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Editorial

Original Articles

PUBLICATION OFFICE:
Department of Community Medicine, Allama Iqbal Medical College / Jinnah Hospital, Allama Shabbir Ahmad Usmani Road Lahore (Pakistan).
Ph +92-42-99231453
Email: journalaimc@gmail.com
drelmo@hotmail.com

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Hope is a Light in your heart
Photography by Ali Rizvi

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Outstanding Reviewer of Vol. 19, Issue 4 (Oct– December 2021)

Dr. Zunaira Kanwal

MPhil (Biochemistry), PhD Scholar
Associate Professor Biochemistry

Dr. Zunaira Kanwal is working as Associate Professor of Biochemistry in AIMC and has been serving the department for past 7 year. She is also a distinguished graduate of AIMC and had been awarded with several medals including a Gold Medal in Biochemistry. She completed her M Phil in Biochemistry with distinction in every course and was awarded with Gold Medal. As a PhD scholar she is currently working on cancer cells in IMBB at University of Lahore. Her 10 research articles have been published in various PMC recognized journals. She desires to be productive in field of education and research.

Dr. Ameena Nasir

MBBS, M. Phil (Physiology)
Assistant Professor Physiology

Dr. Ameena Nasir is a graduate of Allama Iqbal Medical College (AIMC), Lahore. She completed her postgraduation in subject of Physiology from Federal Postgraduate Medical Institute, Lahore in 2016. Later she did Certificate in Medical Teaching from University of Health Sciences, Lahore in collaboration with University of Liver Pool, England and currently pursuing Certificate in Medical Editing from University of Health Sciences, Lahore. Since 2017, she has been serving her Alma Mater, AIMC as Assistant Professor (Physiology) and associated with Journal of AIMC (JAIMC) as peer reviewer.

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'SPANISH FLU' TO COVID-19 PANDEMIC: HISTORICAL PARALLEL AND 'ONE HEALTH' STRATEGY FOR MITIGATING PANDEMICS IN FUTURE

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'Spanish flu' pandemic in 1918 was the biggest calamity experienced by humans in recent past with more than one-third of global population at that time were infected and with an estimated 50-100 million deaths.1 Beginning from few reports of unusual cases of infection in Madrid during late spring of 1918, movement of First World War soldiers facilitated the spread of this deadly infection to North America, Europe, Asia, New Zealand and even in remote Pacific island of Western Samoa.2 This infection was characterized by uncontrolled fever, cough, myalgia, respiratory failure and most people died from secondary bacterial Pneumonia. Lack of antibiotics to treat pneumonia at that time coupled with fatigued health workforce had devastating impact on health care delivery systems.3 Scenes of patient-flooded hospitals, mass graves, oxygen craving by the individuals and shortage of mortuary spaces are few scary depictions of 'Flu' pandemic of 1918, observed as a flashback in Europe, South America and India in existing SARS-COV2 pandemic, after almost 102 years. H1N1 virus was found to be associated with 'Spanish Flu' and later, there was a wide range of antigenic shift in H1N1, owing to its mixing with strains in birds and other animals, which warranted a 'yearly' version of anti-flu vaccines for prevention.

In late December 2019, number of unusual cases of pneumonia was reported in Wuhan, China. Considering SARS infection occurred in Southeast Asia couple of year, these acute respiratory syndrome cases were called SAR-CoV-2. Now known as Covid-19, these cases were traced back to a central animal market place of Wuhan, China. In a time span of few weeks, these sporadic cases turned into an outbreak. This epidemic has now spread to 210 countries.[4] World health Organization declared Covid-19 a Public Health Emergency of International Concern (PHEIC). Globally, to date, there has been more than 272 million confirmed cases and more than five million deaths.[5] First case of Covid-19 was reported in Pakistan on 26th February 2020, and most cases to date linked to importation of infection from Iran, China, Middle-East and European countries. Loose borders and inadequate screening arrangements at port of entries resulted in spread of cases in all provinces of Pakistan. There has been four waves of infection in Pakistan, with approximately one million confirmed cases and more than 28 thousand deaths.[6]

One of the major etiological factors associated with spread of H1N1 infection in 1918 pandemic was the wartime movement of young soldiers from isolated areas to inter-mingle with other nations in Europe, in muddy and humid conditions, which provide fertile ground for the spread of H1N1. Governments and public around the globe were not in a 'listening mode' to follow public health advice from the experts to adopt quarantine and isolation practices. Conspiracy theories were rampant to explain flu events, calling it 'a great game' by medicinal companies, a biological warfare among nations. Similarly, same parallels were observed during current SARS Cov-2 pandemic.

During 1918 pandemic in USA, 'liberty parades' were organized with huge gathering to raise funds for war victims which helped virus to reach millions in a span of weeks and months.[6] Even, there was a political controversy on naming pandemic as 'Spanish flu'; Spain was found 'guilty' of reporting flu cases, albeit, Great Britain, Germany France through propaganda, suppressed news of epidemics from public, which might have saved thousands of lives. Interestingly, in Spain, this flu was labeled as "French Flu".[7]

There has been significant improvement in public health operations since 1918 pandemic. Countries have developed policies to mitigate

disease transmission through designing organizations such as Centers for Disease Control and Prevention (CDC) and implementing disease intelligence and surveillance systems. This gave a window of opportunity for countries to detect cases early and for adopting control measures to reduce morbidity and mortality. World health Organization provided platform for international cooperation and for coordinated efforts against future pandemics, vaccination drive and reducing disparity in health care delivery. Yet, parallel to 1918 pandemic, similar socio-political environment, such as rapid global transportation, inequitable global health investments, resistance to non-pharmacological interventions, and prevalent conspiracy theories about the disease observed in current SARS-Cov-2 pandemic. We must appreciate international efforts to develop effective vaccine in a record time, but even this good work was undermined by conspiracy theorists (incriminating 5-G technology by Chinese, 'Bill Gates's business interests') and 'anti-vaxxers'. Most recently, an organized campaign against wearing mask and vaccinations was seen in many European countries and United States. This shows a disconnect and distrust between the public and the mangers of public health in communicating risk of spreading infection; still, this may be the expression of 'pandemic fatigue', that was also observed during 1918 pandemic.[8,9]

Risk of an outbreak in a regional part of a country transforming into a trans-national pandemic in future is more than ever before. Globalization of trade, disparity in health investments, rise in international travel, urbanizations, interfering with animal ecology and climate change are the domains which have impacted healthcare and it is essential to adopt a 'holistic' approach to tackle health issues and develop a multi-sectoral strategy to prevent pandemics in coming years.[10] There should mechanisms in place in every country to devise an 'information hub' to share data from veterinarians, agriculturalists, live stocks keepers, virologists, meteorologists, environmentalists, marine biologists, economists and health providers. This data should be regularly analyzed to observe trends and predict unusual events. This data sharing should be strengthened by the presence of 'international data hub' for countries to co-ordinate preventive efforts at global level. One such strategy has already been introduced by WHO, CDC, Food and agricultural Organization (FAO), and United Nations Environment program (UNEP), labeled as, 'One Health' initiative.[11] The tripartite definition describes "One Health is an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals and ecosystems. It recognizes the health of humans, domestic and wild animals, plants, and the wider environment (including ecosystems) are closely linked and inter-dependent. The approach mobilizes multiple sectors, disciplines and communities at varying levels of society to work together to foster well-being and tackle threats to health and ecosystems, while addressing the collective need for clean water, energy and air, safe and nutritious food, taking action on climate changes and contributing to sustainable development".[13] 'One Health' Strategy is not a new idea. Its echo can be heard in writings of Hippocrates (400-300 BCE), who identified interdependence of public health and environment. In modern era, this term was coined in 2003 during emergence of 'Severe Acute Respiratory Syndrome-SARS' and subsequent identification of avian influenza strain called H5N1. This event highlighted the link between human and animal health, with its impact on economy and food shortages. The need for rigorous communication of various sectors and multi-sectorial data sharing was felt. Experts from international agencies deemed necessary the inclusion of wildlife, agriculture and zoonotic ecology in responding to human health emergencies and in devising preventive measures, disease control strategies, and event-based surveillance for mitigating future pandemics. [12,13] At global level, 'One Health Commission' is a body responsible for international co-ordination, interaction and support to its member countries. Pakistan is also signatory of 'One health' and preliminary foundation work is in progress. There

are potential economic and health benefits of adopting this concepts as well as sharing of data would enhance capacity both regionally and at global level to improve the health status of communities. Nevertheless, they may be user related barriers pertaining to its planning, resource allocation, ownership and technological differences. However, with commitment and dedication, 'One Health' will not be a mirage and is achievable.

Pandemic threat in future is real; thanks to constant interference and manipulation with nature by human race in terms of deforestation, use of fossil fuel, occupying animal space in the name of development and avaricious pharmaceutical and healthcare industry. In view of this, there is impending risk of more human interactions with antibiotic resistant bacteria and virulent virus strains, environmental degradation and economic conflicts. This would result in catastrophic situations at global scale affecting most nations, frequency of which may be in decades rather than once in a century event. 'One Health' strategy is a way forward to mitigate potential pandemic emergence in future.

Dr. Shahid Mahmood

Editor-in-Chief

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DIAGNOSTIC ACCURACY OF TRANSVAGINAL ULTRASOUND IN POSTMENOPAUSAL BLEEDING

Azra Hasaif,[1] Safia Parveen,[2] Hina Ilyas,[3] Zareen Amjad,[4] Maimoona Javaid,[5] Muhammad Saleem Akhtar[6]

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Abstract

Objective: To determine the diagnostic accuracy of transvaginal ultrasonography in diagnosing the endometrial pathology in females presenting with postmenopausal bleeding.

Methods: Females underwent transvaginal Ultrasonography and endometrial thickness was measured. Then these patients underwent endometrial biopsy through dilation and curettage (D & C) and sample was sent to hospital pathology laboratory for confirmation of endometrial carcinoma. All this information was recorded on Proforma.

Results: In this study the mean age of all females was 58.42 ± 3.92 years with mean parity among the women was 4.90 ± 1.46. The average endometrial thickness was 6.33 ± 3.67 mm. The sensitivity and specificity of endometrial thickness (≥ 4mm) was 97.63% and 87.65% respectively. The positive, negative predictive value and accuracy of endometrial thickness (≥4mm) was 94.29%, 94.67% and 94.4% respectively.

Conclusion: Transvaginal Ultrasonography is highly sensitive, specific and gave good diagnostic accuracy in our study. Being a non-invasive method for diagnosis of endometrial carcinoma in patients with abnormal uterine bleeding TVS should be used instead of invasive pathological procedure.

Keywords: Transvaginal Sonography, Histopathology, Postmenopausal Bleeding, Endometrial Thickness

Postmenopausal bleeding (PMB) is defined as bleeding that occurs 12 months after the last menstrual period. The average of menopause has remained steady, occurring in 80% of women by age 51 and in 95% of women by age 55, with virtually all women experiencing cessation of menses by age 58.[1] Postmenopausal bleeding is often caused by abnormalities of the endometrium, whether they are benign or malignant, 10% -15% Of patients with post menopausal bleeding have endometrial carcinoma.[2] Vaginal bleeding after menopause is not normal and should be evaluated by doctor.[3] Clinical examination constitutes an abdominal and vaginal examination to detect any pelvic masses and a speculum to visualize the vaginal tissue for atrophy and cervix for polyps. Biopsy is the gold standard, which can be obtained by office endometrial sampling or diagnostic D&C.

Hysteroscopy guided biopsies may be carried out in patients where office endometrial sampling fails, in cervical stenosis, persistent bleeding after negative biopsy or inadequate specimen.[4,5] Endometrial thickness measurement by transvaginal ultrasound having a cut-off of 4.0 mm gave 94.8% sensitivity and 46.7% specificity in females with Postmenopausal bleeding to diagnose endometrial pathology.[6] Moreover the overall sensitivity, specificity, positive and negative predictive values for TVS was found 79%, 82%, 84% and 71%, respectively at 4mm.[7] The rationale of this study is to determine the diagnostic accuracy of transvaginal ultrasonography in diagnosing the endometrial carcinoma in females presenting with postmenopausal bleeding taking histopathology as gold standard. Lite-

1. Azra Hasaif 2. Safia Parveen
3. Hina Ilyas 4. Zareen Amjad
5. Maimoona Javaid 6. Muhammad Saleem Akhtar
1-5. Department of Obstetrics and gynecology SLMC Gynae Unit 1
6. *Department of Radiology, SLMC.*

Correspondence:
Dr. Azra Hasaif, *Senior Registrar Obstetrics and Gynecology SLMC Gynae Unit 1. E mail : azrahasaif@outlook.com*

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rature is evident that TVS gave controversial diagnostic accuracy.[6,7] Through this study we want to confirm that TVS is a reliable toll for diagnosis of cause of PMB or not, so that excessive surgeries can be avoided. The objective of the study was to determine the diagnostic accuracy of transvaginal ultrasonography in diagnosing the endometrial carci-noma in females presenting with postmenopausal bleeding taking histopathology as gold standard.

METHODS

Study design: Cross sectional study.

Setting: Department of Obstetrics & Gynecology, Sahiwal teaching hospital Sahiwal.

Duration of study: One year.

Sample size: Sample size of 250 cases is calculated with an expected percentage of sensitivity as 79% with 11% margin of error, 82% specificity with 5% margin of error 7 taking an expected percentage of endometrial carcinomas as 15%. [6]

Sampling Technique: Non probability purposive sampling.

Sample Selection:

Inclusion Criteria: Patients of age 51-75 years with postmenopausal bleeding on patients clinical history.

Exclusion criteria: Females on HRT or on Temoxifin

Data Collection Procedure: 250 females who fulfill the selection criteria was enrolled in the study from OPD of Sahiwal teaching hospital Sahiwal. Informed consent was taken from each patient describing them objective of this study and fact that there is no risk involved to the patient while taking part in this study. Demographic details (name, age, parity, duration of menopause) of patients were noted. All females were undergoing transvaginal Ultrasonography and endo-metrial thickness was measured. Endometrial carci-noma was labeled as positive when using endometrial thickness measurements ≥ 4mm TVS. Then these patients underwent endometrial biopsy through D & C and sample was sent to hospital pathology laboratory for confirmation of endometrial carcinoma. All this information was recorded on Proforma.

Data Analysis: Data was entered and analyzed using computer program SPSS-16. 2×2 tables was generated to calculate sensitivity, specificity, PPV, NPV and diagnostic accuracy of TVS in diagnosing endometrial carcinoma, taking histopathology as gold standard.

RESULTS

In this study the mean age of all females was 58.42 ± 3.92 years. The mean duration of menopause 6.97 ± 2.39 with range of 20 years. The mean duration of postmenopausal bleeding was 4.98 ± 2.14 years. The average endometrial thickness was 6.33 ± 3.67 mm. Table 1

The sensitivity and specificity of endometrial thick-ness (≥4mm) was 97.63% and 87.65% respectively. The positive, negative predictive value and accuracy of endometrial thickness (≥4mm) was 94.29%, 94.67 % and 94.4% respectively. Table 2

DISCUSSION

Menopause is a permanent cessation of mens-truation because of loss of ovarian follicular activity. Natural menopause is said to have occurred after 12 consecutive months of amenorrhoea for which there is no other obvious pathological or physiological cause. Postmenopausal bleeding (PMB), defined as blood loss occurring at least 12 months after menopause, is a common complaint in general gynecological practice. The prevalence of PMB is approximately 10% imme-diately after menopause.[8] Endometrial carcinoma is the most common gyneacologic malignancy and 95% of women with endometrial carcinoma present with PMB.[9]

Main causes include fibroids, polyps, endometrial hyperplasia, carcinoma of endometrium or endocervix, and atrophic vaginitis. Anything that can significantly improve the accuracy of diagnosing the cause of blee-

Table 1: Descriptive Statistics of Age in Years

n	250
Age(years)	58.42±3.92
Duration of Menopause (years)	6.97±3.29
Duration of Post-Menopausal bleeding (years)	4.98±2.14
Endometrial Thickness on TVS (mm)	6.33±3.67

Table 2: Accuracy of TVS Against Histopathology Findings

		Histopathology findings		Total
		Malignant	Benign	
Endometrial Thickness	Malignant	165	10	175
	Benign	4	71	75
Total		169	81	250

Sensitivity	97.63%
Specificity	87.65%
Positive Predictive Value	94.29%
Negative Predictive Value	94.67%
Diagnostic Accuracy	94.4%

ding can reduce the frequency of hysterectomy as a cure.[10,11] Traditionally dilatation and curettage (D and C) used to be the mainstay of investigation for abnormal uterine bleeding but it is not accurate for diagnosing focal intrauterine lesions which are small or located in areas difficult to curette.[11]

The mean age of the patients was 49.5±12.9 years (range, 24-89 years).12 In this study the mean age was 58.42 ± 3.92 years with minimum and maximum ages 53 and 75 years. The age range was 22 years and the most common age was 60 years which is comparable to the above study.

