(4):223-8.
8. Towfighi PP, Brunsvold MA, Storey AT, Arnold RM, Willman DE, McMahan CA. Pathologic migration of anterior teeth in patients with moderate to severe periodontitis. *J Periodontol* 1997;68(10):967-72.
9. Armitage GC. Development of a classification system for periodontal diseases and conditions. *Ann Periodontol* 1999;4(1):1-6.
10. Newman MG, Takei H, Klokkevold PR, Carranza FA. *Carranza's clinical periodontology-e-book: Expert consult: Online: Elsevier Health Sciences* 2014.
11. Jhinga PK, Negi KS, Sharma D, Bhardwaj VK, Vaid S, Nishant N. Interdisciplinary approach for the treatment of pathologic migration in teeth with advanced periodontal disease. *SRM J Res Dent Sci* 2015;6(4):261-4.
12. Moka L, Boyapati R, Salavathi SS, Chintalapani S, Maloth KN, Nagubandi K. Determinants of pathological tooth migration. *J Uni Health Sci* 2018; 7(2):89-93.
13. Nakre PD, Harikiran A. Effectiveness of oral health education programs: A systematic review. *J Int Soc Prev Comm Dent* 2013;3(2):103-15.
14. Phipps KR, Chan BK, Jennings-Holt M, Geurs NC, Reddy MS, Lewis CE, et al. Periodontal health of older men: the MrOS dental study. *Gerodontology* 2009;26(2):122-9.

# Comparison of Surgical Options in Typhoid Ileal Perforation at Tertiary Care Hospital

Inayat Ali Zardari, Abdul Hakeem Jamali, Mashooq Ali Khowaja, Farkhanda Jabeen Dahri, Zulfqar Ali Imtiaz Memon and Altaf Hussain Ghumro

## ABSTRACT

**Objective:** To detect the outcomes of surgical management options in typhoid ileal perforations treated at tertiary care hospital.

**Study Design:** Comparative study

**Place and Duration of Study:** This study was conducted at the Surgical Department of PMC Hospital Nawabshah from January 2017 to December 2018.

**Materials and Methods:** This study included total 100 patients. All patients were admitted from surgical OPD and emergency department of PMCH, Nawabshah. Out of 100, 65 (65%) were females and 35 (35%) were male patients. Age ranged from 30 to 55 and 25 to 45 in females and males respectively. The common mode of presentation was mild to severe pain in abdomen along with distention of abdomen and intermittent/continuous low to high grade fever. Radiological investigations detected free air under right dome of diaphragm. Primary repair, resection, anastomosis and loop ileostomy were made and results were assessed according to condition of the patient.

**Results:** Out of 100, 45 (45%) were found single perforations of less than 1cm and 1.5 to 2 feet away from ileocecal junction whereas 30 (30%) patients had size of perforation less than 2.5 cm with less contaminated abdominal cavity, 25 (25%) patients had single and multiple perforations of more than 2.5cm size with contaminated abdominal cavity.

**Conclusion:** Primary repair is the best surgical option to treat ileal perforations. Ileostomy is the better option to treat large multiple perforation with contamination of abdominal cavity and septicemia patients as compared to resection and anastomosis because ileostomy has local complications and resection anastomosis has systemic complications.

**Key Words:** Ileostomy, Resection, Anastomosis, Primary repair, Typhoid ileal perforation

**Citation of articles:** Zardari IA, Jamali AH, Khowaja MA, Dahri FJ, Memon ZAI, Ghumro AH. Comparison of Surgical Options in Typhoid Ileal Perforation at Tertiary Care Hospital. Med Forum 2019;30(5):100-103.

## INTRODUCTION

Humans can survive only 3 minutes without air and 3 days without water. Human body also works like a machine and it is necessary to accomplish its needs for its maintenance. Water is essential element to life. Human body is composed of 70% water so it is imperative for it to be hydrated. Fresh, clean, and alkaline water is to be used in order to hydrate body and maintain pH level to keep body healthy. If contaminated/infected water is used, many diseases erupt and the most common and fatal of all is typhoid fever.<sup>1</sup> Typhoid disease is caused by *Salmonella typhi* and *salmonella paratyphi*. It is very strange that human is the only reservoir of this organism. It is transmitted through feco-oral route.

It harbors in intestine of a human especially ileum where it causes perforation of the ileum by causing ulcerations in Payers patches. This occurs in the third week of the disease process. Ulcers are usually located within 45 cms of ileocecal junction.<sup>2,3</sup>

The incidence of typhoid ileal perforation is common in developing countries where contaminated water and food is used commonly owing to scarcity of water and fresh food. All African countries, Turkey, South America and Eastern European countries are the countries where the incidence of typhoid ileal perforation is highest.<sup>4</sup>

The common presentation is the abdominal pain, distention of abdomen, vomiting, tender abdomen, dehydration, anemia and tachycardia.<sup>5</sup> In most of the cases, X ray chest and abdomen shows free gas under right dome of diaphragm. Widal-Grube agglutination test is positive at 1:600 dilution.<sup>6</sup>

It is widely accepted now that typhoid ileal perforation is treated surgically only. There are many methods in this regard viz primary closure, excision and closure, resection and primary anastomosis, limited right hemicolectomy and loop ileostomy. These depend upon the size and number of perforations, contamination of abdominal cavity and condition of the small bowel as is

Department of Surgery, PUMHSW, Nawabshah.

Correspondence: Dr. Inayat Ali Zardari, Assistant Professor, Surgical Unit-III PUMHSW, Nawabshah  
Contact No: 0336-3808532  
Email: inayat\_zardari@yahoo.com

Received: January, 2019

Accepted: April, 2019

Printed: May, 2019

found per operatively.<sup>7</sup> So the choice of procedure depends upon the per operative finding of the disease. If the size of perforation is small one and condition of gut is well, primary closure is the better choice to treat. When the perforation is large one in size, number is one or two or more and abdominal cavity is contaminated apart from the edematous and ischemic gut, the choice only is the resection and anastomosis, limited right hemicolectomy and loop ileostomy.<sup>8,9</sup>

The rationale of our study is to compare the outcome of surgical options of typhoid ileal perforation in order to find out the better procedure in our set up for the betterment of populace.

## MATERIALS AND METHODS

This is a comparative study of 100 patients admitted through Emergency/ Surgical Outpatient department (SOPD) in surgical Department of Peoples Medical College Hospital Nawabshah now converted into Peoples University of Medical and Health Sciences for Women (PUMHSW) Nawabshah. This study was conducted from January 2017 to December 2018. This is tertiary care hospital receiving and treating the patients of not only but also other provinces of Pakistan.

All the patients were suffering from abdominal pain, distention and fever, vomiting and tenderness of abdomen. Local examination of abdomen was done to diagnoses the disease and the systemic examination was to assess the general condition of the patient. X Ray Chest/ Abdomen along with Ultrasound of Abdomen was done to help confirm the diagnosis of the disease. X ray showed gas under right dome of diaphragm. They were treated accordingly.

## RESULTS

In this study, total 100 patients were included from all surgical wards of PMCH Nawabshah. Out of 100, 65 (65%) were females and 35 (35%) were male patients.

Out of 100, 45 (45%) were found single perforations of less than 1cm and 1.5 to 2 feet away from ileocecal junction whereas 30 (30%) patients had size of perforation less than 2.5 cm with less contaminated abdominal cavity, 25 (25%) patients had single and multiple perforations of more than 2.5cm size with contaminated abdominal cavity as is shown in table 1 below. The age range of affected was between 25 to 55 years with average age of 40 years.

The procedure of primary repair had multiple complications. These were fistula formation, infected wound, paralytic ileus. Out of 45, only 3 (6.6%) patients presented with fecal fistula and only 4 (8.88%) developed postoperative wound infection, 6 (13.33%) patients developed prolonged paralytic ileus that was relieved by treatment later on. No any presented with burst abdomen.

Out of 30 patients who were treated with resection and end to end anastomosis, 5 (16.6%) patients developed fecal fistula, 3 (10%) came with wound dehiscence, 6 (20%) had infected wound, 10 (33.3%) had paralytic ileus and only 2 (6.66%) developed intra-abdominal abscess as is shown in table 3 below.

Out of 25 patients who were managed by loop ileostomy, 5 (20%) developed skin excoriation, 3 (12%) had transient edema, 2 (8%) came with stomal prolapsed and 1 (4%) had retraction of stoma as is shown in table 4 below.