A thorough evaluation of the uterine cavity is frequently required in gyneacology practice.[12] During the last decades, several methods including transvaginal ultrasonography (TVU), saline infusion sonography, and hysteroscopy, have been developed to assess uterine cavity, with their own advantages and disadvantages. Although TVU is a simple examination allowing clear visualization of most uterine conditions[13], several concerns have been raised regarding its accuracy.[14-16] Hysteroscopy on the other hand, allows direct visualization and sampling of the uterine cavity and has an established diagnostic value for many uterine conditions.[17] However, the latter modality is not as cost-effective and convenient as ultrasonographic imaging modalities, which are associated with relatively less patient discomfort and do not necessitate anesthesia. Thus, currently available modalities are far from being perfect.[18]

Ultrasonographic examination findings were considered normal if a hyperechoic line was observed in the middle of the uterus along with a homogeneous endometrial lining and distinct margin with the myometrium. In premenopausal patients, normal limits of anteroposterior diameter of the endometrium was defined as 4-8 mm in proliferative phase, 8-14 mm in the secretory phase and 6-10 mm in the periovulatory phase. An increase above these limits or presence of heterogeneous echogenicity was considered abnormal.[19]

In postmenopausal patients, a normal endometrium was defined as having a double-wall thickness <5 mm consisting of a thin basal layer. Abnormalities were defined as follows: endometrial polyp, uterine myoma, atrophy, and placental residual material. In addition, a non-specific increase in endometrial echogenicity or presence of fluid in the endometrial cavity is classified as non-specific abnormal finding.[19]

A lot of studies are available with different cut point for endometrial thickness. Among women with postmenopausal uterine bleeding and cancer, 96% will have an abnormal ET (>6 mm). The specificity varies by whether women used hormone therapy. Among nonusers, the specificity was 92%.20 Much less work has been done to evaluate the accuracy of TVU among asymptomatic women. If the same endometrial thickness cutoff is used among asymptomatic women, the false positives will be extremely high, resulting in a very low positive predictive value.[21]

A group of researchers used dilation and curettage (D&C) as a gold standard, to evaluate TVU measurement of ET as a predictor of endometrial cancer in women reporting postmenopausal bleeding (estrogen-progestin therapy [hormone therapy] and nonhormone therapy users). Of the 339 participants, 39(11.5%) were diagnosed with endometrial cancer (four had an ET of 5–7 mm and 35 had an ET > 8 mm) based on histopathology from curettage. No cancers were detected in women with an ET of less than 4 mm. Using a cutoff point of 4 mm, TVU has 100% sensitivity and 60% specificity.[22]

One more study was conducted to see the sensitivity of TVS and other modalities, they found overall

sensitivity and specificity of TVS was 94.1% and 84.8% for TVS.[23] Another study showed sensitivity and Specificity of TVS was 49.7%, and 55.6% respectively and positive predictive value of 63.7% at a cut-off limit of 4 mm.[24] The overall sensitivity, specificity, positive and negative predictive values for TVS in the diagnosis of uterine abnormality was 82%, 68.4%, 84.1%, 65.1% and 77.5%, respectively.[25]

In present study we also found the sensitivity and specificity of endometrial thickness (≥ 4mm) was 97.63% and 87.65% respectively. The positive, negative predictive value and accuracy of endometrial thickness (≥ 4mm) was 94.29%, 94.67% and 94.4% respectively. This study gave better results as compared to to the above cited study. [23-25]

Lastly, transvaginal Ultrasonography is a safe, available and inexpensive method with multiple capacities such as 3D, 4D, Doppler studies and saline infusion (sonohysterography) which can properly diagnose uterine pathologies before hysteroscopy and histopathology. Previous studies have mostly shown that TVS is less invasive than hysteroscopy and in some circumstances may obviate diagnostic hysteroscopy.

CONCLUSION

Transvaginal Ultrasonography is high sensitive, specific and gave good diagnostic accuracy in our study. Being a non-invasive method for diagnosis of endometrial carcinoma in patients with abnormal uterine bleeding should be used instead of invasive pathological procedure. Hence TVS to reduce financial burden of hospital and the patient, improve our practice and to achieve more patients' satisfaction.

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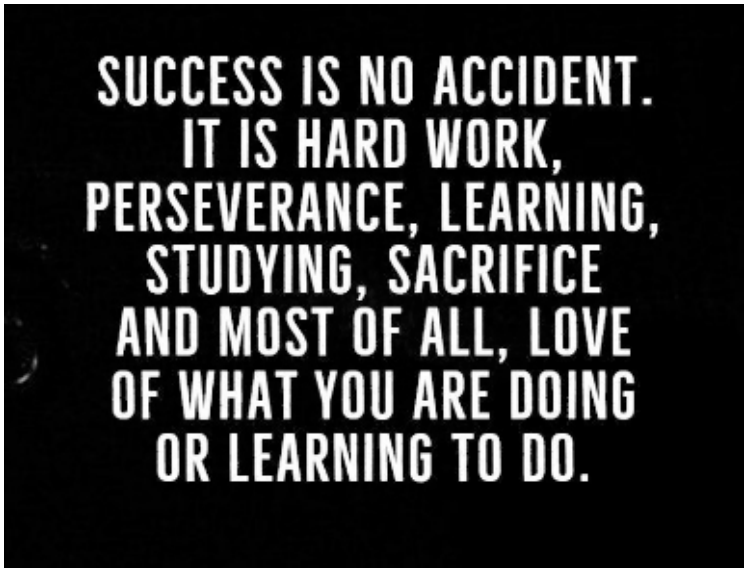

EXPERIENCE OF VARIETY OF INFECTIVE MANIFESTATIONS IN DIABETIC PATIENTS AT SURGICAL FLOOR

Mahboob Alam Chishti,[1] H M Amjad,[2] Abid Hussain,[3] Kamran Cheema,[4] Akmal Shafiq,[5] Muhammad Kareem Ullah,[6] Saeed Mahmood[7]

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Abstract

Background: Diabetes mellitus is a silent killer & its presence in the body is responsible for a lot of manifestations for which patients present in different departments in the hospitals. There is a wide range of infective manifestations for which patients present in surgical outpatients&surgical emergencies as well.

Objectives: This retrospective study was performed to analyze the wide spectrum of infective manifestations in diabetic patients for which they present at surgical floor. This spectrum was observed both, in frank or incidentally diagnosed diabetic patients.

Methods: The study was multicentric & performed at Lahore Medical & Dental College, Lahore from January 2016 to July 2017and Avicenna Medical &Dental College, Lahore from August 2017 to December 2019. All patients presenting in surgical outpatient and surgical emergency were included in the study randomly. The total number of patients were 1000. The whole spectrum of disease manifestations was observed in these patients. This study included frank diabetics as well as incidentally diagnosed diabetic patients.

Results: The spectrum of surgical manifestations included every& any kind of infection in any of the human body organs which can be thought.

Conclusion: Diabetes mellitus is the culprit for causing a wide spectrum of surgical infections in patients being admitted at surgical floor. Oftenly these patients turn out to be borderline or frank diabetics when investigated for their diseases.

Key Words: Surgical Infections, Diabetes Mellitus, Borderline

Deficiency of insulin secretion oraction is responsible for diabetes mellitus (DM) which is a clinical syndrome. In the 21st century, it is considered one of the largest emerging threats to health. Up to 2025, it is estimated that 380 million persons will be effected with DM.[1] Besides the classical complications of the disease, DM has been associated with reduced response of T cells, neutrophil function, and disorders of humoral immunity.[2–4] Consequently, DM increases the susceptibility to infections[4] Such infections, in addition to the repercussions associated with its infectivity, may trigger DM complications such as hypoglycaemia and ketoacidosis.

The main pathogenic mechanisms are: hyperglycaemic environment increasing the virulence of some pathogens; lower production of interleukins in response to infection; reduced chemotaxis and phagocytic activity, immobilization of polymorphonuclear leukocytes; glycosuria, gastrointestinal and urinary dysmotility. Some infections almost always affect only diabetic persons, such as malignant external otitis, rhino cerebral mucormycosis, and gangrenous cholecystitis. In addition to being potentially more serious, infectious diseases in DM may result in metabolic complications such as hypoglycaemia, ketoacidosis, and coma. The

1. Mahboob Alam Chishti
2. H M Amjad
3. Abid Hussain
4. Kamran Cheema
5. Akmal Shafiq
6. Muhammad Kareem Ullah
7. Saeed Mahmood

1. Department of Surgery Avicenna Medical College
2. Department of Surgery Sahiwal Medical College
3-6. Department of Cardiac Surgery Social Security Hospital Lahore
7. Department of Surgery Lahore General Hospital Lahore

Correspondence:
Dr. Mahboob Alam Chishti, *Assistant Professor, Department of Surgery, Avicenna Medical & Dental College, Lahore, Pakistan.*
Email: drmahboobalamchishti@gmail.com

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recommendation of compulsory immunization with anti-pneumococcal and influenza vaccines is essential because of their impact on the reduction of respiratory infections, the number and length of hospitalizations and the number of deaths related to respiratory tract diseases.

More research is needed for clarification of the immunopathogenic mechanisms linking DM and infections and to develop strategies to improve vaccination coverage for diabetic patients.

This article aims to critically review the current knowledge on the mechanisms associated with the greater susceptibility of DM for developing infectious diseases and to describe the main infectious diseases associated with this metabolic disorder in patients with surgical problems.

METHODS

This study was performed at Lahore Medical & Dental College, Lahore from January 2016 to July 2017 and Avicenna Medical & Dental College, Lahore from August 2017 to December 2019. ll patients presenting in outpatient and accident & emergency were included in the study randomly. The wide spectrum of surgical infections was observed. The study included the patients with diagnosed as well as incidentally diagnosed diabetes mellitus.

RESULTS

One thousand patients were included in study. The results included multiple types of infective manifestations with which patients presented at surgical floor.

DISCUSSION

According to some writers, risk factors for complicationsin diabetic patients develop from frequent medical visits which increase the probability of being diagnosed with other diseases. However, this leads to clinical evidence of higher prevalence of infectious diseases among these individuals.[2,3,10]

Major infections associated with diabetes mellitus are respiratory, responsible for a significant number of medical appointments as compared to non-diabetic patients.[4,11–16]

Table 1:

Types of manifestations		Number of patients
Skin & subcutaneous infections		500
Surgical site infections	140	
Boil	50	
Carbuncle	110	
Infected sebaceous cyst	70	
Fournier's gangrene	80	
Meleney's gangrene	50	
Abscesses		300
Intra-abdominal	180	
Post-operative	110	
Visceral	70	
Liver abscess	20	
Renal abscess	05	
Splenic abscess	15	
Pelvic abscess	25	
Appendicular	10	
Perianal	70	
Anterior abdominal wall	45	
Parotid gland	03	
Submandibular gland	02	
Acute cholecystitis		40
Acute pancreatitis		30
Colitis		30
Acute diverticulitis		25
Appendicitis		20
Pelvic inflammatory disease		20
Urinary tract infections		35
LUTI	25	
UUTI (Acute pyelonephritis)	10	

Streptococcus pneumoniae and influenza virus causing respiratory infections are in strong association with DM.[9,15] During influenza epidemics, diabetics areat six times more risk & need hospitalization.[4] Diabetes is also a common coexisting condition and a risk factor for complications in patients with pandemic influenza virus infection.[17-20]

Higher risk of tuberculosis has been observed in individuals with DM[21,22] Nine million new tuberculosis cases were diagnosed in 2009 and 1.7 million persons died from this infection.[21] Multi-resistant tuberculosis, treatment failures and death are more common in these patients.[23] Tuberculosis infection and treatment may complicate the glycaemic control.[24]

Diabeticsare more prone to develop urinary tract infections and complications.[25–27] Inadequate glycaemic control, duration of DM, diabetic microangiopathy,

impaired leukocyte function, recurrent vaginitisand anatomical & functional abnormalities of the urinary tract are responsible for it .[4,25–29]

Asymptomatic bacteriuriahas greater prevalence in diabetic women[25,27–30] Progression to pyelonephritis has been observed by some researchers[28,30] whereas other suggested no serious complications.[11,25,31]

DM has 4–5 times more tendency to develop acute pyelonephritis.[26] Escherichia coli or Proteus sp cause the clinical presentation with bilateral renal involvement which can cause perinephric and renal abscesses, emphysematous pyelonephritis (EP) and renal papillary necrosis.[4,9,32]

Presence of gas in the collecting system or perinephric tissues with necrosis of the renal parenchyma is characteristic of emphysematous pyelonephritis.[30–36] Diabetic women most commonly suffer from it.[16,25,32–36] Abdominal computerized tomography allows the identification of gas in the urinary tract.[9,16,32,33,37,38–40]

Candida is more common for fungal infections in DM[28,41] "Fungal balls" can cause urinary tract obstruction when formed after these infections.[28]

Diabetics also develop emphysematous cystitis more frequently than non-diabetics.[26,40,42,43] Carbon dioxide gas in bladder cavity and wall is pathoganomic for it.[44] E. coli followed by Enterobacter, Proteus, Klebsiella, and Candidaare causative organisms[32] Men are less affected than women.[26,40,44] CT scan is the standard diagnostic tool.[42]

Renal and perinephric abscesses are enteric gram-negative bacilli or polymicrobial infections.[45–47] Around one-third of perinephric abscesses occur in persons with DM.[16,46,47] In case of perirenal suppuration, the overlying skin may show inflammatory reaction.[48]

Gastrointestinal infectious are common in patients with chronic hyperglycaemia[32,49] Some studies show that H. pylori is related to macroangiopathy, neuropathy, and microalbuminuria in diabetic patients with gastritis[53] The H. pylori eradication rate is lower in persons with DM and re-infection rates are higher.[50,51,54,55]

The emphysematous cholecystitis is more frequent in males with DM.[32] Salmonellaenteritidis and Campylobacterare the main pathogens.[32] The clinical presentation is same like non-complicated cholecystitis as right upper quadrant abdominal pain, vomiting and fever.[9] Peritonitis has not been observed. On abdominal palpationcrackles are associated with a worse prognosis.[9] Radiograph or CT scan can detect gas inside the gall bladder which is pathoganomic.[32]

Worldwide more than 170 million people are affected by hepatitis C virus (HCV) and lack of vaccination is the reason for its continuous rise.[56] Chronic infection occurs in approximately 50–80% of the patients which has greater chance to develop liver cirrhosis.

Patients with type 2 diabetes mellites (T2DM) develop HCV infection in 13-33% patients according to several studies from different countries.[57] It can becompared to non-HCV control population which has 4-10% prevalence.[58] The data also suggests that HCV patients are 3 times more prone to develop DM than HCV negative population. Therefore, T2DM is considered an extrahepatic manifestation of HCV infection.[57] HCV positive patients with T2DM develop more severe and rapid liver cirrhosis as compared to non-diabetic patients with HCV infection.[59,60]

About 350 million people are affected with HBV infection worldwide.[60] Relationship of HBV and T2DM is not consistent and only blood glucose abnormalities are reported.[61,62]

An independent association between HBV infection and gestational diabetes has been reported by Lao et al[63] During fingerprint blood glucose monitoring, diabetic patients who shareglucometer without cleaning, can cause high risk of HBV transmission.[64]

In genetically predisposed individuals, coxsackie B4 and B3 can cause development of T1DM.[6] Various mechanisms can explain the role of enterovirus in the pathogenesis of T1DM:[65,66]

Skin and soft tissue infections such as folliculitis, furunculosis, and subcutaneous abscesses are very frequent in diabetic patients. During the disease process or for the first time, these infections may occur[67,68] and can be more severe as well.[4,32,67]

Most common chronic complications of diabetes mellitus are foot infections. They lead patients to hospitalization due to soft tissue infections and osteomyelitis which can result inamputations and death even.[4,9,67,69,70]

The clinical signs in these patients change frequently, often leading to delayed diagnosis.[71] They are divided into moderate or "non-limb threatening" and serious or "limb-threatening" infections.[32,70,72]

Necrotizing fasciitis is characterized by rapid and progressive necrosis of the fascia and subcutaneous tissue, causing microvascular thrombosis, fulminant local tissue destruction and systemic signs of toxicity. Mortality occurs in approximately 40% of the cases.[9,73]

The initial symptoms are fever and intense local pain, followed by areas of skin necrosis with small ulcers that drain a colourless fluid and have unpleasant smell.[16,32] Radiographs can detect the air in the soft tissues.[32]The most affected sites are thorax, abdominal wall, extremities, perineum and groin.[74–76]

Fournier gangrene is a fasciitis that affects the male genitalia. The most common etiologic agents are E. coli, Klebsiella sp., Proteus sp., and Peptostreptococcus.[77,78] The etiology can also be polymicrobial, involving Clostridium, aerobic or anaerobic streptococci and Bacteroides.[32,78]

Invasive external otitis is an infection of the external auditory canal that can extend to the skull base and adjacent regions.[9,16,79] It often affects elderly diabetic individuals and the etiologic agent is usually Pseudomonas aeruginosa.[16,79]

Mucormycosis is a rare opportunistic and invasive infection caused by fungi of the class Zygomycetes.[80,81] The genus most commonly associated with human infections is the Rhizopus, followed by Mucor and Cunninghamella.[82]

This infection occurs in approximately 50% of the cases in individuals with DM due to the greater availability of glucose to the pathogen that causes mucormycosis, the decrease in serum inhibitory activity against the Rhizopus in lower pH, and the increased expression of some host receptors that mediate the invasion and damage to human epithelial cells by Rhizopus.[32,79,83]

Periodontitis is a chronic inflammatory disease characterized by the formation of a periodontal pocket, loss of connective tissue, and alveolar bone resorption, which may sometimes result in tooth loss. It is four times more common in persons with DM and is considered the sixth most common complication of DM.[4,84,85] Periodontitis starts or disseminates insulin resistance, thus worsening glycemic control.[4,16,84–86] Inversely, persistent poor glycemic control has been associated with a greater incidence and progression of gingivitis and periodontitis, producing a vicious circle.[4,85,86]

Approximately 33 million people were infected by the human immunodeficiency virus (HIV) in 2007.[87] The improvements in diagnosis and treatment have translated into an increasing number of patients developing chronic complications including DM.

The increased risk of developing diabetes is related to the HIV itself or its treatment.[88] Insulin resistance is the main mechanism implicated in the pathogenesis of diabetes in HIV patients.[87] Insulin resistance results from high levels of inflammatory cytokines that impair glucose tolerance, leading to the development of T2DM. More recently, some patients were reported to develop autoimmune T1DM after immune restoration during highly active antiretroviral therapy (HAART).[89]

T1DM has been associated with other viral infections including rubella, mumps, Epstein–Barr and cytomegalovirus. The viral infection usually precedes the clinical presentation of T1DM. The causality between enterovirus infections and the diabetogenic process are still unclear.[90]

CONCLUSION

Diabetes mellitus is a syndrome responsible for causing a wide spectrum of surgical infections in patients admitted at surgical floor. These patients are frank diabetics or recently diagnosed diabetics when being investigated for their diseases. Sometimes certain medical infective manifestations also coexist in surgical patients.

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FREQUENCY OF POSTPARTUM HAEMORRHAGE AFTER DELIVERY IN FEMALES PRESENTING WITH HEPATITIS C VIRUS

Anikah Kanwal,[1] Shazia Khalid Khan,[2] Uzma Altaf,[3] Alia Zainab,[4] Uzma Aziz,[5] Farhat Naz[6]

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Abstract

Background: Hepatitis C virus (HCV) causes an infectious disease Hepatitis C, which primarily affects liver. Its prevalence in pregnant women is projected to be between 1 and 8%, worldwide. Individuals with HCV infection have an enhanced risk for haemorrhage due to effects of HCV on coagulation profile and platelets. In pregnancy-associated with HCV infection, multidisciplinary management is required due to potential risk of bleeding complications.

Objective: To assess the frequency of postpartum hemorrhage after delivery in females presenting with hepatitis C virus.

Methods: This study involved 250 HCV positive pregnant women of any parity aged between 20-40 years presenting after ≥ 37 completed weeks of gestation for delivery. Outcome variable was frequency of postpartum hemorrhage. Every patient was asked to give a written informed consent.

Results: The gestational age ranged from 37 weeks to 42 weeks with a mean of 38.62±1.58 weeks. The parity of the patients ranged from 1 to 5 with 32.0% primiparas, 28.0% multiparas (≤3) and 40.0% grand multiparas (≥ 4). 189 (75.6%) patients developed postpartum hemorrhage. No statistically significant difference was observed in the frequency of postpartum hemorrhage across age (p=0.994), gestational age (p=0.773) and parity (p=0.981) groups.

Conclusion: The postpartum hemorrhage frequency was found to be 75.6% amongst HCV positive pregnant women.

Key Words: HCV Positive Pregnancy, Postpartum Hemorrhage, Hepatitis C in Pregnancy

Hepatitis C virus (HCV) causes an infectious disease Hepatitis C, which affects liver primarily.[1] All over the world amongst adults, chronic HCV infection is a major cause of liver disease and an important indication of adult liver transplantation.[2,3]

The prevalence of HCV infection in expectant women is around 1 and 8% and in children between 0.05% and 5%, all over the world. In developing countries, parenteral transmission is still a common cause in children while in developed countries, perinatal transmission is now the leading cause of HCV transmission.[2]

The influence of HCV infection on pregnancy and the effect of pregnancy on HCV infection are inadequately understood.[4] During pregnancy, the maternal immune system must develop tolerance to paternal alloantigens (to prevent maternal immune attack against the fetus) and maintain active immunity against HCV for protection of mother and fetus against infection.[5]

HCV infected women have an enhanced risk for haemorrhage during labour due to effects of HCV on coagulation profile and platelets. The risk for complications during pregnancy is also increased in women with hepatitis C. One recent study has reported that the frequency of PPH was found in 5.6% females who presented with HCV.[7] In a Pakistani study, the frequency of PPH was found to be much greater. It was

1. Anikah Kanwal
2. Shazia Khalid Khan
3. Uzma Altaf
4. Alia Zainab
5. Uzma Aziz
6. Farhat Naz

1. Lady Willingdon Hospital, Lahore.
2,3,6. Department of Gynae Unit 3, Allama Iqbal Medical College Lahore.
4. Fatima Jinnah Medical University, Lahore.
5. Department of Gynaecology, Mansoora Teaching Hospital, Lahore.

Correspondence:
Dr. Anikah Kanwal, Senior Registrar, *Lady Willingdon Hospital.*
E-mail: anikahkanwal@gmail.com

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observed that 80.88% females with HCV had PPH after delivery. In hepatitis C positive women, obstetrical hemorrhagic emergencies (PPH in 292(80.88%) and antepartum haemorrhage in 69(19.11%) of cases) were more frequently observed as compared to hepatitis C negative cases, as quoted from article in JCPSP by Khaskheli et al. in 2014.[8]

Rationale of this study is to find the frequency of postpartum hemorrhage in females presenting with hepatitis C virus. In pregnancy-associated with HCV infection multidisciplinary management is required due to a potential for bleeding complications. I want to find the frequency of postpartum hemorrhage after delivery in females presenting with hepatitis C virus. There is very little data reported regarding the obstetrical hemorrhage related to HCV during pregnancy not only in Pakistan but worldwide as well. Moreover, the reported work shows a remarkable difference between local and international data. So through this study we want to confirm whether HCV can cause PPH in utmost number of cases or only in few cases, as reported by two different studies above. This will help us to identify the magnitude of problem in our society and to trigger further research for the possible causes attributable to this PPH and improve clinical practice. It will also enable us to plan guidelines to prevent PPH in females with HCV in pregnancy. The objective of the study was to assess the fre-quency of postpartum hemorrhage after delivery in females presenting with hepatitis C virus.

- Hepatitis C virus Infection: It was defined as presence of hepatitis C virus DNA in blood of mother before conception of pregnancy as confirmed by ELISA.
- Postpartum hemorrhage: It was labeled if there was >500ml blood loss after normal vaginal delivery or >1000ml blood loss after cesarean section. Blood toss was measured by collecting blood in kidney tray and then measuring in a graduated cylinder for exact volume. Blood loss was also measured by soaked pads which was pre-weighed (dry pad weighed) and then weighed again after soakage where 1mg was equal to 1 ml during first 24 hours of delivery. In case of caesarean section blood volume in suction jar was recorded and blood volume was also calculated by weighing the dry and soaked gauze.

METHODS

Study Design: It is a descriptive case series.

Setting: Research was conducted at Department of Obstetrics and Gynecology, Unit-III, Jinnah Hospital, Lahore.

Duration of Study: Duration of study was 6 months after the approval of synopsis from 30/03/2016 to 29/09/2016.

Sample Size: Sample size of 250 cases was calculated with 95% confidence level, 3% margin of error and taking expected percentage of PPH i.e., 5.6%[7] after delivery in females presenting with hepatitis C virus.

Sampling Technique: Patients were selected by Non-Probability, Consecutive Sampling.

Sample Selection

Inclusion Criteria:

1. Females of age 20-40 years, of any parity presenting at gestational age ≥ 37 weeks for delivery with hepatitis C virus (as per antenatal record and ultrasound).

Exclusion Criteria

1. Multiple pregnancy (on USG)
2. Hydropic pregnancy (on USG)
3. Pregnancy with fibroids (on USG)
4. Un-booked females.
5. Females with comorbid conditions like gestational diabetes (BSR ≥ 186mg/dl) or PIH (BP ≥ 140/90 mmHg), preeclampsia (PIH with proteinuria ≥ +1 on dipstick method), eclampsia (convulsions with PIH)
6. Patients with HCV along with HBV or HEV (on medical record)
7. Patients with bleeding disorders
8. Patients taking anticoagulants.

Two hundred and fifty cases fulfilling inclusion criteria were enrolled in study form labour room of Department of Obstetrics & Gynecology, Jinnah Hospital Lahore. Informed consent was taken.

Demographic information (name, age, gestational age and parity) was also recorded. Patients who were HCV positive were selected to be observed for PPH. Then females were followed till delivery and underwent delivery either through cesa-rean section or normal vaginal delivery. After delivery females were shifted to the ward and were followed-up there till 24 hours. During 24 hours, total blood loss was noted and postpartum hemorrhage was labeled if there was equal and greater than 500ml blood loss after vaginal delivery or equal and greater than 1000ml blood loss after cesarean section (operational definition). All the information was collected on a specially designed proforma (attached). All patients were managed by following standard management protocols.

All the collected data was entered and analyzed through SPSS version 20.0.

1. Numerical variables; age and gestational age have been presented by mean ±SD.
2. Frequency has been calculated for parity.
3. Categorical variable i-e PIH has been presented by frequency and percentage.
4. Data has been stratified for age, gestational age and parity to address effect modifiers. Post-stratification chi-square test has been applied taking p value ≤0.05 as statistically significant.

RESULTS

The age of the patients ranged from 20 years to 40 years with a mean of 26.74±5.25 years. The gestational age of the patients ranged from 37 weeks to 42 weeks with a mean of 38.62±1.58 weeks. The parity of the patients ranged from 1 to 5 with 32.0% primiparas, 28.0% multiparas (≤ 3) and 40.0% grand multiparas (≥4) as shown in Table 1.

189(75.6%) patients developed postpartum hemorrhage as shown in Table 2. There was no statistically significant difference in the frequency of postpartum hemorrhage across age (p=0.994 as shown in Table 3.

DISCUSSION

In developing countries, pregnancy and labor related complications are amongst the major causes of morbidity and mortality in women. PPH is amongst the commonest of such complications in various studies. According to Pakistan Demographic Health Survey 2006-7, the commonest cause of maternal death is PPH. WHO established prevalence of PPH is 34% in Pakistan. It is cause of death in 27% patients with home delivery in 65% of cases[9][10]. This reported frequency of PPH is much higher as compared to that reported in developed countries where it is quoted to be 2-11%.[11] In developed countries, the risk of severe PPH is 1 per 1000 deliveries whereas of death is 3.1 per million maternities. In low resource countries, the risk of death due to PPH is high, ranging from 43%-53%.[12] The manage-

Table 1: *Baseline Characteristics of Study Sample*

Characteristics	Study Sample n=250
Age (years)	26.74±5.25
• 20-30 years	205 (82.0%)
• 31-40 years	45 (18.0%)
Parity	
• Primiparas	80 (32.0%)
• Multiparas (⩽3)	70 (28.0%)
• Grand Multiparas (⩾4)	100 (40.0%)
Gestational Age (weeks)	38.62±1.58
• 37-39 weeks	185 (74.0%)
• 40-42 weeks	65 (26.0%)

Table 2: *Frequency of Postpartum Hemorrhage*

Postpartum Hemorrhage	Frequency	Percentage
Yes	189	75.6
No	61	24.4
Total	250	100

Table 3: *Frequency of Postpartum Hemorrhage across Age Groups n=250*

Age Groups	Postpartum Hemorrhage		Total	P Value
	Yes (n=189)	No (n=61)		
20-30 years (n=205)	155 75.6%	50 24.4%	205 100.0%	0.994
31-40 years (n=45)	34 75.6%	11 24.4%	45 100.0%	
Total	189 75.6%	61 24.4%	250 100.0%	

Chi-square test observed difference was statistically insignificant.

ment goals in PPH are early identification of high risk patients and timely intervention in the form of resuscitation and settling the cause of hemorrhage.[11] Thus there has always been a quest to identify the attributing factors of postpartum hemorrhage to timely recognize this troubling complication.

Hepatitis C virus (HCV) causes an infectious disease Hepatitis C, which primarily affects liver. Its prevalence in pregnant women is projected to be between 1 and 8%, worldwide.[1,2] The influence of HCV infection on pregnancy and the effect of pregnancy on HCV infection are inadequately understood.[4] There is an increased risk for complications during pregnancy in women with hepatitis.[7,8] In pregnancy-associated with HCV infection multidisciplinary management is required due to a potential for bleeding complications. There was very little local and international data regarding the frequency of obstetrical hemorrhage related to HCV infection during pregnancy. Moreover, the reported work showed remarkable difference between local and international data.

The objective of current study was to evaluate the frequency of postpartum hemorrhage after delivery in females presenting with hepatitis C virus. It was a descriptive case series conducted at Department of Obstetrics and Gynecology, Unit-III, Jinnah Hospital Lahore over 6 months after the approval of synopsis from 01/07/2016 to 31/01/2017.

This study involved 250 HCV positive pregnant women of any parity aged between 20-40 years presenting after ≥37 completed weeks of gestation for delivery. Outcome variable was frequency of postpartum hemorrhage. Every patient was asked to provide a written informed consent.

In the present study, the incidence of postpartum hemorrhage was around 189 (75.6%) in HCV positive pregnant women which is alarmingly high. This frequency is much higher than that observed by Money et al. (2014) among similar Indian patients. A possible cause for this conflict can be the limited sample size of study conducted by Money et al. where they included only 108 HCV positive patients while the present study was conducted over a fairly large sample size of 250 patients.[7] The results of the present study are similar to that of Khaskheli et al. (2013) who included 361 HCV positive pregnant women presenting at Liaquat University of Medical and Health Sciences, Jamshoro Sindh and reported similar frequency of postpartum hemorrhage i.e. 80.88%.[8]

The observed frequency of postpartum hemorrhage in the present study is much higher than reported in general pregnant population without HCV.[10] This can be due to derangement of coagulation profile and platelet dysfunction among such patients.[12,13] It can be thus advocated that pregnant woman presenting in their 3rd trimester should be screened for HCV status and those who are positive should have appropriate work up including coagulation profile. These women should also be considered high risk for postpartum hemorrhage so that timely and effective management can reduce the morbidity and mortality associated with postpartum hemorrhage.

CONCLUSION

The frequency of postpartum hemorrhage was found to be 75.6% amongst HCV positive pregnant women. The frequency of postpartum hemorrhage across age (p=0.994), gestational age (p=0.773) and parity (p=0.981) groups showed, no statistically significant difference.

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FULL THICKNESS MUSCLE STITCH AFTER ABDOMINAL DRAIN REMOVAL IN POST OPERATIVE CHRONIC LIVER DISEASE PATIENTS

Mahboob Alam Chishti,[1] H M Amjad,[2] Abid Hussain,[3] Kamran Cheema,[4] Akmal Shafiq,[5] Muhammad Kareem Ullah,[6] Saeed Mahmood[7]

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Abstract

Background: Development of post-operative ascites is a well-known phenomenon in chronic liver disease patients when being operated for general surgical diseases. Control of ascitic leak is a big challenge when drain is removed in these patients post-operatively. For this purpose, different methods had been tried but no one has been effective in solving this problem.

Methods: This study was conducted at Avicenna Medical & Dental College, Bedian Road, Lahore from January 2020 to December 2020. Fifty patients were randomly included in this study. Different methods to control ascitic leak were applied for patients randomly.

Results: It was observed that full thickness anterior abdominal wall muscle stitch after drain removal is the best technique to control the ascitic leak in chronic liver disease patients when being operated for surgical diseases.

Conclusion: After drain removal, in chronic liver disease patients, full thickness muscle stitch through anterior abdominal wall is most successful method to control the ascitic leak.

Key Words: Anterior abdominal wall, Full thickness, Ascitic leak

Perioperative management of patients with cirrhosis who undergo general surgical procedures either elective or emergency is very important to avoid post-operative morbidity and mortality.[1]

Prior to surgery, risk factors for liver disease like chronic alcohol use, blood transfusion, substance use, tattooing or family history of liver disease should be evaluated. Suspicion for chronic liver disease should rise in any patient who has clinical features of cirrhosis, such as palmer erythema, spider nevi, ascites, splenomegaly, leg edema, gynecomastia, testicular atrophy, temporal wasting, parotid gland enlargement or jaundice.[2]

In patients without known liver disease, routine evaluation of liver function tests is not recommended. When liver function tests are abnormal, detailed review of patient's medication, including prescribed as well as over-the-counter and herbal, should also be done to exclude drug-induced liver disease.[3]

Advanced liver disease affects every organ system and is associated with potential life-threatening complications. Preoperative risk stratification of patients with liver cirrhosis, requiring abdominal and nonabdominal surgery, is challenging. It is well known that patients with cirrhosis have increased risk of morbidity and mortality when they require emergency surgery.[4]

Careful selection of patients with liver cirrhosis requiring surgery depends on many factors, including

1. Mahboob Alam Chishti
2. H M Amjad
3. Abid Hussain
4. Kamran Cheema
5. Akmal Shafiq
6. Muhammad Kareem Ullah
7. Saeed Mahmood

1. Department of Surgery Avicenna Medical College
2. Department of Surgery Sahiwal Medical College
3-6. Department of Cardiac Surgery Social Security Hospital Lahore
7. Department of Surgery Lahore General Hospital Lahore

Correspondence:
Dr. Mahboob Alam Chishti, *Assistant Professor Surgery Avicenna Medical College, E-mail: drmahboobalamchishti@gmail.com*

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stage of cirrhosis, type of surgery, timing of surgery (emergent or elective), and associated comorbid clinical conditions like DM, HTN, COPD etc.[5]

Cirrhosis can occur as a result of various causes and has two distinct phases: compensated and decompensated. The presence of complications of cirrhosis, namely, ascites, spontaneous bacterial peritonitis (SBP), variceal bleeding, hepatic encephalopathy, hepatocellular carcinoma, hepatopulmonary syndrome (HPS), and hepatorenal syndrome (HRS), characterizes the decompensated state of the cirrhosis.

Patients with decompensated cirrhosis have a median survival of less than 2 years. Their 1-year mortality rate is 20% in the presence of ascites, and it rises to 57% if the clinical course is complicated with variceal bleeding. Lack of any of these features represents the compensated phase, which has a median survival of more than 12 years.[6]

The other severe complications, including acute liver decompensation and clinical course, may also be complicated by severe coagulopathy, portal vein thrombosis, fluid and electrolyte imbalance, acute renal failure, and sepsis. Other determinants of adverse outcome include emergency surgery, advanced age, and concomitant cardiovascular disease.

Optimal preparation with attention toward cirrhosis complications during perioperative period may decrease the risk of complications or death following surgery. Preparation should include correction of coagulopathy& albumin, treating preexisting encephalopathy, controlling ascites, preventing sepsis, and optimizing renal function.[7]

Although traditionally discouraged, with the advancements in perioperative care, increasing number of patients with cirrhosis are undergoing surgery. Post operatively, they can suffer from above mentioned coplications but in addition a troublesome problem is ascitic leak from drain site when they are removed when indicated.

Different techniques had been used to minimize & control ascitic leak but we experienced that excellent preoperative optimization along with good postoperative care is fundamental to achieve this goal. A full thickness stitch involving ventral abdominal muscles is best technique to stop postoperative drain removal site ascitic leak.

METHODS

This study was conducted at Avicenna Medical & Dental College, from January 2020 to December 2020. Twenty patients were operated for different surgical procedures. Drains were placed in all patients to drain postoperative secretions.

RESULTS

All patients suffered from ascitic leak from drain removal site which was managed by different methods like pressure bandage, skin& subcutaneous stitches (interrupted, continuous & pursting) but as a last resort, full thickness stitch including ventral abdominal wall muscles, in continuous fashion was the most successful method to prevent ascitic leak after drain removal. Before stitch, elevation of wound margins by Allis clamp was successful maneuver to proceed.

DISCUSSION

Preoperatively reduction in ascitic load reduces or minimizes the ascitic leak after drain removal in chronic liver disease patients. There are different approaches for this purpose. The most important step is to drastically reduce your salt intake. Recommended limit is 2,000 mg or less a day. Seeing a nutritional specialist (dietitian) is helpful especially because the salt content in foods is difficult to determine. Salt substitutes — that do not contain potassium — can be used.[8]

Often, patients will require diuretics to treat ascites. Common diuretics are spironolactone and furosemide. These can cause problems with electrolytes and kidney function. It is not a substitute for reducing salt intake. Both are needed to treat ascites.[9]

Sometimes ascites builds up despite use of diuretics and a restricted salt diet. In these cases, patients may need paracentesis to remove large amount of excess fluid.