**Table No.1: Size of perforation with surgical option done in patients.**

S. No	No of pts	Percentage	Size of perforation	Surgical option done
1	45	45%	<1-1.5cm	Primary Repair
2	30	30%	<2.5cm	Resection anastomosis
3	25	25%	> 2.5cm	Ileostomy
Total	100	100%		

**Table No.2: Complications in patients with percentage.**

S.No	Complication	No of patients	Percentage
1	Fecal fistula	3	6.6%
2	Wound infection	4	8.88%
3	Paralytic ileus	6	13.33%
Total		13	28.7%

**Table No.3: Complications in patients with percentage.**

S.No	Complications	No of patients	Percentage
1	Fecal fistula	2	6.6%
2	Wound infection	3	10%
3	Paralytic ileus	3	10%
4	Wound dehiscence	2	6.6%
5.	Intra abdominal abscess	1	3.33%
Total		11	36.5%

**Table No.4: Ratio of complications in patients with percentage.**

S.No	Complications	No of patients	Percentage
1	Skin excoriation	5	20%
2	Transient edema	3	12%
3	Stomal prolapse	2	8%
4	Retraction	1	4%
Total		11	44%

## DISCUSSION

Unlike West, Typhoid ileal perforation is still the common surgical emergency presented as acute abdomen in Pakistan. Its prognosis only depends upon symptoms/signs of the patient and the time of presentation either early or delayed. Fortunately, Early presentation has good prognosis with required surgical procedures. But irony is that there is delayed presentation of patients in state of marked sepsis. Recent advances have proved that surgical treatment is the best option to treat the ileal perforation of typhoid. Various surgical procedures are done keeping in view the multiple factors found per operatively.<sup>10</sup>

In one study, male incidence was found to be increased as compared to females but in our study it is reverse.<sup>11</sup> Female incidence is 65% and male is 35%. One study showed the age ratio of patients suffering from ileal perforation was from 26-31 years. In another study conducted in Pakistan, the patients affected were commonly in their third decade of life<sup>12</sup> but in our study, the average age of patients is 40 years. The common affected in our study was in fourth decade of life.

Postoperative complications are the prognostic determinant of any surgery. One study showed higher rates of complications of primary repair when compared with ileostomy<sup>13</sup> but in our study, the complications rate is lower in the procedure of primary closure. It is 28% whereas in case ileostomy complications are higher upto 40%. But the main difference is that the complications of ileostomy are local and not fatal but the complications of primary repair and resection anastomosis involve systems of the body and patient usually undergoes second surgery. A study conducted in Pakistan showed better prognosis in primary repair as compared to ileostomy regarding the mortality of the patients.<sup>14</sup> The same is found in our study as none of patient died after primary repair.

Regarding the duration of hospital stay, a study showed the decrease in duration of hospital stay in case of loop ileostomy where as the patients of primary repair stayed more days. Same was also seen in another international study.<sup>15</sup> But in our study, the patient of resection and end to end anastomosis stayed more as compared to primary repair and ileostomy because of prolonged paralytic ileus and wound dehiscence/infected wound.

## CONCLUSION

Primary repair is the best surgical option to treat ileal perforations. Ileostomy is the better option to treat large multiple perforation with contamination of abdominal cavity and septicemia patients as compared to resection and anastomosis because ileostomy has local

complications and resection anastomosis has systemic complications.

### Author's Contribution:

Concept & Design of Study: Inayat Ali Zardari  
 Drafting: Abdul Hakeem Jamali, Mashooq Ali Khawaja  
 Data Analysis: Farkhanda Jabeen Dahri, Zulfqar Ali Imtiaz, Memon, Altaf Hussain Ghumro  
 Revisiting Critically: Inayat Ali Zardari, Abdul Hakeem Jamali  
 Final Approval of version: Inayat Ali Zardari

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

- Siddiqui FJ, Rabbani F, Hasan R, Nizami SQ, Bhutta ZA. Typhoid fever in children: some epidemiological considerations from Karachi, Pakistan. *Int J Infect Dis* 2006;10 (3): 215-22.
- Edino ST, Yakubu AA, Mohammed AZ, Abubakar IS. Prognostic Factors in Typhoid ileal Perforation: A Pro-spective Study of 53 Cases. *J National Med Assoc* 2007;99 (9):1042-1045.
- Sheshe AA, Anyanwu LJC, Mohammad AM, Muhammad AB, Obaro SK. Typhoid intestinal perforation: Analysis of the outcome of surgical treatment in Kano, Nigeria. *Arch Med Health Sci [serial online]* 2018 [cited 2019 Apr 18];6:59-63.
- Shaikh GS, Soomro Q, Bhutto AA, Bhatti Y, Alideenari R, Baloch I. Typhoid ileal perforation, experience of 62 cases at Chandka Medical College Hospital, Larkana. *Med Channel* 2009;15:187-90.
- Obaro SK, Hassan-Hanga F, Olateju EK, Umoru D, Lawson L, Olanipekun G, et al. Salmonella bacteremia among children in central and Northwest Nigeria, 2008-2015. *Clin Infect Dis* 2015;61 Suppl 4:S325-31.
- Contini S. Typhoid intestinal perforation in developing countries: Still unavoidable deaths? *World J Gastroenterol* 2017;23(11):1925-1931.
- Slayton RB, Date KA, Mintz ED. Vaccination for typhoid fever in sub-Saharan Africa. *Hum Vaccin Immunother* 2013;9:903-906.
- Obaro SK, Iroh Tam PY, Mintz ED. The unrecognized burden of typhoid fever. *Expert Rev Vaccines* 2017;16:249-260.
- Qamar FN, Azmatullah A, Bhutta ZA. Challenges in measuring complications and death due to invasive Salmonella infections. *Vaccine* 2015;33 Suppl 3:C16-C20.

10. Parry CM, Hien TT, Dougan G, White NJ, Farrar JJ. Typhoid fever. *N Engl J Med* 2002;347:1770-1782.
11. Saxe JM, Cropsey R. Is operative management effective in treatment of perforated typhoid? *Am J Surg* 2005;189:342-344.
12. Talabi AO, Etoneyeku AC, Sowande OA, Olowookere SA, Adejuyigbe O. Predictors of mortality in children with typhoid ileal perforation in a Nigerian tertiary hospital. *Pediatr Surg Int* 2014;30:1121-1127.
13. Date KA, Bentsi-Enchill A, Marks F, Fox K. Typhoid fever vaccination strategies. *Vaccine* 2015;33 Suppl 3:C55-C61.
14. Baker S, Hombach J, Marks F. What Have We Learned From the Typhoid Fever Surveillance in Africa Program? *Clin Infect Dis* 2016;62 Suppl 1:S1-S3.
15. Lee JS, Mogasale VV, Mogasale V, Lee K. Geographical distribution of typhoid risk factors in low and middle income countries. *BMC Infect Dis* 2016;16:732.



# Placebo-Controlled Trial of Pharmaceutical Optimized Hydralazine 25mg (F-6) in Patients with Essential Hypertension

Placebo-Controlled  
Trial of  
Pharmaceutical  
Optimized  
Hydralazine with  
Essential  
Hypertension

Sohail Iqbal<sup>1</sup>, Khurram Shahzad Khan<sup>2</sup>, Farooq Munfaet Ali Khan<sup>2</sup> and Asnad<sup>3</sup>

## ABSTRACT

**Objective:** The objective of this study evaluating biochemical effects and efficacy of optimized Hydralazine 25mg (F-6) as compared to placebo in adult hypertension patients

**Study Design:** Randomized placebo-controlled trial, Double-blind

**Place and Duration of Study:** This study was conducted at the Mohtarma Benazir Bhutto Shaheed Medical College, Biochemistry Department Mirpur, AJK from October 2014 to January 2015.

**Materials and Methods:** In this study we selected 80 patients, from different hospital of Mirpur AJK and 20 patients take as placebo. We measured blood pressure at baseline and after 8 week for both groups that one group received Hydralazine 25mg (F-6) and one group received placebo. Biochemical safety parameter was also measured for both groups. In these parameters we studied protein profile, enzymes/electrolytes, liver function, renal function and complete blood count. In basic metabolism we studied glucose metabolism and lipid metabolism in which triglycerides, LDL-cholesterol, HDL-cholesterol and total cholesterol was included. Microlab 300 was used for analysis of samples for both groups. Merck kits were used for analysis of sample.

**Results:** Baseline systolic blood pressure for Hydralazine 25mg (F-6) was  $148.8 \pm 10.2$  and for placebo was  $148.4 \pm 10.3$ . After 8 weeks was for Hydralazine 25mg (F-6) was  $140.1 \pm 10.4$  and for placebo was  $148.2 \pm 10.2$ . Baseline Diastolic blood pressure for Hydralazine 25mg (F-6) was  $97.6 \pm 6.3$  and for placebo was  $96.9 \pm 6.5$ . After 8 weeks was for Hydralazine 25mg (F-6) was  $86.5 \pm 5.9$  and for placebo was  $96.2 \pm 5.9$ . Blood glucose was observed as no significant variations such as Fasting Blood Glucose (mg/dl)  $98.8 \pm 10.2$  at base line and  $98.7 \pm 10.3$  after 8 weeks. Lipid profile was also observed no significant variation. Such as Total Cholesterol (mg/dl)  $196.8 \pm 42.8$  as baseline and  $195.5 \pm 42.6$  after 8 weeks. LDL - Cholesterol (mg/dl)  $113.9 \pm 32.5$  at base line and  $113.8 \pm 32.6$  after 8 weeks. HDL - Cholesterol (mg/dl)  $54.6 \pm 12.5$  at baseline and  $54.6 \pm 12.5$  after 8 weeks, Triglycerides (mg/dl)  $138.3 \pm 87.5$  at baseline and  $138.7 \pm 88.1$  after 8 weeks. The optimized product was observed best regarding glucose metabolism and also lipid metabolism because both biomolecule metabolisms remain unchanged and not affected with drug.

**Conclusion:** Hydralazine 25mg (F-6) showed best result to achieve and maintain blood pressure for eight weeks. Due to high antihypertensive efficacy it is best choice for blood pressure patients and it is safe for metabolic syndrome patients

**Key Words:** Hypertension, Hydralazine, Biochemical effects

**Citation of articles:** Iqbal S, Khan KS, Khan FMA, Asnad. Placebo-Controlled Trial of Pharmaceutical Optimized Hydralazine 25mg (F-6) in Patients with Essential Hypertension. Med Forum 2019;30(5):104-107.