To correct hypoalbuminemia is also an important

aspect to reduce development of ascites postoperatively in these patients. Oral egg white or infusion of albumin injection is used for this purpose.

To minimize ascitic load before surgical procedures in chronic liver disease patients is very helpful to not develop postoperative ascites. After drain removal, ascitic leak is negligible in fully prepared patients. Even if ascites leak occurs, pressure bandage, superficial stitch is unsuccessful to control it. We have observed that a full thickness stitch including ventral abdominal wall muscles is most successful method to control it. Skin edges elevation is helpful for this stitch.

CONCLUSION

Ascitic leak from drain removal site in chronic liver disease patients has been managed by different methods including pressure bandage, skin & subcutaneous stitches (interrupted, continuous & pursting) but a continuous full thickness stitch including ventral abdominal wall musclesis the most successful method to minimize it. Before stitch, elevation of wound margins by Allis clamp is successful maneuver to proceed.

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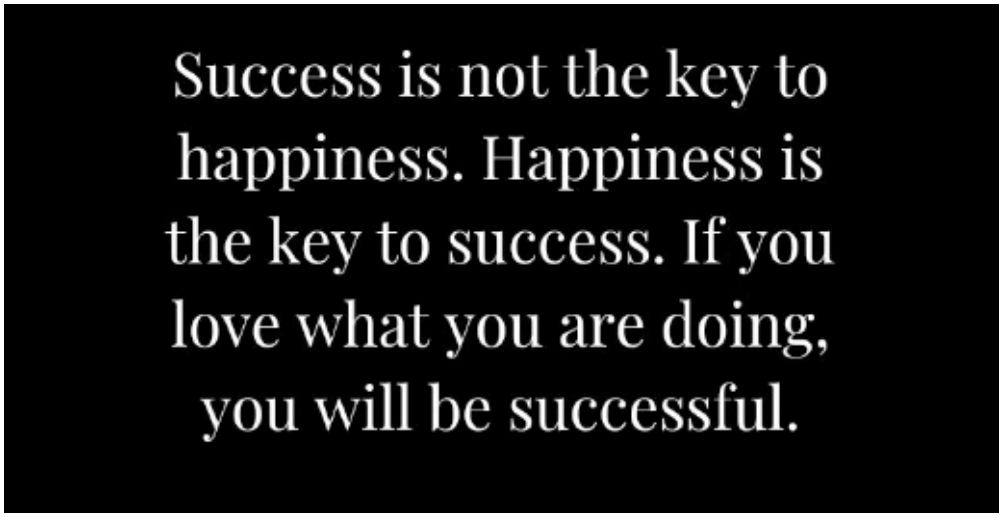

PLASMA D-DIMERS LEVELS IN COVID POSITIVE PATIENTS PRESENTING EARLY IN THE DISEASE

Umer Saeed Ansari,[1] Saman Saeed,[2] Shabbir Hussain,[3] Anum Waqar[4]

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Abstract

Background: Covid-19 pandemic has caused death of more than seven million patients worldwide, and is being countered by rapid diagnostic tests and quarantine. The inflammatory markers serve a pivotal role in estimating the disease progression and early diagnosis of the viral infection. Plasma D-dimer levels in covid positive patients are correlated with increased morbidity and mortality due to acute complications and abnormal coagulation. In this study, plasma D-dimer levels were not significantly elevated in patients who presented during the first week of clinical diagnosis of the disease. Aim of this research was to study the plasma levels of D-dimer (D-dimer) in covid positive patients presenting early in the disease, and to understand its possible role as a diagnostic marker in such patients.

Methods: 300 patients of different age groups, including both males and females, were recruited in this study, who tested positive for covid infection by rRT-PCR method within one week. Quantitative immunological determination of plasma D-dimer was performed by utilizing immunoassay techniques.

Results: Among the 300 covid-positive male and female patients, number of male patients was 201 (67%), while 99 were female patients (33%). Mean plasma D-dimer value was 269 ng/ml. Mean age of all covid positive patients including both males and females was 45 years. High plasma D-DIMER levels were observed in 80 patients (26.6%), whereas, in 220 patients, D- dimer levels were normal (73.3%)

Conclusion: The study has demonstrated that D-dimer (D-dimer) levels in covid-positive patients are not elevated in majority of patients presenting within one week of diagnosis. D-dimer, therefore, do not serve as a suitable biomarker for diagnosis of covid infections in patients presenting early in the disease.

Key Words: Plasma, D-dimer, COVID-19

The SARS-CoV corona virus, which causes SARS is believed to be originated in horse-shoe bats (zoonotic origin), and ultimately jumped to humans in South China in 2002. Eventually it infected more than 8000 people, killing almost 800 patients in the early phase, before it was quelled by countrywide lock-downs, quarantines, rapid diagnostic test and case tracing. When the first corona virus cases were diagnosed in Wuhan in December, and news of an outbreak began to trickle out of the country, few could have predicted the coming pandemic. The WHO declared the outbreak as pandemic, and majority of countries directed their citizens to stay at home to restrict the airborne spread of the infection. The government of Pakistan undertook drastic measures throughout the country, to cope with the spread of the COVID-19 infection, and to simultaneously reduce the mortality.

Fever and cough are purported to be the dominant clinical symptoms worldwide, and in 2020, a systematic review was conducted over 24,000 patients, to determine the prevalence of clinical symptoms in covid

1. Umer Saeed Ansari
2. Saman Saeed
3. Shabbir Hussain
4. Anum Waqar

1. *Assistant Professor Biochemistry, Lahore Medical & Dental College (LMDC), Lahore*
2. *Assistant Professor Physiology, University Medical & Dental College (UCMD), University of Lahore*
3. *Assistant Professor Orthodontic Department, Rashid Latif Medical College, Lahore*
4. *Senior Biochemist, Chughtai Medical Laboratory, Lahore*

Correspondence:
Dr. Umer Saeed Ansari, *Assistant professor Biochemistry, Lahore Medical & Dental College (LMDC), Lahore*

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positive patients. The review was published in June 2020 and concluded that pyrexia and persistent cough are the most dominant symptom in patients with covid infection (Michael C. G et al; 2020)

Currently the gold standard for confirmation of COVID infection is the amplification of viral RNA by real-time reverse transcriptase polymerase chain reaction (rRT-PCR), although it has its own limitations and drawbacks regarding false negativity or false positivity in many individuals reporting in medical laboratories for confirmation of the infection. There is an overwhelming demand for rRT-PCR test country wide, and is also generally termed as nasopharyngeal swab test. The mean incubation period of SARS-CoV corona virus, is about 6 days, the viral load elevates during this period, but the nasopharyngeal swabs for RT-PCR for detection may be falsely negative (Lippi G; 2019)

There is, thus, an overall need for enhanced capacities of medical testing laboratories, trained and skilled personnel and state of the art devices and reagents for screening and rapid diagnosis of patient with covid infections (Li Z et al; 2020). In some countries, such as Italy, the reagents scarcity and less number of specialized medical laboratories compelled the governments to restrict the swab testing to patients exhibiting the clinical symptoms of respiratory depression, which lead to underestimation of covid positive patients in their population (Rubino S; 2020).

In the light of these facts, more blood tests are being performed which help identify the false negative and false positive rRT-PCR results among the general population, showing no acute symptoms of the viral disease.

Overactive blood coagulation functions have been documented in the disease progression of covid infections. Most of the patients in this study who are covid positive on rRT-PCR have initial manifestations such as throat pain, mild fever off and on and flu-like symptoms. Therefore, it has been crucial to indentify the covid positive patients who are at greater risk of developing abnormal coagulation. In this lineD-dimer measurements are routinely performed in clinical practice to rule out the diagnosis of deep vein thrombosis (DVT) or pulmonary embolism (PE), thus indicating an increased risk of abnormal blood clotting in covid positive patients, later in the disease progression. Elevated plasma levels of D-dimer have been found in patients with community-acquired pneumonia associated with a higher mortality rate (Querol J.M; 2004). Recently a study conducted on plasma levels of D-Dimers in covid positive patients correlated the elevated levels of D-dimer with increased morbidity and mortality due to acute complications and abnormal coagulation functions. The study suggested a significantly increased plasma level of D-dimer in patients with severe covid disease, compared with non-severe viral disease and plasma D-dimer greater than 0.5 μg/ml was associated with severe complications in patients with covid. (Hai-HanYu; 2020). Recent studies have documented elevated D-dimer levels in patients with confirmed COVID-19, and have associated this finding with the disease progression. Research work on D-dimer levels has also shown significantly increased levels in patients with COVID-19 who were admitted in the hospital ICUs (Huang C; 2020). Studies have shown wide spread synthesis of pro-inflammatory cytokines in this viral infection. These cytokines further accentuate the risk of vascular permeability, coagulopathy and multi-tissue failure leading to life threatening outcomes (Sayyadi; 2021). A study in year 2020 suggested a correlation among plasma D-dimer (D-DIMER), and severity of COVID-19 infection (Tang N; 2020). However, no conclusive evidence supports the utilization of plasma D-dimer as an evaluation index for covid infection. Measurement of plasma D-dimer levels can prove to be a cost-effective test for early detection of COVID-19-associated coagulopathy and for therapeutic intervention. However, more studies are needed for determining its role as a diagnostic marker early in the disease.

The aim of this research is to study the plasma levels of D-dimer (D-dimer) in covid positive patients presenting early in the disease and to understand its possible role as a diagnostic marker in such patients.

METHODS

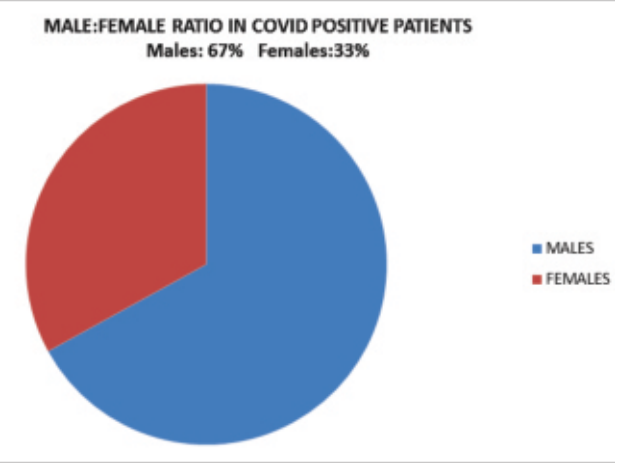
300 patients of different age groups, including both males and females, were recruited in this study, who tested positive for covid infection by rRT-PCR method recently. The study was conducted at Arif Clinical Laboratory, Lahore, and data was collected randomly from patients who reported at the laboratory within one week of the appearance of the signs and symptoms of covid infection. Quantitative immunological determination of plasma D-dimer was performed by utilizing immunoassay techniques.

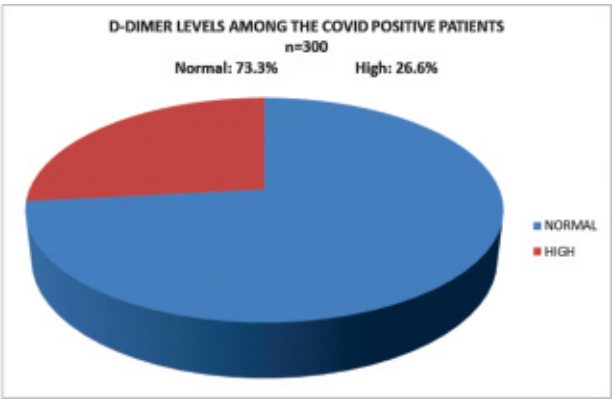
RESULTS

Total number of 300 covid-positive male and female patients were studied (n=300). Number of male patients was 201 (n/m=201) while 99 female patients were positive (n/f=99). Among the 300 covid patients 67% were males, while only 33% patients were females. Overall mean plasma D-dimer value was 269 ng/ml. Mean age of all covid positive patients including both males and females was 45 years. High plasma D-DIMER levels were observed in 80 patients (26.6%), whereas, in 220 patients, D- dimer levels were normal (73.3%).

DISCUSSION

Although elevated plasma levels indicate severe viral infection, but their levels do not rise in the early course of disease in covid positive patients. Elevated D-dimers are proposed to be indirect manifestations of progressively increasing inflammatory processes in the body, associated with high inflammatory cytokines which subsequently activate fibrinolysis and elevate the D-dimer levels in these patients. Recent studies have highlighted high plasma levels of D-dimer associated with the disease progression. In this study, most of the covid positive patients presenting early in this study had normal plasma levels (73.3%) while only 26.6% patients had high levels of D-dimer. Strikingly among the 300 patients randomly selected for confirmation of covid infection, only 33% patients were females, while 67% covid positive patients were males, indicating the high preponderance of covid infection in males.





CONCLUSIONS

The study demonstrates that D-dimer (D-dimer) levels in covid-positive patients is not elevated in majority of patients presenting within one week of diagnosis. D-dimer, therefore, does not appear to be a suitable biomarker for diagnosis of covid infections in patients presenting early in the disease.

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FUNCTIONAL AND RADIOLOGICAL OUTCOME OF SCHATZKER TYPE V AND VI TIBIAL PLATEAU FRACTURES TREATMENT WITH HYBRID EXTERNAL FIXATOR

Muhammad Zafar Iqbal Shahid,[1] Maqsood Akhtar,[2] Abeera Babur,[3] Farheen Qasim,[4] Faizan Majeed[5]

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Abstract

Background: Tibial plateau fractures especially Schatzker type V and VI are mostly accompanied by soft tissue injuries like compartment syndrome and neurovascular involvement. Open reduction and internal fixation is always not a definitive answer for such fractures. Hybrid external fixator is used to maintain articular and axial alignment in such cases.

Objectives: To assess the functional and radiological outcome of Schatzker type V and VI fracture treated with Hybrid external fixator. This prospective study was carried out in orthopaedics department of Services Hospital, Lahore from December 2017 to December 2019.

Methods: A total number of 40 patients with Schatzker type V and VI fractures were included in the study. All these patients were admitted through emergency department of Services Hospital, Lahore. Written consent was taken from each patient for being a part of study. Age range was 20 to 50 years and there were 35 male and 5 females. All patients with poly trauma and neurovascular injury were excluded from study. All these patients were operated and fixed with hybrid external fixator. They were discharged 3 to 5 days after the surgery. These patients were followed in OPD after 2 weeks, 6 weeks, and 3rd, 4th, 5th and 6th month. We used Rasmussen functional and radiological score for the assessment of these fractures.

Results: Mean age was 40 years. There was a male dominance in the sample under study (M35:F5). The most common mechanism of injury was road traffic accident. Rasmussen functional score was excellent for 20, good for 16 and fair for 4 patients. Rasmussen radiological score was excellent in 24 good in 12 and in in 4 patients it was fair.

Conclusion: Hybrid external fixator is a simple and excellent device to treat Schatzker type V and VI fractures with good functional and radiological outcomes.

Keywords: Tibial Plateau, Complex proximal tibia fractures, Hybrid external fixator, Schatzker V and VI fracture, Rasmussen score

Tibial plateau is a bony platform of distal half of knee joint and is composed of medial and lateral condyle separated by inter-condylar eminence where cruciate ligaments and menisci are attached. The medial condyle bears 60 percent weight of knee joint and is thicker than the lateral condyle of tibia. It is concave in shape and located slightly more distally than the lateral condyle. The lateral condyle is thinner weak and convex in shape. Inter-condylar eminence is a bony portion that lies in between two condyles that serve as a point of ACL attachment.[1,4]

Proximal tibial fractures are complex injuries that results from high energy trauma. These are often challenging to the orthopedic surgeon because of

1. Muhammad Zafar Iqbal Shahid
2. Maqsood Akhtar
3. Abeera Babur
4. Farheen Qasim
5. Faizan Majeed

1-5. *Services Institute of Medical Sciences / Services Hospital, Lahore.*

Correspondence:
Dr. Muhammad Zafar Iqbal, *Services Institute of Medical Sciences / Services Hospital, Lahore. E-mail drzafar2014@gmail.com*

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extensive comminution, soft tissue problems, compartment syndrome, articular depression, condylar displacement, skin necrosis and associated neurovascular involvement. Proximal tibial fractures affect the metaphyseal region with or without involvement of the diaphyseal region in 5 to 11% cases. These are 1% of all fractures.[2,3]

In most of the cases it is the axial load that fractures the articular portion of proximal tibia as a result of impaction. When axial load is combined with angular force it causes the comminution of articular as well as metaphyseal region of tibia.[4] These fractures result from the force that is applied through the lower end of femur to the tibial plateau similar to the die punch. Schatzker has divided the proximal tibial fractures in six types out of which type V and type VI are most difficult to treat. Another important point is soft tissue management especially when these are the open. Even if the fractures are closed, they are accompanied with massive swelling and compartment syndrome. Moreover these fractures also result when the force is applied through the lower end of femur.[5]

A lot of treatment options are available to manage these fractures. These include open reduction and stabilization of these fractures with T-plates, L-plates, double plate osteosynthesis, MIPO, intramedullary devices, percutaneous screw fixation and primary Total Knee Replacement. The staged treatment with internal devices application is also used. However all these techniques result in complications especially in the presence of soft tissue injuries, osteoporosis and associated co-morbidities especially in the elderly population. Whether internal or external fixation techniques are used, improper management of soft tissue injury is a factor in the failure of treatment of proximal tibial fractures. There are also external devices like ilizarov fixation and fixation of proximal tibial fractures with hybrid fixators under image intensifier.[6,7,15]

In hybrid external fixator we used the standard ilizarov frame with AO rods and schanz. It is definitive fixation device for these fractures. The hybrid external fixator works on the principles of ligamentotaxis, the fracture fragments are reduced, and the depressed intra-articular fragments were elevated and maintained with the help of either olive wires or k wires.[8]

With open techniques, although fracture is under direct vision and stabilized adequately. There is proper reduction of fracture fragment but still it is disadvantageous as it causes the soft tissue and skin necrosis. When there is extensive comminution and soft tissue damage, internal fixation of these fractures cannot be done. Surgical treatment of these fractures is associated with complications like infection, skin necrosis, malunion, fixation loss and knee joint stiffness.[9]

The hybrid external fixator is a valuable option for treatment of these fractures, especially when associated with skin and soft tissue coverage problems and fractures with compartment syndrome. Other advantages are that it acknowledges the long bone consolidation without additional soft tissue damage. It provides the primary and definitive treatment of proximal tibial fractures. Chances of pin tract infection are less provided the pin tracts are properly looked after.[10,11]

This study is done to see the effectiveness of hybrid external fixator in the management of complex proximal tibia fractures in terms of functional and radiological outcome

METHODS

This study was conducted at department of orthopedic surgery in Services Hospital Lahore from December 2017 to December 2019. A written consent was obtained from each patient on the prescribed proforma. We used Schatzker classification to classify the proximal tibial fractures. A total number of 40 patients presented in emergency department of this hospital were included in the study. All these patients had Schatzker type V and VI fractures. Patients with poly-trauma having bilateral tibial plateau fractures V and VI, neurovascular injury uncontrolled Diabetes Mellitus, peripheral vascular disease and patients not fit for surgery were excluded from study. All these patients underwent X-rays of knee joint AP and lateral views. To know the geometry of postero- lateral and postero-medial fragments each patient had CT scan with 3D reconstruction of proximal tibia.

The age range was 20 to 50 years. There were 35 males and 5 females in this study. 30 patients had Schatzker type V while remaining had type VI fractures. 32 patients had road traffic accident, in 6 patients there was history of fall from height and in remaining 2 patients it was as a result of fight with direct hit at the knee joint. 8 patients had open fracture with a wound in front of knee. Among these 8 patients 3 had GA type 1 fracture while 3 had type B and in remaining it was Gustilo Anderson type 3A injury.

In close fractures hybrid external fixator was applied without opening the fracture site after reduction under C-Arm control. In 3 patients with close fractures we performed the minimal open reduction, depressed fragment was elevated, and hybrid external fixator was applied. While in open fractures the procedure of application of hybrid fixator was preceded by soft tissue debridement, wound irrigation and IV antibiotics. The right leg was involved in 30 patients while in 10 patients it was the left proximal tibial injuries.

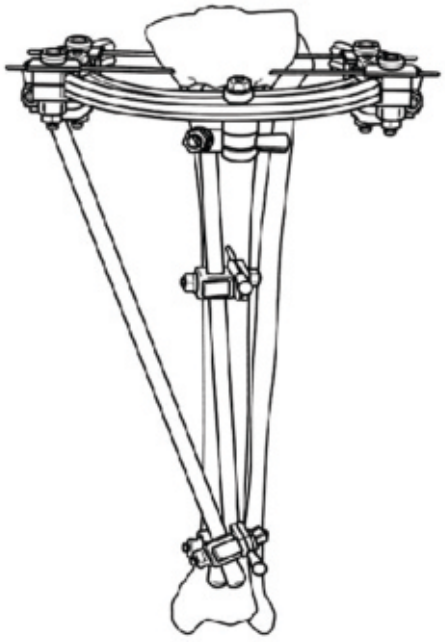

Fig 1: *Diagrammatic presentation of Hybrid External Fixator*

After application of hybrid fixator all patients were instructed for care of pins to avoid the pin tract infection and to start Knee ROM. All patients with open wounds were having dressing and antibiotics for 4-7 days. All patients were discharged from the hospital on an average of 3-5 days after surgery. They were followed in OPD after 2 weeks, 6 weeks and thereafter 3rd, 4th, 5th and 6th month. We used Rasmussen functional and radiological score for the assessment of these fractures.[18] Data was analyzed by using SPSS version 25. A p value of less than 0.005 was considered as significant.

RESULTS

Mean age in our study group was 40.32 + 5.64 years ranging from 20-50 years. There was male dominance with 35 male and 5 female in our study. 30 patients had Schatzker type V while 10 patients presented with type VI fractures. All the patients were operated within 36 hours after admission. Average Operating time was 55 minutes. Mean stay in hospital was 5 days with a range from 3 to 12 days.

In this study union was seen on average of 4 months (4-6 months) except in 3 patients. These 3 patients took longer time for union (6-7) months. Hybrid external fixator was well tolerated in all the patients. The average range of motion achieved at knee joint was 0-115 degree with 2 patients having extension lag of 20 degree.

The Rasmussen functional score was excellent for 20 patients (Score 28.2) and good for 16 patients (Score 20) while for 4 patients (Score11) it was fair. Rasmussen radiological grading was excellent for 24 patients, good for 12 patients and fair for 4 patients. There were no poor results in both functional and radiological Rasmussen assessment.

There was no systemic complication except in 3 patients. They were having deep infection which was treated with wound debridement, irrigation and IV antibiotics until ESR and CRP returned to the normal.

One patient had DVT which was detected timey and it was managed with LMW Heparin. 15 patients had pin tract infection (37%) which were superficial and managed with pin tract care and oral antibiotics in OPD.

4 patients had mal-union less than 15 degree of valgus while in 1 case there was skin necrosis. This

patient required secondary flap rotation by plastic surgery department.

Rasmussen functional and radiological score

A. Subjective complaints
- a. Pain
  - No pain 6
  - Occasional pain 5
  - Constant pain after activity 4
  - Significant rest pain 0
- b. Walking capacity
  - Normal walking capacity (in relation to age) 6
  - Walking outdoors for at least 1 h 4
  - Short walks outdoors for >15 min 2
  - Walking indoors only 1
  - Wheel-chair/bedridden 0

B. Clinical signs
- a. Extension
  - Normal 6
  - Lack of extension (0-10°) 4
  - Lack of extension > 10° 2
- b. Total range of motion
  - >140° 6
  - >120° 5
  - >90° 4
  - >60° 2
  - >30° 0
- c. Stability
  - Normal stability in extension and 20° of flexion 6
  - Abnormal instability 20° of flexion 5
  - Instability in extension < 10° 4
  - Instability in extension > 10° 2
- Maximum 30
- Excellent 27-30
- Good 20-26
- Fair 10-19
- Poor <10

A. Articular depression
- Not present 6
- <5 mm 4
- 6-10 mm 2
- >10 mm 0

B. Condylar widening
- Not present 6
- <5 mm 4
- 6-10 mm 2
- >10 mm 0

C. Angulation (valgus/varus)
- Not present 6
- <10° 4
- 10-20° 2
- >20° 0
- Maximum 18
- Excellent 18
- Good 12–17
- Fair 6–11
- Poor <6

DISCUSSION

Table 1: *Demographic Distribution of Schatzker V and VI Fractures*

Variables (n=40)	Schatzker type V (n=30)	Schatzker type VI (n=10)
Age Mean 40.32 + 5.64 years min= 20 max= 50 years		
20-30yrs	16 (80.0%)	4 (20.0%)
31-40yrs	8 (61.5%)	3 (38.5%)
41-50yrs	6(66.5%)	3(33.5%)
Gender		
Male	30 (85.7%)	5 (14.3%)
Females	3 (60.0%)	2 (40.0%)

Table 2: *Rasmussen Functional Score Table*

S/no	Grading n=40	Functional score
1	Excellent (27-30)	20 (50.0%)
2	Good (20-26)	16 (40/0%)
3	Fair (10-19)	4 (10/0%)
4	Poor (<10)	0 (0.0%)

Table 3: *Rasmussen Radiological Score Table*

S/no	Grading n=40	Radiological score
1	Excellent (max 18)	24 (60.0%)
2	Good (12 -17)	12 (30.0%)
3	Fair (6-11)	4 (10/0%)
4	Poor (<6)	0 (0.0%)

Proximal tibial fractures are always challenging to the orthopaedic surgeons. These are caused by high energy trauma like Road traffic accident especially after motorbike accidents followed by fall from height

and rarely by direct blow. In elderly people proximal tibial fractures may result of trivial trauma such as history of slip and fall on the floor because bones are osteoporotic with poor bone stock[4].

Proximal tibial fractures are usually associated with skin compromise, blister formation, soft tissue abrasions, intra articular comminution, ligamentous injury, meniscal damage and compartment syndrome. Type V and VI fractures can also result in neurovascular damage. These fractures also result in instability and deformity either varus or valgus at the knee joint which further complicate the situation.[1,2]

In management of these fractures one should restore the axial and varus /valgus mal-alignment, maintain the joint congruity by elevating the depressed articular fragments, soft tissue management and early physiotherapy of knee joint. Patient should be instructed for early weight bearing under the care of trained physiotherapist. Long period of immobilization of knee joint results in the stiffness which is very difficult treat.[3]

Although ORIF of these fractures is advantageous in terms of direct reduction and visualization of fracture fragments[6] but still the soft tissue compromise and wound infection are higher with such fixation devices.[5,7,9] The hybrid external fixator is a valuable option to treat Schatzker type V and VI fractures. It eliminates the delay in surgery because of presence of swelling and results in early rehabilitation of patient. The problem of knee stiffness is also minimized with hybrid external fixator by early start of knee movement, which is very common in Schatzker type V and VI fractures.[8] In our study we fixed the fracture with minimal invasive techniques under image intensifier that resulted in short operative time, minimal blood loss, less soft tissue compromise and wound was managed properly. Even in the presence of open fracture we can apply hybrid external fixator as definitive treatment. Early fixation of Schatzker V and VI fractures with hybrid external fixator results in the short hospital stay.

A lot of studies show the hybrid external fixator is a good device for the definitive management of proximal tibial fractures especially type V and VI. In our study the fracture united in mean period of 16.20 ± 3.2 weeks with no intra-articular collapse after removal of the fixator.

Savolainen et al treated 33 patients with proximal tibia fractures out of which 20 patients had high energy trauma, with hybrid external fixator. According to him hybrid external fixator is a safe device for proximal tibia fractures. In his study he reported the union time of 20 weeks which is comparable to our study.

In the study done by Vankaeash et al. the mean union time was 13.3 weeks with delayed union in 2 cases.

J B Gross et al concluded that hybrid external fixator has satisfactory outcome with several advantages associated with it such as shorter operative time, less bleeding, shorter hospital stay and lower infection rate. He reported union rate of 80% which is comparable with our study.[10]

In 2019 TA Bhat et al reviewed 25 cases with proximal tibial fractures fixed with hybrid external fixator and reached to the conclusion that this fixation method is reliable and effective alternate of locking plates in selective patients.[11]

The study done by Dar Reyaz and Latoo et al Hybrid External Fixator for complex tibial plateau fractures, a minimally invasive technique" has reported the fair reduction results without compromising the already compromised soft tissue in Schatzker type V and VI. The infection rate and union time reported in our study is comparable with the literature.[12]

In the study done by Konstantinos Kateros et al. the average union time was 15.5 weeks (range 13-19 weeks) for these complex tibial fractures. All these fractures were treated with hybrid external fixator. He demonstrated that hybrid external fixator is safe in terms of low complication rates and has good functional outcome.[13]

The study done by Rubash et al found that hybrid external fixator is an excellent treatment in Schatzker type V and VI fractures with extensive oft tissue injury. It facilitates the patient in early weight bearing and has good functional outcome.[14]

In the management of High energy Tibial plateau

fractures treated with hybrid external fixator Babis C George et al concluded that Schatzker type V and VI fractures are serious injuries with great impact on the residual limb. Hybrid external fixator as a definitive treatment for these high energy bi-condylar fractures has been proved to be beneficial. They concluded that it not only provides osseous stabilization but also help in the healing of severed soft tissue envelop.[15]

The severed soft-tissue is always a critical predictor of functional outcome. The stripping of the skin and subcutaneous tissue results in devascularization of bone and a higher rate of infection. Infection rates markedly decreased and outcomes greatly improved when a less invasive technique was used. Lee et al reported on 36 tibial plateau fractures treated with a less invasive stabilization system. Two of them had a deep infection and one had extensive skin necrosis and required plastic surgery. Most of the authors who had good results with the internal fixation of such fractures have used the external fixator as a preliminary step to help soft-tissue healing before internal fixation. Fixation of the fracture using the hybrid external fixator avoids extensive soft-tissue dissection and decreases the incidence of deep infection and devascularization.[15,16,17]

In our study there was no systemic complication except 3 patients who developed wound infection which got resolved with IV antibiotics and debridement. There was associated superficial pin tract infection in 4 patients and it was treated with proper pin tract care and oral antibiotics. This rate of infection is comparable with the literature.[11,12]

All these studies support the use of hybrid external fixator in Schatzker type V and VI fractures especially those who have compromised skin and those with open fractures.

CONCLUSION

Our study shows that management of proximal tibial fractures with hybrid external fixator has good functional outcomes. Early active mobilization of the knee joint is essential to prevent the fracture disease. Hybrid external fixator is advantageous in this respect as early mobilization can be achieved with it especially in case of complex tibial fractures (Schatzker Type V, VI).

Even the hybrid external fixator successfully provide the continuous excess to care the soft tissue especially in case of open wounds without further compromise.

Conflict of Interest None

Funding Source None

Limitation of the Study

In our study the sample size was small. Moreover the follow up period for the patients under the study was relatively short. There was no comparative arm involved in the study.

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ASSOCIATION OF MECONIUM STAINED LIQUOR WITH ACIDIC CORD BLOOD GASES IN FEMALES UNDERGOING CESAREAN SECTION

Shazia Sehgal,[1] Maria Jabeen,[2] Aliza Rafaqat,[3] Shazia Khalid,[4] Farhat Naz,[5] Irum Inam[6]

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Abstract

Objective: The objective of this study was to determine the association of acidic cord blood gases with meconium staining in amniotic fluid in females undergoing cesarean section.

Methodology: It was a case control study. 100 females, fulfilling selection criteria were selected from the labor room of Department of Obstetrics & Gynecology, Jinnah Hospital, Lahore. Demographic information (name, age, gestational age, parity and BMI) was obtained along with informed consent. Patients were stratified into two groups, one with meconium staining of liquor during caesarean and the other without meconium staining. Within one minute after delivery, blood samples were obtained from the cord and were sent to the laboratory of the hospital for assessment of cord blood gases. Acidic blood gases and acidic pH were labeled (as per operational definition) if present.

Results: Hundred patients with ages ranging from a minimum of 18 to a maximum of 40 took part in the study. Minimum gestational age of the women in the study was 37 weeks and maximum gestational age was 42 weeks (mean 39.14 ± 1.54 weeks). The BMI of the women ranged from 22 to 32 with the mean being 27.70 ± 2.67. 54% of patients were having their first baby and 46% of patients were multiparous. Acidic cord blood gases were detected in 48% cases and were normal in the rest of the 52% patients. By comparing the presence of acidic cord blood gases in females with or without meconium it was found that there was significant association of acidic cord blood and meconium stained liquor with an odds ratio of 21. After stratification of age, acidic cord blood gases were distributed equally over the ages < 30 and >30, with Odds ratio more than 1 in both age groups. Same was the case with gestational ages <40 weeks and >40 weeks, and with BMI <28 and >28. Thus suggesting that in our study, the acidotic cord blood vessels were associated most significantly with meconium staining regardless of the maternal age, gestational age or BMI of the mother.

Conclusion: Acidic cord blood gases were found in a total of 48% patients (48/100), out of which more than 83% (40/48) were those who also had meconium stained amniotic fluid. Presence of acidic cord blood gas was significantly associated in females with meconium staining of liquor.

Key words: Acidotic Cord Blood Gas, Caesarean Section, Meconium.

Meconium is a thick, black-green, odorless material present in the fetal intestine during the third month of gestation. It is formed by the accumulation of debris which includes desquamated cells from the intestine and skin, lanugo hair, gastrointestinal mucin, fatty particles from the vernix caseosa, amniotic fluid, and intestinal secretions. It contains glycoproteins which are blood group specific and a small amount of lipid and protein that decreases with increasing gestation.[1,2] The black-green color of meconium is because of bile pigments. Meconium is sterile, but if it is aspirated into the lung, it may cause the release of

1. Shazia Sehgal
2. Maria Jabeen
3. Aliza Rafaqat
4. Shazia Khalid
5. Farhat Naz
6. Irum Inam

1-6: Department of Obstetrics and Gynaecology

Correspondence:
Dr. Shazia Sehgal, *Department of Obstetrics and Gynaecology, AIMC/Jinnah Hospital, Lahore.*

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cytokines and other vasoactive substances that lead to inflammatory responses in the fetus and newborn.[3] In patients with aspiration of meconium, pulmonary function improves if proinflammatory cytokines decrease after the first 96 hours of life.[4]

Meconium present in the amniotic fluid can be aspirated during fetal gasping or in the initial breaths taken by the baby after delivery. Normally, fetal breathing activity removes the fluid present in the lungs, out of the trachea.[5] The presence of prolonged hypoxia stimulates fetal breathing centres and initiates gasping that can lead to inhalation of meconium stained amniotic fluid.[6] Many stillborns were seen to have meconium in their lungs[6] and in those who died soon after birth without a history of aspiration at delivery.[7,8] Thus aspiration of the meconium stained liquor in the first few hours of birth poses a risk and the neonatal period can be severely affected if the child does develop aspiration.

Meconium aspiration syndrome (MAS) is defined as respiratory distress in newborn infants born through meconium-stained amniotic fluid (MSAF) whose symptoms cannot be otherwise explained.[9] In the newborn, MAS can present with varying degrees of severity ranging from mild respiratory distress to life-threatening respiratory failure.

Meconium aspiration syndrome is a significant cause of infant mortality in developed as well as in developing countries. In the United States, a retrospective multi-center study was conducted on full-term infants born over a period of 10 years, and it reported a 1.8 percent incidence rate of meconium aspiration syndrome (MAS).[10]

The incidence of meconium staining of amniotic fluid varied across different gestational ages. It was seen to be highest in post term babies, followed by term babies and the lowest in preterm ones. This was best illustrated by a large English multicenter study that reported rates of MSAF in preterm, term, and post term infants of 5.1, 16.5, and 27.1 percent, respectively.[11]

Meconium staining of the amniotic fluid was seen to be majorly linked to a gestational age beyond 37 weeks and was seldom seen with a gestational age less than 34 weeks.[12]

It was suggested that the passage of meconium could be caused by increased peristalsis and relaxation of the anal sphincter due to increased vagal outflow which is seen with umbilical cord compression or increased sympathetic inflow in compensation for hypoxia.[13]

It is worth mentioning here that there are multiple literatures which have an entirely contradictory claims and suggest that meconium passage could only be a physiologic process and that the presence of meconium in the amniotic fluid at birth is due to the impaired clearance of the meconium in utero.[14,15] Thus it is important to collect data and to research this dilemma, so as to clarify which of the two contrasting conjectures is valid.