## INTRODUCTION

<sup>1</sup>. Department of Pharmacology / Physiology<sup>2</sup> / Biochemistry<sup>3</sup>, Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur, AJK.

Correspondence: Dr. Asnad, Associate Professor of Biochemistry, Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur, AJK.

Contact No: 0332-3698204

Email: drasnadkhan@gmail.com

Received: October, 2018

Accepted: February, 2019

Printed: May, 2019

Morbidity and mortality are the risk factor of cardiovascular diseases and hypertension. With the help of adequate blood pressure we can manage easily. Mostly prescribed Hydralazine for the treatment of hypertension which act as vasodilator. Absorption of this drug is very high after the oral administration and significant first-pass metabolism. The guideline of blood pressure of 140/90mmHg treatment is 130/85 mmHg according World Health Organization (WHO) and it was actually 140/90 mmHg on previous guideline of WHO.<sup>1-6</sup> For renal diseases one risk factor is high blood pressure.<sup>7</sup> Angiotensin-converting enzyme (ACE) is also play important role in controlling of blood pressure. It has significant role macroalbuminuria with renal diseases and this result also observed in microalbuminuria patients.<sup>8</sup>

For the treatment of hypertension, mostly prescribed Hydralazine which act as vasodilator. Absorption of this drug is very high after the oral administration and significant first-pass metabolism<sup>9</sup>. According the acetylation of the drug, the Oral availability t range between 10 and 35 %, is reported. Hydralazine has high physiochemical stability, low dose (50–100 mg) and its short biological half-life (2–4 h). So these properties of the drug facilitate researcher to formulate the drug into once-a-day CR formulation<sup>10–12</sup>. This drug has very affective property as antihypertensive in severe hypertension in pregnancy. It is mostly prescribed in pregnancy.<sup>11</sup> Headache, nausea, and vomiting are side effects which are common and its deteriorating pre-eclampsia symptoms which are mimic. Olmesartan have superior tolerability and antihypertensive efficacy<sup>13</sup>. For effectiveness and tolerance in patient medoxomil and amlodipine besylate sowed result with hypertension<sup>14</sup>. Amlodipine besylate alone and with combination with benazepril hydrochloride with valsartan and with perindopril showed good result<sup>15,16</sup>. The objective of this study, determining biochemical basic metabolism and efficacy of pharmaceutical optimized product Hydralazine 25mg (F-6) in patients with essential hypertension in also in placebo for comparison.

## MATERIALS AND METHODS

This was multicenter, randomized, placebo-controlled, comparative study. Patient was randomized to receive optimized Hydralazine 25mg (F-6) once daily and Placebo once daily for 8 weeks. The study was conducted in Department of Biochemistry, Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur, AJK from October 20 14 to January 2015. Patients were selected from four different hospitals of Mirpur AJK. In this study we selected 80 patients, from different hospital of Mirpur AJK and 20 patient take as placebo. We measured blood pressure at baseline and after 8 week for both groups that one group received Hydralazine 25mg (F-6) and one group received placebo. Biochemical safety parameter was also measured for both groups. In these parameters we studied protein profile, enzymes electrolytes, liver function, renal function and complete blood count. In basic metabolism we studied glucose metabolism and lipid metabolism in which triglycerides, LDL-cholesterol, HDL-cholesterol and total cholesterol was included. Microlab 300 was used for analysis of samples for both groups. Merck kits were used for analysis of sample.

## RESULTS

Baseline systolic blood pressure for Hydralazine 25mg (F-6) was  $148.8 \pm 10.2$  and for placebo was  $148.4 \pm 10.3$ . After 8 weeks was for Hydralazine 25mg (F-6) was  $140.1 \pm 10.4$  and for placebo was  $148.2 \pm 10.2$ .

Baseline Diastolic blood pressure for Hydralazine 25mg (F-6) was  $97.6 \pm 6.3$  and for placebo was  $96.9 \pm 6.5$ . After 8 weeks was for Hydralazine 25mg (F-6) was  $86.5 \pm 5.9$  and for placebo was  $96.2 \pm 5.9$ . Blood glucose was observed as no significant variations. Such as Fasting Blood Glucose (mg/dl)  $98.8 \pm 10.2$  at baseline and  $98.7 \pm 10.3$  after 8 weeks. Lipid profile was also observed no significant variation. Such as Total Cholesterol (mg/dl)  $196.8 \pm 42.8$  as baseline and  $195.5 \pm 42.6$  after 8 weeks. LDL - Cholesterol (mg/dl)  $113.9 \pm 32.5$  at base line and  $113.8 \pm 32.6$  after 8 weeks. HDL - Cholesterol (mg/dl)  $54.6 \pm 12.5$  at baseline and  $54.6 \pm 12.5$  after 8 weeks, Triglycerides (mg/dl)  $138.3 \pm 87.5$  at baseline and  $138.7 \pm 88.1$  after 8 weeks. The optimized product was observed best regarding glucose metabolism and also lipid metabolism because both biomolecule metabolisms remain unchanged and not affected with drug.

**Table No.1: Baseline characteristics**

	Hydralazine 25mg (F-6) (n=60)	Placebo (n=20)
Age (years)	$50.3 \pm 8.2$	$50.5 \pm 8.6$
Male / Female (%)	41.2 / 58.8	35.5 / 64.5
Body weight (Kg)	$70.2 \pm 12.5$	$70.5 \pm 12.4$
BMI (kg/m <sup>2</sup> )	$27.1 \pm 2.9$	$27.2 \pm 2.8$
SBP sitting (mmHg)	$148.9 \pm 10.2$	$148.4 \pm 10.3$
DBP sitting (mmHg)	$97.6 \pm 6.3$	$96.9 \pm 6.5$

**Table No.2: Ambulatory blood pressure monitoring. Mean values of blood pressure**

	Hydralazine 25mg (F-6) (n=60) Systolic BP - 24 hours (mmHg)	Placebo (n=20)	P-value
Baseline	$148.8 \pm 10.2$	$148.4 \pm 10.3$	NS
Week 8	$140.1 \pm 10.4$	$148.2 \pm 10.2$	0.0036
	Diastolic BP - 24 hours (mmHg)		
Baseline	$97.6 \pm 6.3$	$96.9 \pm 6.5$	NS
Week 8	$86.5 \pm 5.9$	$96.2 \pm 5.9$	0.0002

NS: Non significant, *p*: probability

## DISCUSSION

For stroke one is risk factor is high blood pressure.<sup>17</sup> Dementia and cognitive impairment are present in high blood pressure patient and it is present with metabolic syndrome.<sup>18,19</sup> In table No1, baseline characteristics are

present. The study was conducted in Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur, AJK from October 20 14 to January 2015

**Table 3: Baseline Biochemical characteristics**

	Hydralazine 25mg (F-6) (n=60)	Placebo (n=20)
	Fasting Blood Glucose (mg/dl)	
Baseline	98.8 ± 10.2	98.4 ± 9.4
Week 8	98.7 ± 10.3	98.5 ± 9.3
	Total Cholesterol (mg/dl)	
Baseline	196.8 ± 42.8	195.7 ± 34.5
Week 8	195.5 ± 42.6	195.3 ± 34.7
	LDL (mg/dl)	
Baseline	113.9 ± 32.5	119.5 ± 26.5
Week 8	113.8 ± 32.6	119.7 ± 27.3
	HDL (mg/dl)	
Baseline	54.6 ± 12.5	48.5 ± 12.2
Week 8	54.3 ± 12.7	48.9 ± 12.5
	Triglycerides (mg/dl)	
Baseline	138.3 ± 87.5	146.2 ± 87.2
Week 8	138.5 ± 88.1	144.7 ± 87.5

In this study we selected 80 patients, from different hospital of Mirpur AJK and 20 patient take as placebo. We measured blood pressure at baseline and after 8 week for both groups that one group received Hydralazine 25mg (F-6) and one group received placebo. Biochemical safety parameter was also measured for both groups. In these parameters we studied protein profile, enzymes electrolytes, liver function, renal function and complete blood count. In basic metabolism we studied glucose metabolism and lipid metabolism in which triglycerides, LDL-cholesterol, HDL-cholesterol and total cholesterol was included. Microlab 300 was used for analysis of samples for both groups. Merck kits were used for analysis of sample. The antihypertensive efficacy result was present in table No.2. The optimized product showed significant efficacy for systolic and diastolic blood pressure. Baseline systolic blood pressure for Hydralazine 25mg (F-6) was  $148.8 \pm 10.2$  and for placebo was  $148.4 \pm 10.3$ . After 8 weeks was for Hydralazine 25mg (F-6) was  $140.1 \pm 10.4$  and for placebo was  $148.2 \pm 10.2$ . Baseline Diastolic blood pressure for Hydralazine 25mg (F-6) was  $97.6 \pm 6.3$  and for placebo was  $96.9 \pm 6.5$ . After 8 weeks was for Hydralazine 25mg (F-6) was  $86.5 \pm 5.9$  and for placebo was  $96.2 \pm 5.9$ . Blood glucose was observed as no significant variations Such as Fasting Blood Glucose

(mg/dl)  $98.8 \pm 10.2$  at base line and  $98.7 \pm 10.3$  after 8 weeks. Lipid profile was also observed no significant variation. Such as Total Cholesterol (mg/dl)  $196.8 \pm 42.8$  as baseline and  $195.5 \pm 42.6$  after 8 weeks. LDL - Cholesterol (mg/dl)  $113.9 \pm 32.5$  at base line and  $113.8 \pm 32.6$  after 8 weeks. HDL - Cholesterol (mg/dl)  $54.6 \pm 12.5$  at baseline and  $54.6 \pm 12.5$  after 8 weeks, Triglycerides (mg/dl)  $138.3 \pm 87.5$  at baseline and  $138.7 \pm 88.1$  after 8 weeks. The optimized product was observed best regarding glucose metabolism and also lipid metabolism because both biomolecule metabolism remain unchanged and not affected with drug. However, some drugs used in the treatment of hypertension, such as diuretics and beta-blockers, are known to be able to promote harmful alterations in lipid metabolism, especially in glucose metabolism. 70.2% of the patients treated with Hydralazine 25mg (F-6) to achieve and maintain for eight week. It means it has high antihypertensive efficacy it is best choice for blood pressure patients and is it is safe for metabolic syndrome patients

## CONCLUSION

Hydralazine 25mg (F-6) showed best result to achieve and maintain blood pressure for eight weeks. Due to high antihypertensive efficacy it is best choice for blood pressure patients and it is safe for metabolic syndrome patients.

### Author's Contribution:

Concept & Design of Study: Sohail Iqbal  
 Drafting: Khurram Shahzad Khan  
 Data Analysis: Farooq Munfaet Ali  
 Khan, Asnad  
 Revisiting Critically: Sohail Iqbal, Khurram Shahzad Khan  
 Final Approval of version: Sohail Iqbal

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. Sykowsky PA, D'Agostino RB, Belanger AJ, Kannel WB. Secular Trends in Long Term Sustained Hypertension, Long Term Treatment and Cardiovascular Morbidity. The Framingham Heart Study 1950-1990. Circulation 1996; 93: 697-703.
2. MacMahon S, Peto R, Cutler J, et al. Blood Pressure, stroke, and coronary heart disease. Part 1, prolonged differences in blood pressure: prospective observational studies corrected for regression dilution bias. Lancet 1990; 335: 765-77.
3. Diretrizes IV. Brasileiras de Hipertensão Arterial - Sociedade Brasileira de Hipertensão; Sociedade Brasileira de Cardiologia e Sociedade Brasileira de Nefrologia. Hipertensão 2003;5(4):126-63.

4. Chobaniam AV, Bakris GL, Black HR, et al. Seventh report of the Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure- JNC 7. Hypertension 2003; 42: 1206-52.
5. 2003 European Society of Hypertension - European Society of Cardiology guidelines for management of arterial hypertension. J Hypertens 2003;21:1011-53.
6. Hansson L, Zanchetti A, Carruthers SG, Dahlöf B, et al on behalf of HOT Study group. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomized trial. Lancet 1998;351:1755-62.
7. Lewis EJ, Hunsicker LG, Bain RP, Rohde RD. The effect of angiotensin converting enzyme inhibition on diabetic nephropathy. N Engl J Med 1993;329: 1456-62.
8. Marre M, Chatellier G, Leblanc H, Guyene TT, Menard J, Passa P. Prevention of diabetic nephropathy with enalapril in normotensive diabetics with microalbuminuria. BMJ 1988;297: 1092-95.
9. Wulff K, Lenz K, Krogsgaard AR, Holst B. Hydralazine in arterial hypertension. Randomized, double-blind comparison between conventional and slow-release preparations, Ugeskr. Laeger 1980;142:1862-1865.
10. Talseth T, Fauchald P, Pape JF. Hydralazine slow-release: Observations on serum profile and clinical efficacy in man. Curr Ther Res Clin Exp 1977;21: 157-168.
11. Adir J, Janda SM, Curry CL, Taylor RE, Poku CD, Rotenberg KS. Comparative efficacy and safety of immediate - release and controlled - release hydralazine in black hypertensive patients. Clin Ther 1987;9:640-650.
12. Passa P, Leblanc H, Marre M. Effects of enalapril in insulin dependent diabetic subjects with mild to moderate uncomplicated hypertension. Diabetes Care 1987;10:200-04.
13. Pedersen MM, Schmitz A, Pedersen EB, Danielsen H, Christiansen JS. Acute and long-term renal effects of angiotensin converting enzyme inhibition in normotensive, normoalbuminuric insulin-dependent diabetic patients. Diabet Med 1988;5: 562-69.
14. Garg R, Yusuf S. Overview of randomized trials of angiotensin-converting enzyme inhibitors on mortality and morbidity in patients with heart failure. Collaborative Group on ACE Inhibitor Trials. JAMA 1995;273:1450-6.
15. Indications for ACE inhibitors in the early treatment of acute myocardial infarction: systematic overview of individual data from 100,000 patients in randomized trials. ACE Inhibitor Myocardial Infarction Collaborative Group. Circulation 1998;97:2202-12.
16. Randomised placebo-controlled trial of lisinopril in normotensive patients with insulin-dependent diabetes and normoalbuminuria or micro-albuminuria. The EUCLID Study Group. Lancet 1997;349:1787-92.
17. Bernard RC, Carl JP, John OP, Jaroslav SI, Galina C, et al. Effects of ranolazine with atenolol, amlodipine, or diltiazem on exercise tolerance and angina frequency in patients with severe chronic angina. JAMA 2004;291:309-316.
18. Khalida B, Najaf AG, Naheed A. Comparative studies of cimetidine derivative "temalastine" for potential energy calculation by Kitaigorodskii and Lennard-Jones functions. Pak J Biochem Mol. Biol 2010;43:81-86.
19. Afshan N, Naheed A, Khalida B, Najaf AG and Farhat B. Conformational analysis geometry optimization of nucleosidic antitumor antibiotic showdomycin by Arguslab 4 software. Pak J Pharmacol 2009;22:78-82.

# Different Causes of Anaemia in Elderly Patients

Causes of  
Anaemia in  
Elderly Patients

Madiha Islam<sup>1</sup>, Amna Arooj<sup>2</sup>, Mona Aziz<sup>3</sup> and Sadia Taj<sup>4</sup>

## ABSTRACT

**Objective:** To find out the frequency of dissimilar causes of anemia in elderly patients

**Study Design:** Cross-sectional study

**Place and Duration of Study:** This study was conducted at the Department of Haematology, Shaikh Zayed Hospital, Lahore from March 2015 to September 2015.

**Materials and Methods:** A total of 600 cases were enrolled after fulfilling the inclusion criteria. Anemic patients of both genders between 66-86 years were included.

**Results:** Mean age was  $73.14 \pm 4.05$  years. Male patients were in majority 430(71%). Anemia due to iron insufficiency was found in 178 (29.7%) cases, anemia which was related to megaloblastic cause was noted in 72 (12%) cases, myelodysplastic syndrome related anemia in 56 (9.3%), anemia due to chronic inflammation was found in 150 (25%) of cases, 56 (9.3%) of cases had anemia which was caused by chronic kidney disease, anemia which was linked with endocrinopathy was present in 60 (10%) cases and in 28(4.66%) cases anemia was of unexplained origin.

**Conclusion:** The majority of the cases had iron insufficiency related anemia in the elderly age. So it is recommended that iron therapy should be given to the elderly patients.

**Key Words:** Iron deficiency anemia, Megaloblastic anemia, Myelodysplastic syndrome related anemia, Elder patients

**Citation of articles:** Islam M, Arooj A, Aziz M, Taj S. Different Causes of Anaemia in Elderly Patients. Med Forum 2019;30(5):108-112.

## INTRODUCTION

According to world health organization (WHO), anemia in elderly patients is defined as concentration of haemoglobin less than 12g/dl in female gender and less than 13g/dl in male gender.<sup>1</sup> Incidence of the anemia in female and male after age (65 y) was 11% and 10% respectively according to the study of Third National Health and Nutritional Examination Survey (NHANES III). After 50 years, the prevalence of anemia in elderly increases rapidly. By the age of 84 years or older anemia occurrence rate in elderly reached up to 19.9%.<sup>2</sup>

<sup>1</sup>. Department of Pathology, M. Islam Medical & Dental College Gujranwala.

<sup>2</sup>. Department of Pathology, Sahiwal Medical College Sahiwal.

<sup>3</sup>. Department of Haematology & Blood Bank, Shaikh Zayed Medical Complex Lahore.

<sup>4</sup>. Department of Haematology, Fatima Memorial Medical & Dentistry College Lahore.

Correspondence: Dr. Madiha Islam, Assistant Professor of Pathology, M. Islam Medical & Dental College Gujranwala.