METHODS

This is a case control study which was done in the Gynae & Obstetrics department in Jinnah Hospital, Lahore, over a span of six months. 100 females fulfilling selection criteria were enrolled in the study and informed consent was obtained. Demographic information (name, age, gestational age, parity and BMI) was also obtained. During delivery, amniotic fluid was assessed for presence or absence of meconium staining and two groups were formed on the basis of that. Within one minute after delivery, blood samples were obtained from the cord and were sent to the laboratory of the hospital for assessment of cord blood gases. Reports were assessed and levels were noted. Acidotic blood gases and acidic pH were labeled (as per operational definition) if present. All this information was collected through a pre-designed proforma (attached). Data was analyzed via SPSS version 20. Quantitative variables like age, gestational age and BMI were analysed by mean and standard deviation. Qualitative variables like parity and acidotic blood gases were converted to frequency and percentage. Odds ratio (OR) was calculated to measure association between meconium staining and acidotic blood gases. OR >1 was considered as significant and the chi square test was applied.

Data was stratified for age, gestational age, parity and BMI. Adjusted OR was calculated for stratified groups. Adjusted OR >1 was considered as significant and post stratification chi square test was applied with P-value < 0.05 considered as statistically significant.

RESULTS

Of the 100 patients, minimum age was 18 and maximum age was 40, and mean age was 28.84 ± 7.02 years. The minimum gestational age was found to be 37 weeks and maximum gestational age was 42 weeks with mean and standard deviation was 39.14 ± 1.54 weeks. BMI of women participating in the study ranged from 22 to 32, with mean and standard deviation 27.70 ± 2.67. 54 (54%) patients had a parity of 1 and there were 46 (46%) patients with parity 2. Acidotic cord blood gases were found in 48 (48%) patients while the rest of the 52 (52%) patients did not show acidosis. Of the 48 patients who had acidotic cord blood, 40(83%) also had meconium staining of liquor. By comparing the presence of acidotic cord blood gases in females with or without meconium it was found that there was significant association of meconium staining and acidosis, with and OR = 21.00

After stratification of age, acidic cord blood gases were distributed over the age <30 and >30, with Odds ratio more than 1 in both age groups. Same was the case with gestational ages <40 weeks and >40 weeks, and with BMI <28 and >28. Thus suggesting that in our study, the acidotic cord blood vessels were associated most significantly with the meconium staining and both acidic cord blood gases and meconium staining together, were seen across different groups after stratification.

Table 1: Descriptive Statistics (n =100)

	Minimum	Maximum	Mean	Std. Deviation
Age	18	40	28.84	7.02
Gestational Age	37	42	39.14	1.54
BMI	22	32	27.70	2.67

Table 2: Distribution of Parity

Parity	Frequency	Percent
1	54	54
2	46	46
Total	100	100.0

Table 3: Distribution of Study Group

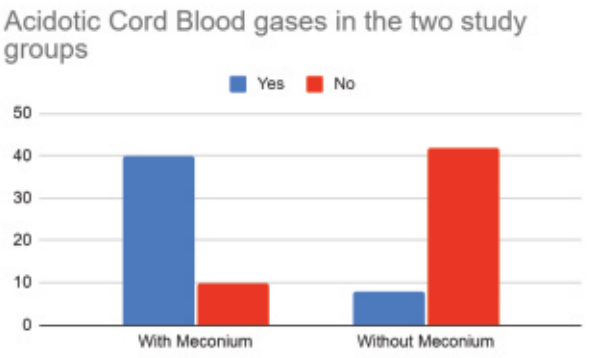
Study Group	Frequency	Percent
With Meconium Staining	50	50
Without Meconium Staining	50	50
Total	100	100.0

Table 4: Distribution of Acidotic Cord Blood Gases

Acidotic Cord Blood Gases	Frequency	Percent
Yes	48	48
No	52	52
Total	100	100.0

Table 5: Comparison of Acidotic Cord Blood Gases in females with and without Meconium Staining (n = 100)

Study Group	Acidotic Cord Blood Gases		Total	Odds Ratio
	Yes	No		
With Meconium	40	10	50	
Without Meconium	8	42	50	21.0
Total	48	52	100	



Graph 1. *Comparison of Acidotic Cord Blood Gases in Females with and without Meconium Staining (n=100)*

Table 6: Stratification of Acidotic Cord Blood Gases in Females with Respect to Age (n = 100)

Study Group	Acidotic Cord Blood Gases		Total	Odd Ratio
	Yes	No		
Age < 30 years				
With Meconium	22	6	28	14.67
Without Meconium	4	16	20	
Age ≥ 30 years				
With Meconium	18	4	22	29.25
Without Meconium	4	26	30	

Table 7: Stratification of Acidotic Cord Blood Gases in females with respect to Gestational Age (n = 100)

Study Group	Acidotic Cord Blood Gases		Total	Odd Ratio
	Yes	No		
Gestational Age < 40 Weeks				
With Meconium	24	4	28	28.00
Without Meconium	6	28	34	
Gestational Age ≥ 40 Weeks				
With Meconium	16	6	22	18.67
Without Meconium	2	14	16	

Table 8: Stratification of Acidotic Cord Blood Gases in Females with Respect to BMI (n = 100)

Study Group	Acidotic Cord Blood Gases		Total	Odd Ratio
	Yes	No		
BMI ≤ 28				
With Meconium	28	2	30	84.00
Without Meconium	4	24	28	
BMI > 28				
With Meconium	12	8	20	6.75
Without Meconium	4	18	22	

DISCUSSION

The objective of the research was to determine the association of acidic cord blood gases with meconium staining in amniotic fluid in females undergoing cesarean section. In this regard the present case control study was conducted at the Department of Obstetrics & gynecology Unit-III, Jinnah Hospital Lahore. One hundred females undergoing caesarean section who fulfilled the inclusion criteria were included in the study using probability consecutive sampling.

Ages of the patients enrolled in the research were between 18 and 40, (Mean age 28.84+7.02). The minimum gestational age was found 37 weeks and maximum gestational age was 42 weeks with mean and standard deviation was 39.14 ± 1.54 weeks. BMI of the patients ranged from 22 to 32 with a mean of 27.70 ± 2.67.

A study conducted in a hospital in Iran showed that out of 323 pregnancies with meconium-stained amniotic fluid at 36-42 weeks' gestation, 68 (21%) had a pH less than 7.20 in umbilical arterial blood, 21 (7%) had a pH less than 7.15, and only three newborns (0.9%) had true metabolic acidemia. At birth, of the 74 newborns with normal electronic fetal heart rate (FHR) tracings, eight (11%) had an umbilical arterial pH less than 7.20.

There was a significantly higher frequency of acidemia (defined as pH less than 7.20) in newborns with both baseline and periodic FHR abnormalities. Patients who had umbilical artery blood pH less than 7.20 had a statistically significant association with meconium stained liquor in contrast to the patients who had an umbilical artery blood gas pH more than 7.20. The results of this study are validated by our research which revealed the same results. However, there was no significant difference in the frequency of manifestation of meconium aspiration syndrome in the infants belonging to either group.[16]

In our study, 54% of patients in which parity was 1 and 46% of patients with parity of 2 or more. Acidotic cord blood gases were found in 48% patients while Acidotic Cord Blood Gases were not found in 52% patients. By comparing the presence of acidotic cord blood gases in females with or without meconium it was found that there was significant association of meconium staining and acidic cord gases with an OR = 21.00.

In a previously conducted case control study, meconium aspiration was seen to be present in a significant amount of patients who had meconium stained liquor during caesarean section. The rate of MAS was highest in patients whose gestational age was more than 37 weeks, and the majority of the patients with MAS were grouped in gestational age beyond 42 weeks. Factors independently associated with severe MAS were identified to be the following; thick meconium amniotic fluid, fetal tachycardia as seen on CTG, Apgar score ≤3 at 1 minute, and birth in a level III facility.[17]

Another study assessed two factors, cardiotocography and meconium staining of liquor and analysed them in relation to fetal acidemia. The study revealed that although the meconium staining of liquor doesn't always mean that the neonate is in distress and has acidemia, the absence of meconium staining in the

research was significantly seen to be associated with better outcomes for the neonate. Fetal acidemia was also predicted using the changes seen on cardiotocography and fetal heart rate abnormalities on CTG were linked to fetal acidemia and meconium staining both.[18] These results are in congruence with our research which also suggests that absence of meconium staining of liquor poses a risk of fetal acidemia, and presence of meconium staining is not always dangerous, however if seen, should make the doctor wary and cognizant that there might be ongoing fetal distress, so they can deploy resources to appropriately manage the baby.

CONCLUSION

After careful stratification of the results across factors such as maternal age, gestational age, BMI etc, we came upon the conclusion that the presence of meconium stained liquor at the time of caesarean is indeed associated with fetal acidemia and distress. A statistically significant association was found between the two and our study results are supported by multiple researches done in the past. Patients who exhibit meconium staining should be managed meticulously after they are delivered so as to minimize neonatal mortality especially due to meconium aspiration syndrome.

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MENSTRUAL DISORDERS IN UNDERGRADUATE MEDICAL STUDENTS

Nargis Iqbal,[1] Faiza Nisar,[2] Khulood Mukhtar,[3] Mehreen Nisar,[4] Nazia Nawaz,[5] M. Zia-ul- Miraj,[6] Amna Rafique,[7] Nosheen Salman[8]

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Abstract

Background: Menstrual disorders are quite common in early twenties and in stressful environment especially in medical schools. Sometimes these disorders are so severe to affect day to day activities and performances. Early detection and timely management is vitally important.

Objectives: To determine the Prevalence of Menstrual Disorders in undergraduate medical students and to provide appropriate suggestion and treatment in order to get good academic result.

Methods: A Quantitative Cross Sectional Study was carried out in Obstetrical and Gynae Department of Al-Aleem Medical College affiliated with Gulab Devi Educational Complex on 200 willing unmarried female students after approval from IRB. Non probability convince sampling technique was used 50 from each class.

Results: The response rate in this study was 100%, 25% from each 1st, 2nd, 3rd, and 4th year. The mean age of the students was 21+- 1.25 years, 67% were day scholar and only 33% hostel-lite, major chunk 71% were tension prone. Two third (67%) of the girls had regular menstruation, irregularity was observed in 33%. The mean age of menarche was 12.79+-1.21. The prevalence of menstrual disorders like Dysmenorrhea was 41.50%, Pre-menstrual syndrome 34.50% and menstrual flow abnormality was 24.00%. P-Value was highly significant in association between menstrual disorders and menstrual cycle.

Conclusions: In our study commonest disorders were dysmenorrhea, premenstrual syndrome and menstrual flow abnormalities. Early detection, Proper counselling sessions and time treatment could help the students both in health and academics leading to professional dedicated doctors for the Community.

Key Words: Female Medical Students, Dysmenorrhea, Premenstrual Syndrome, Menorrhagia, Oligomenorrhea, Amenorrhea.

Menstruation is defined as the" periodic uterine bleeding from the vagina throughout reproductive life of a female regulated by Hypothalamic Pituitary Ovarian Axis".[1,2] The average duration of menstrual cycle is 4-5 days, average flow of blood is 35-45 ml and 89% menstrual cycle last for 7-8 days and it may ranges between 21-35 days.[3] Menstrual disorders are quite common in puberty and young Girls especially medical students.[4,5] Common Menstrual disorders could be Menorrhagia- blood loss more than 80 ml/ cycle and 8 days on regular basis, Dysmenorrhea-blood loss accompanied with cramping pain, Premenstrual Syndrome- menstruation with mood swings e.g. stress, anxiety, headache, bloating that interfere routine work and lifestyle, Polymenorrhea frequent menstrual loss, cycle less than 21 days apart, Amenorrhea or Oligomenorrhea no periods or scanty periods.[6,7,8] The menstrual cycle is considered to be an important factor reflecting the functional and concentrating potentiality of female especially medical student. Various evidence based studies reported a strong

1. Nargis Iqbal
2. Faiza Nisar
3. Khulood Mukhtar
4. Mehreen Nisar
5. Nazia Nawaz
6. M Zia-UL- Miraj
7. Amna Rafique
8. Nosheen Salman

1-8. Al-Aleem Medical College/Gulab Devi Educational Complex, Lahore, Pakistan.

Correspondence:
Dr. Nargis Iqbal, Department of Gynaecology. Al-Aleem Medical College/Gulab Devi Educational Complex, Lahore, Pakistan.

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correlation between stress, anxiety and menstrual disorder.[9,10] Medical students belong to a great risk group for developing menstrual disorders because of their life style, increased study pressure, lack of proper sleep, irregular food intake and poor exercise habits. According to literature review most of the menstrual disorders could be prevented by early detection and proper timely management.[11,12] The objectives of the study were be to find out the prevalence of menstrual disorders in our students, so that remedies to eliminate in future can be streamlined in order to get good academic performance.

METHODS

After approval from Institutional Review Board, a quantitative cross sectional study was carried out on 200 willing unmarried girls, 50 from each 1st, 2nd, 3rd, and 4th year MBBS over a period of three months from 1st April to 30th June 2021. Non probability convince sampling technique was used, the purpose of the study, importance of menstrual disorders and how to fill the Performa was explained to all participants in 10-15 minutes. Data was collected by handing over 18 items self-structured (previously piloted) questionnaire to all 200 female medical students after informed consent apart from demographic data. Fifteen to twenty minutes later filled Performa's was collected from all participants. All the data was entered, rechecked and then analyzed using SPSS version 20. The Descriptive Statistics was used to check the frequency, percentage and responses of all quantitative variables. P-Value was calculated by using Chi-square test.

RESULTS

The response rate in this study was 100%, 25% from each 1st, 2nd, 3rd, and 4th year. The mean age of the students was 21±1.25 years, 67% were day scholar and only 33% hostel-lite, major chunk 71% were tension prone. Two third (67%) of the girls had regular menstruation, irregularity was observed in 33%. The mean age of menarche was 12.79±1.21. The prevalence of menstrual disorders like Dysmenorrhea was 41.50%, Pre-menstrual syndrome 34.50% and menstrual flow abnormality was 24.00%. Table l highlight the Menstrual cycle, Types of menstrual disorder, its nature

Table 1: *Menstrual Cycle & its Disorders (n=200)*

Cycle Length		
Menstrual Days	**No of students**	**Percentage**
< 21 days	25	12.50
21- 35	134	67.00
➢ 35	41	20. 50
Duration of bleeding		
1 – 2 days	23	11.50
3 – 5	143	71.50
➢ 5	34	17.00
No. of Pads/ Day		
1 – 2	39	19.50
3 – 5	135	67.50
➢ - 5	26	13.00
Menstrual Disorders		
Dysmenorrhea	83	41.50
Mild	19	22.89
Moderate	48	57.83
Severe	16	19.27
Pre-Menstrual Syndrome	69	34.50
Mood Swings	62	89.85
Headache	45	65.21
Migraine	19	27.53
Edema	18	26.08
Breast Tenderness	25	36.23
Depression	21	30.43
MenstrualFlow Abnormality	48	24.00
Menorrhagia	20	41.66
Poly-menorrhagia	8	16.67
Oligo-menorrhea	12	25.00
Amenorrhea	5	10.41
Metrorhagia	3	6.25

Table 2: *Association of Dysmenorrhea, PMS, Menstrual Flow Abnormalities with Menstrual cycle (n=200)*

Variables	**Dysmenorrhea**		
Menstrual Cycle		**Chi-square**	**P-Value**
Regular (n=134) **Irregular** (n=66)	83 (41.50%)	0.316	0.034
	Premenstrual	**Syndrome**	
Regular (n=134) **Irregular** (n=66)	69 (34.50%)	0.231	0.055
	Menstrual Flow	**Abnormalities**	
Regular (n=134) **Irregular** (n=66)	48 (24.00%)	0.512	0.047

and severity. Association of menstrual disorders with menstrual cycle were shown in Table ll.

DISCUSSION

Menstruation is a symbol of normal reproductive health, any abnormality may affect the physical, mental, social, psychological and executional wellbeing of an individual. Menstrual disorders are the major gynecological issues among adolescent and especially in medical students because of stressful environment.[13,14] In our study mean age of the students was 21 ±1.25 years tallying with other studies.[9,11] The 2/3rd of the girls (67%) were having regular menstrual cycle and in 1/3rd (33%) irregular menstrual cycle was observed, these findings were resembling with other studies.[13,14] The mean age of menarche in the study was 12.79± 1.21, which was mimicking with other researchers.[4,9]

Dysmenorrhea is defined as painful menstrual flow, quite prevalent in anxiety prone females and is supposed to be the commonest menstrual disorders[15]. It is divided into three categories mild (Able to perform routine activities) moderate (Require some medication) and severe (Absence from class/workplace plus medication. In our study the commonest menstrual disordered observed was dysmenorrhea its prevalence was 41.5% this was consistent with studies conducted by Kulshrestha S. and Kedar K.'[16,17] but differ from others who reported premenstrual syndrome was top in their studies.[9] Majority of the students (57.83%) in this study were suffering from moderate degree of dysmenorrhea and most of them were tension prone and only 19.27% required bunk from the class these findings were similar with other studies.[7,18] Premenstrual syndrome is quite common among menstrual disorders and is associated with certain Physical, Behavioral and psychological symptoms in second half of menstrual cycle due to increased progesterone in the blood stream.[19,20] In our study the prevalence of Premenstrual syndrome was 34.50%, second commonest menstrual disorder in this study and this finding was tallying with other researches,[8,21] but Indu V9, reported high prevalence (85.24%) in his study. Mood swings, headache, and breast tenderness were the commonest presentation in PMS apart from edema, migraine and depression, these findings are similar with other studies.[9,19,22] The menstrual flow abnormality is common usually after menarche and in stress-full environment. Medical students experienced a great degree of stress during academic years and suffer with different menstrual irregularities.[23] The Prevalence of menstrual flow abnormalities in our study was 24.0% which was tallying with other studies,[6,8] high prevalence was observed in a study conducted by Indu V9. Among the blood flow abnormalities menorrhagia was the commonest 41.66%, second was Oligomenorrhea 25% these findings were mimicking with other studies.[9,16,17] P- Value less than 0.05 is considered to be statistical significant, association between menstrual disorder and menstrual cycle highlight the significant P-Value in this study.

CONCLUSION

Menstrual irregularities are quit common in medical students, it may affect their health and academic performance. In our study commonest disorders were dysmenorrhea, premenstrual syndrome and menstrual flow abnormalities. Early detection, Proper counselling sessions and timely treatment could help the students both in health and academics leading to professional dedicated doctors for the Community.