Contact No: 0322-7362972

Email: roofidr@yahoo.com

Received: November, 2018

Accepted: March, 2019

Printed: May, 2019

Anemia was least common between the age of 50–64 in females while between the age of 17 and 49 years the occurrence in men was lowest. Significantly, in both gender, after the 5<sup>th</sup> decade of life the incidence of anemia augmented. Although in males age-linked prevalence of anemia was more dramatic. At the age of 75 or older anemia was more frequent in men than in women.<sup>3</sup> This sex disproportion has been examined in other studies as well<sup>4,5</sup> predicted that between the ages 75–84 years, 14.7–16.0% of male and 8.0–11.9% of female had WHO-defined anemia. In the elderly age 85 years and older prevalence rate of anemia was 29.6–30.7% in male gender and 16.5–17.7% in female gender.<sup>6</sup>

Anemia in elderly have numerous etiologies, like anemia due to iron insufficiency (15-23%), anemia due to chronic inflammation (15-35%), anemia related to chronic kidney diseases (8%), endocrinopathies (hypothyroidism) related anemia (<5%), anemia associated with deficiency of vitamin B12 or deficiency of folate (0-14%), anemia due to myelodysplastic syndromes (0-5%) and unexplained anemia (17-45%).<sup>7</sup>

## MATERIALS AND METHODS

This cross-sectional study was carried out at Department of Hematology, Shaikh Zayed Hospital Lahore from 15<sup>th</sup> March 2015 to 14<sup>th</sup> September 2015. A total of 600 cases were included. Patients of both genders between the age of 66-86 years having anemia were included. Patients with history of iron, vitamin

B12, folate and erythropoietin therapy in last two months and history of blood transfusion in last 30 days were excluded. Complete blood picture (CBC) including Hemoglobin (Hb) and those patients which were found to be anemic were investigated for Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH) [using Abacus+ hematological auto analyzer], peripheral smear, and Bone Marrow aspiration (where indicated). Serum Iron, Total Iron binding Capacity (TIBC), serum TSH, serum urea and serum creatinine levels were carried out in Biochemistry Laboratory, Shaikh Zayed Hospital [using Dimension RXL auto analyzer]. All this information and the causes of anemia (anemia due to iron insufficiency, anemia related to chronic inflammation, anemia related to chronic kidney disease, anemia due to endocrinopathies, anemia due to vitamin B12 or folate deficiency, myelodysplastic syndromes related anemia and unexplained anemia) were recorded. The data was analysed using SPSS-20.

## RESULTS

The mean age of 73.14±4.05 years were enrolled for this study (Fig. 1). Male patients 430(71%) were in majority as compared to female patients 170 (28.3%). Anemia related to iron insufficiency was present in 178 (29.7%) of cases and was absent in 422 (70.3%) of cases. Anemia due to megaloblastic cause was noted in 72 (12%) of cases and was absent in 528 (88%) of the cases. Anemia related to myelodysplastic syndrome was present in 56 (9.3%) cases while absent in 544 (90.7%) cases. Chronic inflammation related anemia was seen in 150 (25%) of cases while 450 (75%) cases did not have this condition. Chronic kidney disease related Anemia was present in 56 (9.3%) while absent in 544 (90.7%) cases. Anemia related to endocrinopathies was noted in 60 (10%) cases and was not present in 540 (90%) of cases. Anemia due to Unexplained reasons was seen in 28 (4.66%) of cases.

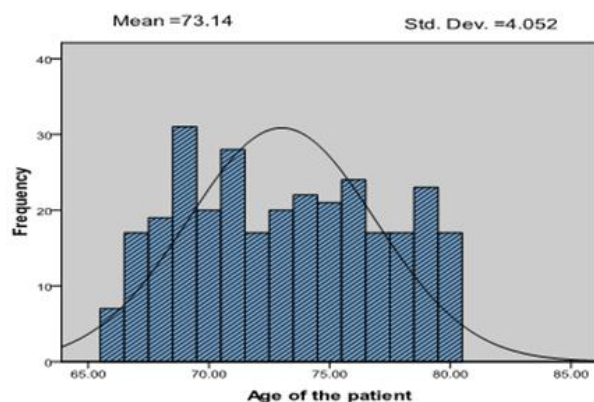


Figure No. 1: Distribution of age

The Prevalence of Anemia related to Iron insufficiency was high (34.7%) in patients among age group 75-85 years as compared to patients among age of 65-75 years

i.e.(27.2%). Similarly, prevalence of Anemia due to unexplained reasons was also more in the patients of age 75-85 years having percentage of 7.1% in comparison to 3.5% among the age group of 65-75 years. Whereas Anemia due to Megaloblastic causes 28%, Anemia related to Myelodysplastic syndromes 21%, Chronic inflammation related Anemia 50%, Chronic kidney disease related Anemia 22% and Anemia related to endocrinopathies 20% was more prevalent among patients of age group 65-75 years as compared to patients of age 75-85 (Table 1).

Anemia due to iron insufficiency and chronic inflammation related Anemia were the common anemia present among male gender having percentage of 29.8% and 27%. Also, anemia due to megaloblastic cause and anemia related to endocrinopathies were noted with the prevalence of 13% and 10.7% respectively. Like male gender, anemia due to iron insufficiency and anemia related to chronic inflammation were most common causes among female gender having percentages of 29.4% and 17% respectively whereas anemia related to Megaloblastic causes, anemia related to myelodysplastic syndromes, Chronic kidney disease related Anemia, Anemia related to endocrinopathies and Anemia due to unexplained causes were almost equal among female gender. The prevalence of anemia related to myelodysplastic syndromes and chronic kidney disease related anemia was found more in female gender as compared to male gender (Table 2).

Table No. 1: Comparison of prevalence according to age

Reasons of anemia	Age group		P value
	65-75 years	75-85 years	
Anemia related to iron insufficiency			
Yes	110(27.2%)	68(34.7%)	0.117
No	294(72.8%)	128(65.3%)	
Anemia due to megaloblastic cause			
Yes	56(13.9%)	16(8.2%)	0.106
No	348(86.1%)	180(91.8%)	
Anemia related to myelodysplastic syndrome			
Yes	42(10.4%)	14(7.1%)	0.247
No	362(89.6%)	182(92.9%)	
Chronic inflammation related anemia			
Yes	100(24.8%)	50(25.5%)	0.497
No	304(75.2%)	146(74.5%)	
Chronic kidney disease related anemia			
Yes	44(10.9%)	12(6.1%)	0.130
No	260(89.1%)	184(93.9%)	
Anemia related to endocrinopathies			
Yes	40(9.9%)	20(10.2%)	0.541
No	264(90.1%)	176(89.8%)	
Anemia due to unexplained reasons			
Yes	14(3.5%)	14(7.1%)	0.131
No	390(96.5%)	919(92.9%)	

**Table No. 2: Comparison of prevalence according gender**

Gender		P value	
Reasons of anemia	Male (n=430)		Female(n=170)
Anemia related to iron insufficiency			
Yes	128(29.8%)	50(29.4%)	0.532
No	302(70.2%)	120(70.6%)	
Anemia due to megaloblastic cause			
Yes	56(13.0%)	16(9.4%)	0.256
No	374(87%)	154(90.6%)	
Anemia related to myelodysplastic syndrome			
Yes	38(8.8%)	18(10.6%)	0.362
No	292(91.2%)	152(89.4%)	
Chronic inflammation related anemia			
Yes	116(27%)	34(20%)	0.133
No	314(73%)	136(80%)	
Chronic kidney disease related anemia			
Yes	36(8.4%)	20(11.8%)	0.241
No	394(91.6%)	150(88.2%)	
Anemia related to endocrinopathies			
Yes	46(10.7%)	14(8.2%)	0.343
No	384(89.3%)	156(91.8%)	
Anemia due to unexplained reasons			
Yes	12(2.8%)	16(9.4%)	0.020
No	418(97.2%)	154(90.6%)	

Socioeconomic status shows group with low socioeconomic status individuals had anemia related to Iron insufficiency in 27.9% cases, anemia related to megaloblastic causes in 15.8% cases, MDS related anemia in 8.7% cases, Anemia of chronic inflammation in 24% cases, Chronic kidney disease related anemia in 7.7% cases, anemia related to endocrinopathies in 12% cases and Unexplained anemia in 3.8% cases. While individuals in other group had anemia related to Iron Insufficiency in 32.5% cases, anemia related to megaloblastic causes in 6% cases, MDS related anemia in 10.3% cases, anemia of chronic inflammation in 26.5% cases, anemia of chronic kidney disease in 12% cases, anemia related to endocrinopathies in 6.8% cases and Unexplained anemia in 6.0% cases. The frequency of megaloblastic anemia was greater in low socioeconomic group and this difference showed statistical significance (Table 3).

Chronic kidney disease related anemia and anemia due to unexplained causes were found bit more prevalent among patients having malnutrition i.e., 10.7% each as compared to 8.9% and 2.7% while anemia related to iron insufficiency, anemia related to megaloblastic causes, MDS related anemia, chronic inflammation related anemia and anemia related to endocrinopathies were found more among other group of patients (Table 4).