Study Limitations As this study was carried out in one tertiary care hospital the results of the study could not be generalized.

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Conflicts of Interest I don't have any conflicts of interest regarding the study.

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Author's Contributions NI conceptualized the idea and made research proposal, FN collected the data, KM, NN, helped in entering data and made tables, MN, helped in analyzing data and Editing, ZM supervised the study.

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If you don't like something, change it. If you can't change it, change your attitude.

OUTCOME OF PRIMIGRAVIDA WITH UNENGAGED VERSUS ENGAGED FOETAL HEAD AT ONSET OF LABOUR

Rubeena Badar Khan,[1] Muntaha Sarosh,[2] Kalsoom Waheed,[3] Mahboob Alam Chishti,[4] Zareen Amjad,[5] Abid Hussain,[6]

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Abstract

Objectives: To compare the frequency of cesarean section in primigravidae who present with engaged foetal head and unengaged foetal head at the onset of labour.

Methods: A total of 120 patients after admission in labour room at onset of labourwere enrolled in the study keeping in view the inclusion criteria. Informed consent was taken. Patients with unengaged fetal head were placed in group A(n=60) and those with engaged fetal head in group B(n=60). Each patient was followed for the entire duration of labour according to standard protocol and course of labour was recorded on partogram. Caesarean section was performed in case of failed progress of labour, failed descent of head, non-reactive CTG (fetal distress) or meconium stained liquor. Frequency of caesarean section in both groups was noted. Labour outcome in terms of caesarean section and its indications were also evaluated. Data was entered in a predesigned proforma. SPSS version 21was used to analyze collected data.

Results: Frequency of cesarean section in Group A (primigravidae with unengaged fetal head at onset of labour) was recorded as18% (n=11) while 82% (n=49) delivered vaginally. In the Group B (primigravidae with engaged fetal head at onset of labour) 8% (n=5) delivered by caesarean section and remaining 92% (n=55) delivered vaginally. Thus it shows a significant difference in the mode of delivery between the two groups.

Conclusion: We concluded that the frequency of cesarean section in primigravidae with unengaged fetal head at onset of labour is significantly higher than engaged fetal head.

Key Words: Primigravidae, engaged fetal head, Unengaged fetal head at term, cesarean delivery.

Parturition is a process encompassing complete set of mechanisms from fetal head engagement to delivery of baby. Meanwhile it is also a risky time for mother and fetus especially in primigravida and needs vigilant assessment and timely interventions to avoid any expected and unexpected complications. Traditionally it is said that fetal head engagement occurs by 38 weeks of pregnancy in majority of primigravida woman1and is confirmatory evidence that pelvic inlet is adequate. Unengagement of head in Primigravida has long been considered a possible sign of cephalo-pelvic disproportion, and associated with high risk of obstructed labour and a predictor of cesarean section. Surgical interventions are quite higher, latent phase is prolonged and first stage is prolonged due to improper adaptation of fetal head and misdirection of uterine expulsive forces. Prolonged labour exposes mother to high risk of infection, ketosis and obstructed labour, while fetus is endangered by asphy-

1. Rubeena Badar Khan
2. Muntaha Sarosh
3. Kalsoom Waheed
4. Mahboob Alam Chishti
5. Zareen Amjad
6. Abid Hussain

1,2. Department of Obstetrics & Gynaecology Avicenna Medical College, Lahore.
3. *Department of Obstetrics &* Gynaecology, Services Hospital, Lahore
4. *Department of Surgery Avicenna Medical College, Lahore.*
5. *Department of Obstetrics &* Gynaecology, Sahiwal Medical College, Sahiwal.
6. Department of Cardic Surgery, Social Security Hospital, Lahore.

Correspondence:
Dr. Rubeena Badar Khan, *Department of Obstetrics &* Gynaecology Avicenna Medical College, Lahore.
E-mail: rubeenaabadarkhan@gmail.com

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xia and infection.[2] It is said by few researchers that Higher the fetal station at onset of labour more the risk of dysfunctional labour patterns and c/section due to arrest disorders and management of these patients by cesarean section has its financial effects and restriction of future family size for the patients.[3]

Overall mortality rate from cesarean section is 6/100000, that is 6-7 times higher than vaginal delivery. Cesareans done after a trial of labour have higher rates of mortality and morbidity as compared with vaginal delivery or elective cesarean section.[4] Although majority of researchers found that unengaged head at term or onset of labour in primigravidae entitles them as a high risk patients as result of their studies showed higher rate of c/sections and other mentioned complications[4,5] but many researchers also concluded that unengaged fetal head can be delivered vaginally[1,4,5] and engaged fetal head does not affect mode of delivery,[6] generating a question mark on significance of fetal head engagement in relation to mode of delivery.

We wanted to conduct this study as existing literature has a grey area and it is not conclusive whether unengaged head in primigravidae is associated with increased c/section rate, so this study will help us to establish the relationship of head level in early active labour in nulliparas with mode of delivery and the possible high risk cases could be identified early. It will help us to optimize patient management in best interest of patients based on evidence.[5,6]

If high risk patients can be predicted at the onset of labour they can be offered cesarean section instead of facing prolonged course of labour to avoid unnecessary time and morbidity of prolong labour, failed operative vaginal delivery followed by late cesarean delivery with increased cost and complications. Secondly if identified early; these high risk Primigravida would be referred to tertiary care hospital for safe delivery.[5,6]

Engagement: It is defined as the stage at which widest part of the fetal head has passed through the pelvic inlet. Engaged fetal head is the head at or below 0 station on pelvic examination. Foetal head at- 3,-2 or -1 is considered as unengaged head.

Cesarean Section: Operative delivery performed through an abdominal incision for the indications like fetal distress during labour (assessed by CTG), failure to progress (assessed by partogram, cervical dilatation <1 cm/4 hrs) & meconium stained liquor (visual assessment on p/v examination and liquor on sterile pad) and others.

METHODS

Outcome of Primigravida with unengaged versus engaged head at onset of labour: was conduc-ted in the Department of Obstetrics & and Gynaecology, Avicenna hospital Lahore for the period of one year, from January2020 to December 2020. Primigravida at term (37-41 weeks) with cephalic presentation, Singleton Pregnancy & estimated fetal weight 2.5-3.8 kg (all assessed by ultrasound) with onset of uterine contractions and cervical dilatation of 1.5 to 3cm were included in the study. The exclusion criteria was patients with placenta previa (diagnosed by ultrasound), IUGR (diagnosed on Doppler Ultrasound), previous uterine surgery, multiple pregnancy (diagnosed on ultrasound), fetal distress (On CTG) at time of admission, spinal deformity, antenatal h/o medical disorders (PIH, GDM, Thyroid disorder).

Patients were selected after their admission in labour room at the onset of labour. Non-Probability purposive sampling technique was used. Sample size of 120cases (60 in each group) was estimated using 5% level of significance after taking informed consent and reassuring patients regarding expertise, care and confidentiality. A Prospective cohort study was carried out. Patients with unengaged fetal head were placed in group A and those with engaged fetal head in group B. Each patient was followed throughout the labour; bishop scoring, uterine contractions monitoring and CTG was done at regular intervals according to standard protocols and labour was augmented with ARM or oxytocin infusion if needed, course of labour was recorded on Partogram, c/section was done in case of failed progress of labour, non-reactive CTG (fetal distress) or meconium stained liquor. All the required data was entered in Proforma that included labour

outcome in terms of c/section and its indications.

The collected data was transferred and analyzed using SPSS version 21. The quantitative variable like age was analyzed by measuring mean and standard deviation. Qualitative variables like c/section were measured by frequency and percentage; data was stratified for use of oxytocin in both groups. Relative risk>1 was considered significant.

RESULTS

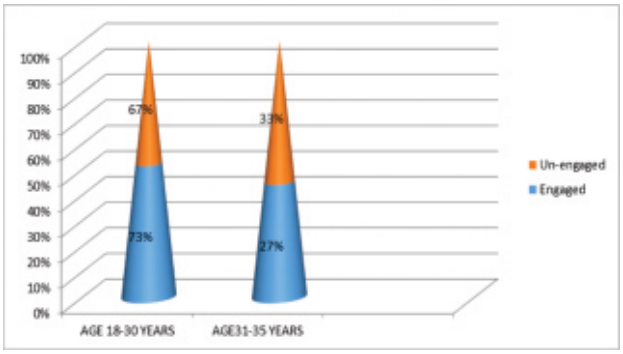
A total of 120 cases (60 in each group) fulfilling the inclusion criteria were enrolled to compare the frequency of cesarean section in primigravidae with engaged and unengaged fetal head at onset of labour.

Age distribution of the patients in both groups was as follows, 73% (n=44) in engaged and 67% (n=40) in un-engaged group were found to be in 18-30 years of age group while remaining 27% (n=16) in engaged and 33% (n=20) in un-engaged group were between 31-35years of age , Mean+ SD was calculated as 27.54 +3.21 and 27.54+3.21 years respectively. (Table No. 1)

Frequency of cesarean section in primigravidae with engaged and unengaged fetal head was recorded as 8%(n=5)and 18%(n=11) respectively and remaining 92% (n = 55) in engaged group and 82% (n=49) in unengaged group delivered vaginally. Relative risk was 0.5037, Z statistic was 2.073 while P value was calculated as 0.0382, which shows a significant difference between the two groups. (Table No. 2)

Table 1: Age Distribution (n=120)

Age (in years)	Engaged (n=60)		Un-engaged (n=60)	
	No. of patient	%	No. of patient	%
18-30	44	73	40	67
31-35	16	27	20	33
mean±sd	27.54±3.21		27.54±3.21	



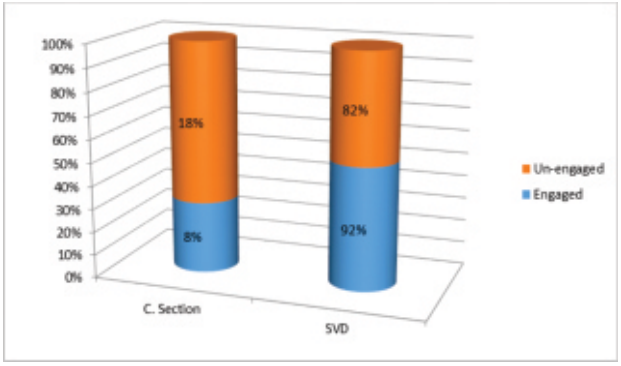
Stratification for cesarean section with regard to use of oxytocin was recorded in Table No. 3, where out of 5 cases in engaged group 3 were augmented with oxytocin, on the other hand 10 out of 11 women with an unengaged foetal head were augmented. (Table No. 3)

Table 2: Mode of Delivery in Primigravida with Engaged and Unengaged Fetal Head(n=120)

Mode of Delivery	Engaged (n=60)		Un-engaged (n=60)	
	No. of patient	%	No. of patient	%
C. Section	5	8	11	18
SVD	55	92	49	82

Relative risk = 0.5037
Z statistic = 2.073
P value = 0.0382

Mode of Delivery in Primigravida with Engaged and Unengaged fetal head(n=120)



When we evaluated different indications for caesarean section in each group; Failed progress of laour and Failed descent of foetal head in women with unengaged foetal head were the significant ones, 4 and 3 patients (n=11) respectively, as shown in Table 4.

DISCUSSION

Table 3: Need of Augmentation with Oxytocin(n=16)

Use of oxytocin	Engaged (n=5)	Un-engaged (n=11)
Yes	3	10
No	2	1

Labour is an important event with a unique experience in a woman's life, which gives her the greatest

satisfaction as she delivers her own child. Much of energy is expended during this time. Hence the term 'labour' used to describe this process. Primigravida are

Table 4: Indications for Cesarean Section(n=16)

Indication	Engaged (n=5)	Un-engaged (n=11)
Failed progress of labour	1	4
Fetal Distress	2	2
Meconium stained liqour	1	2
Failed descent of head	1	3

one of the importantgroups at risk and high fetal station in primigravidas in labouror near term may indicate a threat to the normal progress of labour because of cephalo-pelvic disproportion or obstruction of the fetal passageway through pelvis by tumor or the placenta. Unengaged head in primigravida at term raises apprehension thus engagement of fetal head is considered the cardinal observation in a pregnant woman at term or at onset of labour.

In our study, out of 120 cases (60 cases in each group), frequency of cesarean section in primigravidae with engaged and unengaged fetal head at onset of labour was recorded as 8% (n=5) and 18% (n=11) while remaining 92% (n=55) and 82% (n=48) respectively delivered vaginally, which shows a significant difference between the two groups. Our findings are in agreement with Chaudhry S5 who also concluded that operative delivery rate was more in unengaged vertex group i.e 16.8% as compared to 5.3% in engaged head group (p=0.0000). Another study by Iqbal S6 concluded that c/section rate was 5% in unengaged head and 15% in engaged head group (p=0.00), which is in contrast to our findings. Sally Segal[7] came up with a view that an engaged fetal head does not affect mode of delivery showing c/section rate of 13.8% (95% CI 0.95-2.3; p=0.08)and same conclusion was drawn by Salim NA et al8.Study by Noura9 shows a vaginal delivery rate of 79.3% and c/section rate of 20.7% in patient with unengaged head p=0.06.

Ambwani et al[10] stated that the rate of caesarean section was 34% in women with unengaged head at term thus considering high foetal head as a risk factor for dysfunctional labour and a strong predictor of caesarean section. Major indications for caesarean section were failed progress of labour and failed descent of head as was evident in the current study also. According to Debby11, 82.9% of women with unengaged head delivered vaginally and 17.1% had a caesarean section which is quite comparable to ours as well.

Friedman et al[12] stated that in primigravidas with high head, latent phase is prolonged and mean duration of labour was 14.4 hrs. In our series, in majority of the cases labour also lasted more than 12 hours. Major causes in these patients were improper adaptation of fetal head, high station at the beginning of labour, deflexed head, misdirection of uterine expulsive forces, high incidence of rupture of membranes and ineffective uterine contractions.

However there were no neonatal deaths and there were no serious maternal complications except third degree perineal tear. These results were consistent with the results of many studies.[5,9,10] There was greater need for augmentation with oxytocin in women with unengaged groupit is evident in our study also. According to a study by Saqib et al[13] the most important predictor for normal vaginal delivery in women with unengaged head was natural onset of labour and this was also observed in our study where women with unengaged head with spontaneous onset of labour were more likely to deliver vaginaly. Thus nulliparous women with unengaged foetal head should be induced cautiously along with counseling for an increased need for caesarean section.[14] The cesarean section after trial of labour carries more risk of maternal as well as neonatal morbidity and mortality.[15]

In light of the above findings, we are of the view that "There is difference in rate of c/section in Primigravide with unengaged versus engaged fetal head at onset of labour" and high risk women can be predicted at the onset of labour. They can be offered cesarean section instead of facing prolonged course of labour to avoid unnecessary time and morbidity of prolong labour, failed operative vaginal delivery followed by late cesarean delivery, increased cost and complications.

CONCLUSION

We concluded that the frequency of cesarean section in primigravidae with unengaged fetal head at onset of labour is significantly higher than engaged fetal head

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POSTOPERATIVE PAIN AND APPETITE IN PEDIATRIC PATIENTS UNDERGOING MONOPOLAR TONSILLECTOMY AND COLD STEEL TONSILLECTOMY

Shuman Roy,[1] Ali Husnain Sheikh,[2] Muhammad Dawood Saleem,[3] Nighat Arif,[4] Najaf Abbas,[5] Gull e Zahra Kamla[6]

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Abstract

Objectives: To compare postoperative pain and appetite in pediatric patients undergoing partial tonsillectomy via monopolar diathermy and total tonsillectomy via cold steel technique.

Methods: A total of 102 children aged 2 to 10 years admitted for total or partial tonsillectomy were considered for this study. In Group-A, all children had partial tonsillectomy (PT) with monopolar cautery (n=55) and total tonsillectomy (TT) was done using cold steel technique in Group-B (n=47). All cases were discharged and sent home on day-1 and were asked to follow up on day-10. In terms of post-operative outcome, all children were assessed for post-operative pain and appetite.

Results: In a total of 102 children, 56 (54.9%) were male. Overall, mean age was noted to be 4.4+2.6 years. There were 64 (62.7%) children who belonged to rural areas of residence. Significant difference was noted in terms of severity of pain between children of both study groups as there were 13 (27.7%) children in Group-B who had severe pain in comparison to 6 (10.9%) in Group-A (p=0.0471). In terms of appetite, 41 (74.5%) children in Group-A reported good appetite in comparison to 14 (29.8%) in Group-B. In terms of appetite there was a significant difference between both groups (p<0.0001).

Conclusion: Children undergoing monopolar tonsillectomy were having significantly less severity of pain and significantly improved appetite in comparison to those who underwent cold steel tonsillectomy.

Keywords: Tonsillectomy, pain, appetite.

Tonsillectomy is described as surgical excision of the palatine tonsils. Tonsillectomy is a routine procedure done by Ear, Nose and Throat (ENT) specialists all around the globe. Pediatric age groups are most commonly involved in tonsillectomy.[1] Data from United States of America reveals that around half a million tonsillectomy procedures are performed annually among children aged below 15 years.[2]

Most commonly seen indications for tonsillectomy include recurrent attacks of sore throat and obstructive sleep apnea (OSA).[3] There is no consensus about minimum age for performing tonsillectomy in children but researchers suggest children even younger than 3 years to have safe outcomes following tonsillectomy.[4] Complications like bleeding, velopharyngeal insufficiency and dehydration may occur after tonsillectomy but one important concern following tonsillectomy in younger age groups is inability of the children to eat properly.[5] A systemic review evaluating 6 studies comparing effectiveness of partial tonsillectomy (PT) versus total tonsillectomy (TT) revealed that children who underwent PT were having more favorable outcomes in comparison to those who had TT. The systemic review also found that PT was linked

1. Shuman Roy
2. Ali Husnain Sheikh
3. Muhammad Dawood Saleem
4. Nighat Arif
5. Najaf Abbas
6. Gull e Zahra Kamla

1-3. Akhtar Saeed Medical and Dental College, Lahore
4. Islamic International Medical College
5. Islam Medical College Sialkot
6. Fatima Memorial Medical and Dental College, Lahore

Correspondence:
Dr. Shuman Roy, *Senior Registrar Akhtar Saeed Medical and Dental College, Lahore*

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with less emotional distress but there was no statistically significant difference in terms of quality of life between the two approaches. It was also seen that children undergoing PT started normal diet 4 days earlier than those who underwent TT.[6]

There is scarcity of local literature regarding various outcome aspects of different tonsillectomy approaches so the present study was designed to compare postoperative pain and appetite in pediatric patients undergoing partial tonsillectomy by monopolar cautery and total tonsillectomy by and cold steel method.