**Table No.3: Comparison of prevalence according to economic status**

Reasons of anemia	Low socio-economic status		P value
	Yes (n=336)	No (n=234)	
Iron deficiency anemia			
Yes	102(27.9%)	76(32.5%)	0.234
No	264(72.1%)	158(67.5%)	
Megaloblastic anemia			
Yes	58(15.8%)	14(6.0%)	0.007
No	308(84.2%)	220(94%)	
Myelodysplastic syndrome anemia			
Yes	32(8.7%)	24(10.3%)	0.402
No	334(91.3%)	210(89.7%)	
Anemia of chronic inflammation			
Yes	88(24%)	62(26.5%)	0.365
No	278(76%)	172(73.5%)	
Anemia of chronic kidney disease			
Yes	28(7.7%)	28(12%)	0.147
No	338(92.3%)	206(88%)	
Anemia of endocrinopathies			
Yes	44(12%)	16(6.8%)	0.102
No	322(88%)	218(93.2%)	
Unexplained anemia			
Yes	14(3.8%)	14(6%)	0.276
No	352(96.2%)	220(94%)	

**Table No.4: Comparison of prevalence malnutrition**

Reasons of anemia	Malnutrition		P value
	Yes (n=150)	No (n=450)	
Iron deficiency anemia			
Yes	42(28%)	136(30.2%)	0.417
No	108(72%)	314(69.8%)	
Megaloblastic anemia			
Yes	12(8%)	60(13.3%)	0.152
No	138(92%)	390(86.7%)	
Myelodysplastic syndrome anemia			
Yes	18(12%)	38(8.4%)	0.241
No	132(88%)	412(91.6%)	
Anemia of chronic inflammation			
Yes	38(25.3%)	112(24.9%)	0.526
No	112(74.7%)	338(75.1%)	
Anemia of chronic kidney disease			
Yes	16(10.7%)	40(8.9%)	0.398
No	134(89.3%)	40.5(91.1%)	
Anemia of endocrinopathies			
Yes	10(6.7%)	50(11.1%)	0.189
No	140(93.3%)	400(88.9%)	
Unexplained anemia			
Yes	16(10.7%)	12(2.7%)	0.009
No	134(89.3%)	438(97.3%)	

## DISCUSSION

Anemia in elderly patients is related to increased mortality and morbidity and it is a very frequently found condition in this population, especially in those who are hospitalized. The purpose of this study was to find out the frequencies of different underlying conditions that lead to anemia in elderly population. There is controversy in literature regarding definition of anemia in older population. In 1960s WHO criteria were established in a group lacking individuals older than 65 years, (6, 8) thus making their general applicability in the elderly to be questioned. By using a threshold of less than the mean minus two SDs<sup>7,9</sup> or by using percentiles other definitions are established. WHO definition was used in this study because it is used in the majority of studies published as the literature contains no generally accepted definition of anemia in the older population.<sup>11,12</sup>

In the present study, the mean age of patients was 73.14±4.05 years. In a study done by Artz et al. mean age of patients was calculated 76.0 years.<sup>13</sup> Another study done by Merchant et al. showed mean age of 78.2 years.<sup>14-16</sup> The mean age of our study population is comparable with these studies.

In present study there were (430) 71% males and 170(29%) females which show high prevalence of anemia in elderly men. This sex difference has been observed in other studies as well. Study done by Skjeebakken et al<sup>4</sup> included 26530 participants from community aged 24 years and above and found that prevalence of anemia in males aged 65 years and above was 29.6% and those of females was 16.5%. Similarly Salive et al<sup>5</sup> studied 3946 elderly people and of those who were anemic 41% were males and 21% were females. This difference in sex distribution can be explained on the basis of lower normal haemoglobin level of elderly women (postmenopausal) as compared to men by WHO.

In the present study, frequency of IDA was found to be 29.7%, ACD was found in 25% elderly patients, anemia related to chronic kidney disorder in 9.3%, anemia related to endocrinopathies in 10%, megaloblastic anemia in 12% cases, MDS related anemia in 9.3% and unexplained anemia in 4.66% elderly patients.

In a similar study done by Artz et al<sup>19</sup> frequency of different causes of anemia in elderly was IDA in 23%, ACD in 35%, chronic kidney disease in 8%, anemia related to endocrinopathies in less than 5%, megaloblastic anemia in 14%, MDS related anemia in 5% and unexplained anemia in 45%.<sup>17</sup>

In NHANES III prevalence of different causes of anemia in elderly group was IDA 16.6%, megaloblastic anemia 2.0%, ACD 19.7%, anemia related to chronic kidney disorder 8.2% and Unexplained Anemia 33.6%.<sup>12,16</sup> Another study done INCHIANT showed IDA 17.4%, megaloblastic anemia 10.5%, ACD 24.4%, anemia related to chronic kidney disorder 10.5% and unexplained anemia 37.2%.<sup>16,17</sup>

According to another study done by van Houwelingen et al<sup>8</sup>, the five most prominent causes of anemia were ACD (30-45%), Iron deficiency (15-30%), megaloblastic anemia (5-10%), MDS related anemia (5%) and Unexplained anemia (15-25%).

Present study and comparative studies show Nutrition deficiency anemia and anemia of chronic disorder as prominent causes of anemia in aged population. Anemia due to iron insufficiency is however having more frequency as compared to other studies. This may be because we included elderly patients in hospital setting who have more comorbidities like dental issues and gastrointestinal bleeds as compared to other community population based studies.

Present study shows high prevalence of anemia related to endocrinopathies as compared to other studies by van Houwelingen et al<sup>8</sup> and Artz et al.<sup>19</sup> This can be explained on the basis that other studies in comparison has been done on community dwelling ambulatory population as compared to hospitalized cohort in our study.

Similarly our present study shows low prevalence of Unexplained anemia because it is more frequent in community dwelling individuals who have occult malignancies and undiagnosed hidden cases of MDS as a cause of unexplained anemia and once the patient comes to hospital as in our study multiple investigations and labs help to reach a definitive diagnosis.<sup>7,18</sup>

Depending on their clinical setting the causes of anemia differ in elderly population. However, anemia related to chronic inflammation and anemia related to iron insufficiency are the most common treatable forms of anemia both in hospitalized and community-dwelling elderly populations.<sup>19</sup>

According to this study anemia related to chronic renal disease was found in about 9% of the elderly patients assessed. While according to previous studies, anemia related to chronic renal disease showed prevalence of about 17.5%, but these studies used criterion for chronic kidney disease as glomerular filtration rate (GFR) of <30 mL/min.<sup>19,20</sup>

We divided our study cohort into two age groups. Similarly we divided our study population into two groups on the basis of gender, socioeconomic status and malnutrition. This was intended to see any differences in types and pattern of anemia between the two groups. The frequency of unexplainable anemia was greater in group having malnutrition.<sup>20,21</sup>

We also found that frequency of megaloblastic anemia was greater in low socioeconomic group. According to a study, people in lower socioeconomic groups have double the risk of megaloblastic anemia as compared to those who belong to middle or upper class (9, 21). This can be explained by lack of vitamin B12 and folate in their diet because these are expensive sources of food and partly explained by poor dentition in old age.



## CONCLUSION

Iron deficiency anemia is found as the most frequent cause of Anemia in our study cohort. SO the elderly population must be considered accordingly for the treatment of such cases.

### Author's Contribution:

Concept & Design of Study: Madiha Islam  
 Drafting: Amna Arooj, Mona Aziz  
 Data Analysis: Sadia Taj  
 Revisiting Critically: Madiha Islam, Amna Arooj  
 Final Approval of version: Madiha Islam

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

## REFERENCES

1. Bross MH, Soch K, Smith-Knuppel T. Anemia in older persons. *Am Fam Physician* 2010; 82: 480-7
2. Vanasse GJ, Berliner N. Anemia in elderly patients: an emerging problem for the 21st century. *ASH Education Program Book* 2010; 271-5
3. Stevens GA, Finucane MM, De-Regil LM, Paciorek CJ, Flaxman SR, Branca F, et al. Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995–2011: a systematic analysis of population-representative data. *Lancet Glob Health* 2013; 1: e16-e25
4. Skjelbakken T, Langbakk B, Dahl IMS, Løchen ML. Haemoglobin and anaemia in a gender perspective: The Tromsø Study. *Eur J Haematol* 2005;74:381-8.
5. Salive ME, Cornoni-Huntley J, Guralnik JM, Phillips CL, Wallace RB, Ostfeld AM & Cohen HJ. Anemia and hemoglobin levels in older persons: relationship with age, gender, and health status. *J Am Geriatr Soc* 1992; 40: 489-96
6. Organization WH. Nutritional anaemias: report of a WHO scientific group [meeting held in Geneva from 13 to 17 March 1967. 1968.
7. Beutler E, Waalen J. The definition of anemia: what is the lower limit of normal of the blood hemoglobin concentration? *Blood* 2006;107: 1747-50.
8. van Houwelingen AH, den Elzen WP, Mooijaart SP, Heijmans M, Blom JW, de Craen AJ, et al. Predictive value of a profile of routine blood measurements on mortality in older persons in the general population: the Leiden 85-plus Study. *PloS one* 2013; 8: e58050.
9. Tettamanti M, Lucca U, Gandini F, Recchia A, Mosconi P, Apolone G, et al. Prevalence, incidence and types of mild anemia in the elderly: the "Health and Anemia" population-based study. *Haematologica* 2010; 95: 1849-56.
10. Denny SD, Kuchibhatla MN, Cohen HJ. Impact of anemia on mortality, cognition, and function in community-dwelling elderly. *Am J Med* 2006;119: 327-34
11. Petrosyan I, Blaison G, Andrès E, Federici L. Anaemia in the elderly: an aetiological profile of a prospective cohort of 95 hospitalised patients. *Eur J Int Med* 2012; 23: 524-8.
12. den Elzen WP, Willems JM, Westendorp RG, de Craen AJ, Assendelft WJ, Gussekloo J. Effect of anemia and comorbidity on functional status and mortality in old age: results from the Leiden 85-plus Study. *Can Med Assoc J* 2009; 181: 151-7.
13. Guralnik JM, Eisenstaedt RS, Ferrucci L, Klein HG, Woodman RC. Prevalence of anemia in persons 65 years and older in the United States: evidence for a high rate of unexplained anemia. *Blood* 2004; 104: 2263-8.
14. Inelmen E, D'Alessio M, Gatto M, Baggio M, Jimenez G, Bizzotto M, et al. Descriptive analysis of the prevalence of anemia in a randomly selected sample of elderly people living at home: some results of an Italian multicentric study. *Aging Clin Exp Res* 1994;6: 81-9.
15. Eisenstaedt R, Penninx BW, Woodman RC. Anemia in the elderly: current understanding and emerging concepts. *Blood Rev* 2006; 20: 213-26.
16. Ferrucci L, Guralnik JM, Bandinelli S, Semba RD, Lauretani F, Corsi A, et al. Unexplained anaemia in older persons is characterised by low erythropoietin and low levels of pro-inflammatory markers. *Br J Haematol* 2007; 136: 849-55
17. Ania BJ, Suman VJ, Fairbanks VF, Melton LJ. Prevalence of anemia in medical practice: community versus referral patients. Presented at Mayo Clinic Proceedings 1994.
18. Merchant AA, Roy CN. Not so benign haematology: anaemia of the elderly. *Br J Haematol* 2012; 156: 173-85
19. Artz AS, Thirman MJ. Unexplained anemia predominates despite an intensive evaluation in a racially diverse cohort of older adults from a referral anemia clinic. *J Gerontol A-Biol J* 2011; 66: 925-32. Terrier B, Resche-Rigon M, Andres E, Bonnet F, Hachulla E, Marie I, Rosenthal E & Cacoub P. (2011). Prevalence, characteristics and prognostic significance of anemia in daily practice. *QJM*: hcr230
20. Terrier B, Resche-Rigon M, Andres E, Bonnet F, Hachulla E, Marie I, et al. Prevalence, characteristics and prognostic significance of anemia in daily practice. *QJM* 2011;230.
21. Drewnowski A, Shultz J. Impact of aging on eating behaviors, food choices, nutrition, and health status. *J Nutr Health Aging* 2001; 5(2):75-9.

# Clinical Presentation of Hepatitis C Virus in Urban and Rural Patients

Hepatitis C Virus  
in Urban and  
Rural Patients

Marifat Shah

## ABSTRACT

**Objective:** The objective of this study was to determine the clinical presentation of hepatitis C and comparison of these features of hepatitis C among urban and rural areas.

**Study Design:** Descriptive / Cross sectional study

**Place and Duration of Study:** This study was conducted at the Jinnah Teaching Hospital attached to the Jinnah Medical College, Peshawar from October, 2017 to December, 2018

**Materials and Methods:** This cross sectional descriptive study was conducted on 100 consecutive patients. The participants were diagnosed for hepatitis C by suggesting Anti-HCV antibody through immune chromatographic technique (ICT) followed by ELISA and PCR (qualitative) to confirm; and ultrasound abdomen to detect ascites and any hepatic parenchymal changes. Patient's names, age, sex, marital status, address (rural and urban) and clinical presentations were recorded. Descriptive statistics were calculated in SPSS 20.0.

**Results:** Comparison was made for clinical presentations of Hepatitis C between rural and urban areas using chi-square test.  $P\text{-value} \leq 0.05$  was considered significant. Male were  $n=40(40\%)$  and female were  $n=60(60\%)$ . The mean age was  $41.78 \pm 14.19$  years. The age ranged from 17 to 75 years. Most of the participants were married  $n=95(95\%)$ . The clinical presentation of hepatitis C were generalized body aches, jaundice, lethargy, fever, arthralgia, ascites, and malaise etc. The most common presentation of hepatitis C in our sample was generalized body aches  $n=45(45\%)$ . Of total the  $n=7(7\%)$  cases reported arthralgia. Jaundice was found in  $n=5(5\%)$  participants. Lethargy was found in  $n=7(7\%)$  cases. Five (5%) cases presented with ascites. Malaise was reported by 7 cases. Nine (9%) cases were asymptomatic.

**Conclusion:** The difference in clinical presentations of hepatitis C between urban and rural areas was not statistically significant ( $P > 0.05$ ). This showed that the main role in clinical presentation of Hepatitis C is genetic and environment may have fewer roles.

**Key Words:** Hepatitis C, clinical presentations, rural, urban

**Citation of articles:** Shah M. Clinical Presentation of Hepatitis C Virus in Urban and Rural Patients. Med Forum 2019;30(5):113-116.

## INTRODUCTION

Generally the term Hepatitis refer to inflammation of the liver, may resulting from many causes like viral, bacterial, fungal, parasitic organisms, alcohol, drugs, autoimmune diseases, and metabolic diseases.<sup>1</sup> More than 50% of cases of acute hepatitis in the America are presented mainly in the emergency department.<sup>2</sup>

Round about 55% to 85% of patients develop chronic hepatitis C post exposure to hepatitis C virus (HCV). The objective of hepatitis treatment is to eradicate the virus, attain a sustained virologic response (SVR), and intercept disease progression to avoid late complications.<sup>3</sup>

Treatment of hepatitis with interferon based regimens are no longer recommended; as oral, direct acting antiviral agents are now recommended as the first line treatment. Complications of HCV in long-term comprise of cirrhosis and hepatocellular carcinoma (HCC).<sup>4,5</sup>

Most patients are asymptomatic during initial exposure to the HCV.<sup>6</sup> Approximately 30% of individuals present with features like fatigue, arthralgia, or jaundice, associated with a transient increase in serum amino-transferases, especially alanine amino-transferase,<sup>7</sup> but fulminant hepatic failure is a rare occurrence.<sup>8</sup> A spontaneous eradication of hepatitis C virus infection happens in 15%-30% of patients, while in the residual percentage the infection becomes chronic.<sup>9, 10</sup> Nevertheless, another study reported that after acute infection, up to 45% of young healthy individuals may produce a vigorous antibodies and cellular mediated immune responses, which results in the spontaneous eradication of the viral agent.<sup>11</sup>

Hoofnagle reported that extra-hepatic presentation may result in a poor health related quality of life. The symptoms of these comprise of fatigue, anorexia, muscles aches, joint pain, irritation, and headaches.<sup>7</sup> Fatigue is possibly the most common and disabling

Jinnah Medical College, Peshawar

Correspondence: Dr. Marifat Shah, Assistant Professor,  
Jinnah Medical College, Peshawar.  
Contact No: 0346-9041984  
Email: marifats@hotmail.com

Received: January, 2019  
Accepted: March, 2019  
Printed: May, 2019

extra-hepatic symptom of hepatitis C, found in almost 50% of the affected patients. Shakil et al.<sup>12</sup> reported that fatigue was found in about 61% of US blood donors who were affected by HCV. In another study on 239 participants with various causes of liver disease (including HCV) were examined in an outpatient setting, 70% had some form of musculoskeletal pain, and 54% had fatigue.<sup>13</sup>

## MATERIALS AND METHODS

This cross sectional descriptive study was carried out at Jinnah Teaching Hospital attached to the Jinnah Medical College, Peshawar, from October, 2017 to December, 2018 on 100 consecutive patients. Sampling was done using convenient sampling technique. Approval was taken from ethical review committee of the hospital. After detailed explanation to the participants regarding the purpose of the study a verbal informed consent was taken.

A detail history was taken followed by relevant examination. All participants were diagnosed for hepatitis C by history, examination and appropriate laboratory investigations. The participants were diagnosed for hepatitis C by suggesting Anti-HCV antibody through immune chromatographic technique (ICT) followed by confirmation with Enzyme-linked immune sorbent assay (ELISA) and qualitative Polymerase chain reaction (PCR). Abdominal ultrasound was also advised for each patient to look for the presence of Ascites and any parenchymal liver disease or focal mass lesion e.g. hepatocellular carcinoma. Patient's name, age, sex, marital status, addresses (rural and urban) and clinical presentations were recorded in pre-structured proforma. Pakistani nationals, both genders, age above 15 years and cooperative patients were included in this study.

The collected data were analyzed using SPSS version 20.0. Mean and standard deviation were calculated for quantitative variables like age. Frequency and percentages were computed for qualitative variables like sex, marital status, address (rural and urban) and clinical presentations of Hepatitis C. Comparison were made for clinical presentations of Hepatitis C between rural and urban areas using chi-square test. P-value less than or equal to 0.05 ( $\leq 0.05$ ) was considered significant.

## RESULTS

The total participants were hundred (100), in which male were n=40(40%) and female were n=60(60%). The mean age was  $41.78 \pm 14.19$  years. The age ranged from 17 to 75 years. Most of the participants were married n=95(95%). Half of the sample belong to urban n=50(50%) and half to rural areas n=50(50%). The most common age group was 31-45 years n=31(31%) followed by 46-60 years n=29(29%) and 15-30 years

n=28(28%). The least number of participants were in age group 61-75 years n=12(12%). The details of frequency of age groups, gender, marital status and rural/urban are given in table 1.

**Table No.1: Frequency of age groups, genders, marital status and rural/urban area**

Variable		Frequency	Percent
Age group	15-30	28	28.0
	31-45	31	31.0
	46-60	29	29.0
	61-75	12	12.0
	Total	100	100.0
Gender	Male	40	40
	Female	60	60
	Total	100	100
Marital status	Married	95	95
	Unmarried	5	5
	Total	100	100
Urban/Rural	Urban	50	50
	Rural	50	50
	Total	100	100

**Table No.2: Frequency of clinical presentations of Hepatitis C**

Clinical presentations of Hepatitis C	Frequency	Percent
GBA	45	45
GBA, Routine screening	3	3
Routine screening(asymptomatic)	9	9
Lethargy, GBA	3	3
Maliase, Burning sensation	1	1
GBA, Arthralgia	2	2
Maliase	1	1
Arathalgia, Malaise	1	1
GBA, Ascites	1	1
Acute Hepatic (Jaundice)	5	5
Feverish, Malaise	1	1
GBA, pain RHC	2	2
Feverish , Legs aches	4	4
Arthralgia	7	7
Ascites	5	5
A/N screen	6	6
Lethargy, Burning sensation	1	1
Lethargy, Malaise	3	3
Total	100	100

\*GBA, generalized body aches; A/N, antenatal; RHC, right hypochondrium

The clinical presentation of hepatitis C were generalized body aches, jaundice, lethargy, fever, arthralgia, Ascites, and malaise etc. The most common presentation of hepatitis C in our sample was

generalized body aches n=45(45%). Of total the n=7(7%) cases reported arthralgia. Jaundice was found in 5% participants. Lethargy was found in n=7(7%) cases. Five (5%) cases presented with ascites. Malaise was reported by 7 (7%) cases. Nine (9%) cases in this study were asymptomatic and were found during routine screening for different tasks (preoperative, blood donation, going abroad etc). The six (6%) antenatal(A/N) cases were also found during the routine A/N screening (seemingly asymptomatic). Rests of details are given in table 2.

Comparison of clinical presentation of Hepatitis C between urban and rural areas showed that the difference between the two were not statistically significant ( $P=0.468$ ). The details are given in table 3.

**Table 3: Comparison of clinical presentation of Hepatitis C between urban and rural areas**

Clinical presentation of Hepatitis C	Address				P-value*
	Urban		Rural		
	n	%	n	%	
GBA	21	21	24	24	0.468
GBA, Routine screening	1	1	2	2	
Routine screening	6	6	3	3	
Leg aches	0	0	0	0	
Lethargy, GBA	2	2	1	1	
Maliase, Burning sensation	0	0	1	1	
GBA, Arthralgia	2	2	0	0	
Malaise	1	1	0	0	
Arathalgia, Malaise	1	1	0	0	
GBA, Ascites	1	1	0	0	
Acute Hepatic (Jaundice)	3	3	2	2	
Feverish, Maliase	0	0	1	1	
GBA, pain RHC	0	0	2	2	
Feverish , Legs aches	2	2	2	2	
Arthralgia	3	3	4	4	
Ascites	4	4	1	1	
A/N screen	3	3	3	3	
Lethargy ,Burning sensation	0	0	1	1	
Lethargy, Malaise	0	0	3	3	

\*Pearson Chi-Square Test

## DISCUSSION

In study we determined the clinical features/manifestations of hepatitis C in our population. Due to environmental and genetic variations the manifestations

of hepatitis C may be variable in various populations. Hepatitis C virus is inconsistent because of the features of the viral RdRp (RNA-dependent RNA polymerase), increase rate of replication, and large population samples. The characteristics of Darwinian evolution of HCV are the appearance of the HCV genotypes, including six main variants and a large number of subtypes.<sup>14</sup>

Our findings showed that the clinical presentation of hepatitis C were generalized body aches, jaundice, lethargy, fever, arthralgia, ascites, and malaise etc. Fatigue is a complex symptom that includes a variety of complaints encompassing malaise, lethargy, lassitude and tiredness. The fatigue comprises the most common complaint among the hepatitis patients.<sup>15</sup> The incidence of fatigue in hepatic pathologies is less clearly defined. Fatigue is usually an integral part of the clinical features of individuals affected by autoimmune hepatitis, frequently paralleling liver inflammation as detected by serum alanine aminotransferase quantification or liver biopsy findings, and response is frequently fairly quick to the immunosuppressive therapy.<sup>16,17</sup> In viral hepatitis the acute presentations are often associated with feelings of fatigue or malaise, which slowly subsides as the patient recovers clinically (e.g. from hepatitis A). Though, the scenario in patients with chronic viral hepatitis appears to be more debatable. Specially, a significant frequency of patients with chronic hepatitis C who are followed in tertiary care centers, or who are used as a participant in clinical trials, complain of fatigue or decreased vitality, which has a direct negative impact on their health related quality of life.<sup>18</sup>

Our findings showed that the most common presentation of hepatitis C in our sample was generalized body aches. A study Barkhuizen et al.<sup>13</sup> on 239 participants with various causes of liver disease (including HCV) were examined in an outpatient setting, 70% had some form of musculoskeletal pain, and 54% had fatigue. These results are similar to our findings.

In the present study the comparison of clinical presentation of Hepatitis C between urban and rural showed the difference between the two areas were not statistically significant ( $P=0.468$ ). This showed the main role in clinical presentation of Hepatitis C is genetic and environment has fewer roles. No such study has been traced in literature on comparison of clinical presentation of Hepatitis C between urban and rural areas.

However, this study is cross sectional design and small sample study; so more studies of randomized clinical trial design are required to further explore this area.

## CONCLUSION

- The clinical presentations of hepatitis C were generalized body aches, jaundice, lethargy, fever, arthralgia, ascites, and malaise
- The most common presentation of hepatitis C in our sample was generalized body aches
- The difference in clinical presentations of hepatitis C between urban and rural areas were not statistically significant ( $P>0.05$ ).

**Author's Contribution:**

Concept & Design of Study: Marifat Shah  
Drafting: Marifat Shah  
Data Analysis: Marifat Shah  
Revisiting Critically: Marifat Shah  
Final Approval of version: Marifat Shah

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

**REFERENCES**

1. Grewal US, Walia G, Bakshi R, Chopra S. Hepatitis B and C Viruses, their coinfection and correlations in chronic liver disease patients: A tertiary care hospital study. *Int J Appl Basic Med Res* 2018;8(4):204-9.
2. Poynard T, Cacoub P, Ratzu V, Myers R, Dezaillies M, Mercadier A, et al. Fatigue in patients with chronic hepatitis C. *J Viral Hepat.* 2002; 9(4):295-303.
3. Yoon EL, Sinn DH, Lee HW, Kim JH. Current status and strategies for the control of viral hepatitis A in Korea. *Clin Molecul Hepatol.* 2017; 23(3):196-202.
4. Jawad A. Hepatitis C. *BMJ* 2017;358: j2861(<https://doi.org/10.1136/bmj.j2861>).
5. Terrault NA. Care of Patients Following Cure of Hepatitis C Virus Infection. *Gastroenterol Hepatol* 2018;14(11):629-34.
6. Villano SA, Vlahov D, Nelson KE, Cohn S, Thomas DL. Persistence of viremia and the importance of long-term follow-up after acute hepatitis C infection. *Hepatol* 1999;29(3):908-14.
7. Hoofnagle JH. Hepatitis C: the clinical spectrum of disease. *Hepatol* 1997;26(S3):15S-20S.
8. Kodali S, McGuire BM. Diagnosis and management of hepatic encephalopathy in fulminant hepatic failure. *Clin Liver Dis* 2015;19(3):565-76.
9. Deutsch M, Papadopoulos N, Hadziyannis ES, Koskinas J. Clinical characteristics, spontaneous clearance and treatment outcome of acute hepatitis C: a single tertiary center experience. *Saudi J Gastroenterol* 2013;19(2):81-9.
10. Wang CC, Krantz E, Klarquist J, Krows M, McBride L, Scott EP, et al. Acute hepatitis C in a contemporary US cohort: modes of acquisition and factors influencing viral clearance. *J Infect Dis* 2007;196(10):1474-82.
11. Gerlach JT, Diepolder HM, Zachoval R, Gruener NH, Jung M-C, Ulsenheimer A, et al. Acute hepatitis C: high rate of both spontaneous and treatment-induced viral clearance. *Gastroenterol* 2003;125(1):80-8.
12. Shakil AO, Conry-Cantilena C, Alter HJ, Hayashi P, Kleiner DE, Tedeschi V, et al. Volunteer blood donors with antibody to hepatitis C virus: clinical, biochemical, virologic, and histologic features. *Ann Int Med* 1995;123(5):330-7.
13. Barkhuizen A, Rosen HR, Wolf S, Flora K, Benner K, Bennett RM. Musculoskeletal pain and fatigue are associated with chronic hepatitis C. *Ame J Gastroenterol* 1999;94(5):1355.
14. Pawlotsky J-M. Hepatitis C virus genetic variability: pathogenic and clinical implications. *Clin Liv Dis* 2003;7(1):45-66.
15. Swain MG. Fatigue in liver disease: pathophysiology and clinical management. *Canad J Gastroent Hepatol* 2006;20(3):181-8.
16. Ferrari R, Pappas G, Agostinelli D, Muratori P, Muratori L, Lenzi M, et al. Type 1 autoimmune hepatitis: patterns of clinical presentation and differential diagnosis of the 'acute' type. *J Hepatol* 2004;97(7):407-12.
17. Czaja AJ, Freese DK. Diagnosis and treatment of autoimmune hepatitis. *Hepatol.* 2002;36(2):479-97.
18. Kenny-Walsh E. Clinical outcomes after hepatitis C infection from contaminated anti-D immune globulin. *New Engl J Med* 1999;340(16):1228-33.