METHODS

This prospective study was conducted from 19/08/2021 to 18/08/2021 at Akhtar Saeed Trust Hospital Lahore.

Approval from institutional ethical committee was acquired. Informed written consent was sought from all study participants or their parents/ guardians. A total of 102 children aged 2 to 10 years admitted for total or partial tonsillectomy were considered for this study. Children known to have mental retardation, congenital heart disease or herediatary disorders were not enrolled. Children having sickle cell disease, musculoskeletal disorders, hearing loss or any sort of chronic pain were also excluded. Children having past history of any kinds of surgery were also not included.

In Group-A, all children under went PT with monopolar cautery was performed (n=55) while TT was done using cold steel technique in Group-B (n=47).[7] Post-procedure, all children were prescribed oral analgesic and oral antibiotic for 7 days. All cases were discharged and sent home on day-1 and were asked to follow up on day-10. In terms of post-operative outcome, all children were assessed for post-operative pain and appetite. Post-operative pain was assessed using facial pain scale where pain was categorized in 3 categories. Mild pain was labeled with a score between 1 to 3, moderate with scores 4 to 6 while severe pain was labeled showing scores between 7 to 10. Post-operative appetite was measure using visual analog scale scaling between 1 to 10cm.[15] For this, parents/ guardians were asked to mark the location that represented the appetite of their child. The distance of less than 4 cm was labeled as "poor appetite", between 4 to 7 cm as "acceptable appetite" and between 7 to 10 cm as "good appetite".

All study information was recorded on a customized proforma designed for this research. Data was analyzed using SPSS version 26.0. Frequency and percentages were calculated for qualitative variable while mean and standard deviation represented quantitative data. Chi-square test was used to observe significant difference regarding study variables in between both study groups, considering p value < 0.05 as significant.

RESULTS

In a total of 102 children, 56 (54.9%) were male. Overall, mean age was noted to be 4.4+2.6 years while 64 (62.7%) were aged less than 5 years. Table 1 is showing distribution of characteristics between children of both study groups and no statistically significant difference was noted ($p>0.05$).

Table 2 is showing comparison of outcome variables in between both study groups. Significant difference was noted in terms of severity of pain in between children of both study groups as there were 13 (27.7%) children in Group-B who had severe pain in comparison to 6 (10.9%) in Group-A ($p=0.0471$). In terms of appetite, 41(74.5%) children in Group-A had reported good appetite in comparison to 14 (29.8%) in Group-B. In terms of appetite, there was significant difference in between children of both study groups ($p<0.0001$).

Table 1: *Characteristics of Children in Both Study Groups*

Characteristics		Group-A (n=55)	Group-B (n=47)	P-Value
Gender	Male	31 (56.4%)	25 (53.2%)	0.7483
	Female	24 (43.6%)	22 (46.8%)	
Age (years)	<5	34 (61.8%)	30 (63.8%)	0.8341
	≥5	21 (38.2%)	17 (36.2%)	

DISCUSSION

Tonsillectomy is a commonly performed procedure all around the world. It is perceived as a minor procedure as cases are usually sent home on the same day following surgery.[8] Up until 1930s, PT was a commonly considered approach but there was always fear of regrowth. On the other hand, TT has always been considered to be followed by significant amount of pain, less appetite and occasional hemorrhage. In TT, tonsillar capsule is completely removed while in PT, the capsule is preserved while tonsils are shaved away adopting various instruments.[9]

Table 2: Comparison of Outcome Variables in Both Study Groups

Outcome		Group-A (n=55)	Group-B (n=47)	P-Value
Severity of Pain	Mild	16 (29.1%)	7 (14.9%)	0.0471
	Moderate	33 (60.0%)	27 (57.4%)	
	Severe	6 (10.9%)	13 (27.7%)	
Appetite	Poor	4 (7.2%)	11 (23.4%)	<0.0001
	Acceptable	10 (18.2%)	22 (46.8%)	
	Good	41 (74.5%)	14 (29.8%)	

In the present study, children having PT were operated using monopolar cautry while cold steel technique was adopted for children undergoing TT. It was seen children in monopolar tonsillectomy groups were having significantly less severity of post-operative pain (p=0.0471) as well as significantly better appetite (p<0.0001) in comparison to those children who underwent cold steel tonsillectomy. Handler SD et al evaluating 1445 who underwent TT, post-surgery bleeding rate was observed to be 2.6% while the authors concluded that pain is inevitable in the post-surgery period which can significantly impair appetite of the patients.[10] El Sayed Ahmad et al from Lebanon concluded that patients undergoing monopolar tonsillectomy were noted to have significantly improved appetite and less severity of pain in comparison to those who underwent cold steel technique which is very similar to what we noted in the present research.[7]

Eriksson M et al analyzing children undergoing tonsillectomy adopting various approaches revealed that children undergoing TT were having concerning post-surgery pain and less appetite.[8] In Pakistan, our study is the 1st one comparing monopolar approach in PT cases and cold steel approach in TT. Koltai C et al comparing children undergoing TT and PT regarding outcomes found that children undergoing PT were having significantly better outcomes in terms of safety and reliability as it was seen that these children were having less post-srugery pain, comparatively faster recovery and improved quality of life.[11] A study from Brazil done by Vieira et al concluded that children under 12 years of age undergoing monopolar electrocautry were having clinically significantly less post-surgery pain without any additional rates of complications.[12]

It is a fact that suitable post-surgery oral intake of food and liquids following any approach of tonsillectomy is vital as it helps promoting recovery of the children undergoing tonsillectomy.[13,14] To elaborate this further, dehydration can initiate a vicious cycle of decreased intake of fluids which can in turn further lead to less food intake and subsequently contribute to post-surgery morbidity and recovery.[14]

Our study had some limitations as well. As per protocols of the study, we were limited to evaluating outcomes like severity of pain and appetite, we were unable to record any other morbidity or complications. We only noted short-terms outcomes in the present study, so studies should also be conducted evaluating long-term outcomes following different techniques and approaches of tonsillectomy. As this was a single center study with a relatively small sample size, the findings of this study need further evaluation by conducting more multi-center studies involving larger sample sets.

CONCLUSION

Children undergoing partial tonsillectomy by monopolar tonsillectomy were having significantly less severity of pain and significantly improved appetite in comparison to those who underwent total technique by cold steel methods.

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FOLIC ACID SUPPLEMENTATION FOR PREVENTION OF PRETERM DELIVERY IN FEMALES PRESENTING IN THIRD TRIMESTER OF PREGNANCY

Shamila Ijaz Munir,[1] Mariam Riaz,[2] Yasmeen M. Din,[3] Amna Ahsan,[4] Saira Fayyaz[5]

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Abstract

Background: Preterm birth complicates 12% of deliveries and accounts for many fetal anomalies. During pregnancy, fetal growth causes an increase in the total number of rapidly dividing cells, which leads to increased requirements for folate and subsequent decrease in serum folate concentration which has been proposed as trigger for preterm delivery. Many recent studies claimed that folic acid supplementation in pregnant women during 3rd trimester resulted in considerably lower frequency of preterm delivery and advocated routine folic acid supplementation in future.

Objective: The objective of this study is to determine the frequency of preterm delivery with folic acid supplementation in females presenting during third trimester of pregnancy.

Methods: This study is descriptive case series and was conducted in Obstetrics and Gynaecology department of Sir Ganga Ram Hospital, Lahore from 1st September, 2019 to 28th Feb,2020. Total of 170 pregnant women aged between 18-40 years presenting between 24-28 weeks of gestation were enrolled after informed consent. These patients were advised to take folic acid 5mg/day until delivery. Outcome variable was frequency of preterm delivery which was labeled if the delivery occurred before 37 completed weeks of gestation as calculated from last menstrual period.

Results: The mean age was 26.7±4.9 years. There were 139 (81.8%) primiparas and 31 (18.2%) multiparas. The mean gestational age was 26.0±1.4 weeks while the mean BMI was 24.5±3.3 Kg/m2. Preterm delivery occurred in 11 (6.5%) patients. There was no statistically significant difference in the frequency of preterm delivery across various subgroups based on patient's age (p-value=0.999), parity (p-value=0.996), gestational age (p-value=0.959) and BMI (p-value=0.896).

Conclusion: Folic acid supplementation in pregnant women in 3rd trimester decreases the occurrence of preterm delivery along with associated maternal and neonatal morbidity.

Key Words: Preterm Delivery, Folic Acid, 3rd Trimester.

Preterm birth is the leading cause of neonatal mortality and complicates 12% of deliveries worldwide. This incidence is even higher in developing countries. Preterm births account for 75% of perinatal mortality and more than half the long-term morbidity. Although most preterm babies survive, they are at increased risk of neurodevelopmental impairments, respiratory distress and gastrointestinal complications.[1] Preterm birth also causes one in three children with visual impairment, one in five with mental retardation, and almost half with cerebral palsy. These short-and long-term sequelae make the prevention of preterm birth a need of hour and an utmost public health priority.[2]

During pregnancy there is increased requirements of folate for development and growth of fetus. Folate (vitamin B9) is an essential nutrient that is required for DNA replication and as a substrate for a range of enzymatic reactions involved in amino acid synthesis

1. Shamila Ijaz Munir
2. Mariam Riaz
3. Yasmeen M. Din
4. Amna Ahsan
5. Saira Fayyaz

1-4. Ganga Ram Hospital, Lahore.
5. Lahore General Hospital, Lahore.

Correspondence:
Prof. Dr. Shamila Ijaz Munir, *Ganga Ram Hospital, Lahore.*

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and vitamin metabolism. Folate deficiency has been associated with abnormalities in both mothers (anemia, peripheral neuropathy) and fetuses (congenital abnormalities). Dietary supplementation with folic acid around the time of conception has long been known to reduce the risk of neural tube defects (NTDs) in the offspring.[3] Inadequate folate intake leads to decrease in serum folate concentration, resulting in a decrease in erythrocyte folate, a rise in homocysteine concentration, and megaloblastic changes in the bone marrow and other tissues with rapidly dividing cells.[4]

Supplementation with folic acid is internationally recommended from preconception until 12 weeks of pregnancy. Another recommendation by the World Health Organization is that women of reproductive age should take weekly iron and folic acid supplements, especially in populations where the prevalence of anemia is high, i.e. above 20%.[5]

Studies have suggested that supplementary folic acid in early-to-mid pregnancy may be protective for neural tube defects, low birth weight and small for gestational age neonates.[6] The beneficial effect of folic acid intake before and shortly after conception is well recognized, whereas the effect of supplementation during the second and third trimesters is controversial and poorly documented.[7] Indirect evidence suggests that folate may indeed be important in the timing of labor. In observational studies, a shorter duration of pregnancy has been associated with low serum folate levels and with the absence of folic acid intake during pregnancy.[8] One study has showed that the frequency of preterm delivery was only 7.6% with folic acid intake.[9] But another study showed it to be 22.6%.[10] Preterm delivery is a leading cause of perinatal morbidity and mortality in our country therefore its association with folic acid supplementation is of major interest.[11]

Rationale of this study is to assess the frequency of preterm delivery with folic acid supplementation in females presenting during the third trimester of pregnancy. Literature has shown that folic acid can be helpful in preventing preterm delivery. But evidence regarding folic acid intake during the third trimester is scarce. Even there is no local literature/data available which can help in obtaining the evidence regarding the role of folic acid supplementation during the third trimester. Moreover, the available literature showed controversial evidence in this regard. So through this study we wanted to confirm the role of folic acid supplementation in pregnant females to prevent preterm delivery. This will help us to achieve local evidence, improve our practice and in making better public health policies at national level.

METHODS

Females of age 18-40 years presen-ting for routine antenatal check up at gestational age of ≥ 24weeks and ≤28 weeks (on LMP) were included.

Females with existing risk factors for preterm delivery like, multiple pregnancy(on USG), gestational or essential hypetension (BP ≥140/90mmHg), preeclampsia (BP ≥140/90mmHg + proteinuria ≥ +1 on dipstick), eclampsia (convulsions with BP≥ 140/90mmHg), gestational or chronic diabetes (BSR>186mg/dl), deranged LFTs (AST>40IU, ALT>40IU), deranged RFTs (serum creatinine>1.2mg/dl), PPROM or pla-cental abruption (on USG) were excluded from study.

There demographic profile i.e. name, age, gestational age, parity, BMI was noted. Females were advised to take folic acid supplementation 5 mg/day till delivery. Females were advised to present in the labour room in case of active labour. If a female presented in active labour and underwent delivery before 37 weeks of gestation, then preterm delivery was labeled. All this information was recorded on performa.

All the collected data was entered and analyzed through SPSS version 21.0. Numerical variables; age, gestational age and BMI have been presented by mean±SD. Categorical variables i-e parity and preterm delivery have been presented as frequency and percentage. Data has been stratified for age, parity, gestational age at presentation and BMI to address effect modifiers. Post-stratification chi-square test has been applied with p-value ≤0.05 considered as significant.

RESULTS

The age of the patients ranged from 18 years to 40 years with a mean of 26.7±4.9 years. Majority (n= 92, 54.1%) of the patients were aged between 25-34 years followed by 18-24 years (36.5%) and 35-40 years (9.4%). There were 139(81.8%) primiparas and 31(18.2%) multiparas. The gestational age of the patients ranged from 24 weeks to 28 weeks with a mean of 26.0±1.4 weeks. The BMI of these patients ranged from 21.0 Kg/m^2 to 34.8 Kg/m^2 with a mean of 24.5±3.3 Kg/m^2. Majority (n=115, 67.7%) of the patients had normal BMI while 32(18.8%) patients were overweight and another 23(13.5%) patients were obese as shown in Table 1.

Preterm delivery occurred in 11(6.5%) patients as shown in Table 2. There was no statistically significant difference in the frequency of preterm delivery across various subgroups based on patient's age (p-value = 0.999), parity (p-value=0.996), gestational age (p-value=0.959) and BMI (p-value=0.896) as shown in Table 3.

DISCUSSION

Preterm birth is the dominant cause of fetal morbidity and mortality and accounts for respiratory distress syndrome, necrotizing enterocolitis, neurodevelopment behavior abnormalities and almost half with cerebral palsy.[2] During pregnancy, rapid fetal growth leads to increased requirements for folate and subsequent decrease in serum folate concentration[4] which has been proposed as a trigger for preterm delivery.[6] Therefore it is not surprising that many recent studies claimed that folic acid supplementation in pregnant women during the 3rd trimester resulted in considerably lower frequency of preterm delivery and advocated routine folic acid supplementation in future.[9,10] These studies have varied in the exposure of interest. Some have examined folic acid sources from supplements or diet, some have measured folate in serum and others have been trend analyses based on folic acid fortification of the food supply which has led to variability of results and controversy.[7-10] Moreover, there was no such local published material which necessitated the present study.

Table 1: Baseline Characteristics of Pregnant Women Receiving Folic Acid Supplementation

Characteristics	Study Sample n=170
Age (years)	26.7±4.9
18-24 years	62 (36.5%)
25-34 years	92 (54.1%)
35-40 years	16 (9.4%)
Parity	
Primiparas	139 (81.8%)
Multiparas	31 (18.2%)
Gestational Age (weeks)	26.0±1.4
24-26 weeks	94 (55.3%)
26-28 weeks	76 (44.7%)
BMI (Kg/m^2)	24.5±3.3
20-25 Kg/m^2	115 (67.7%)
25-30 Kg/m^2	32 (18.8%)
30-35 Kg/m^2	23 (13.5%)

Table 2: Frequency of Preterm Delivery in Pregnant Women Receiving Folic Acid Supplementation

Preterm Delivery	Frequency (n)	Percentage (%)
Yes	11	6.5
No	159	93.5
Total	170	100.0

Table 3: Stratification of Preterm Delivery across Various Subgroups of Pregnant Women Receiving Folic Acid Supplementation

Characteristics	N	Preterm Delivery n (%)	P-value
Age (years)			
18-24 years	62	4 (6.5%)	0.999
25-34 years	92	6 (6.5%)	
35-40 years	16	1 (6.3%)	
Parity			
Primiparas	139	9 (6.5%)	0.996
Multiparas	31	2 (6.5%)	
Gestational Age (weeks)			
24-26 weeks	94	6 (6.4%)	0.959
26-28 weeks	76	5 (6.6%)	
BMI (Kg/m^2)			
20-25 Kg/m^2	115	7 (6.1%)	0.896
25-30 Kg/m^2	32	2 (6.3%)	
30-35 Kg/m^2	23	2 (8.7%)	

Chi-square test, observed difference was statistically insignificant

In the present study, the mean age of the patients was 26.7±4.9 years. We observed that the majority (54.1%) of the patients were aged between 25-34 years followed by 18-24 years (36.5%) and 35-40 years (9.4%). A similar mean age of 27.6±5.9 years has been reported by Yasmin et al. (2017) among pregnant women receiving folic acid supplementation at Jinnah Postgraduate Medical Centre, Karachi.[12] Li et al. (2014) reported comparable mean age of 25.6±3.9 years among Chinese women.[13] A similar age groups distribution has been reported by Shaw et al. (2011) who reported that 52.2% of the American women receiving folic acid supplementation during pregnancy were aged between 25-34 years followed by 18-24 years (34.3%) and 35-40 years (13.5%).[14]

In the present study, there were 139(81.8%) primiparas and 31(18.2%) multiparas. Zheng et al. (2016) reported that 80.3% of Chinese women receiving folic acid supplementation during pregnancy were primiparas.[15] A higher frequency of primiparas (91.9%) among Chinese such women has also been reported by Li et al.[13]

We observed that the mean BMI was 24.5±3.3 Kg/m^2. Majority (67.7%) of the patients had normal BMI while 32 (18.8%) patients were overweight and another 23(13.5%) patients were obese. A similar mean BMI of 23.9±4.1 Kg/m^2 has been reported by Yasmin et al. among such women at Jinnah Postgraduate Medical Centre, Karachi.[12] Shaw et al. reported it to be 24.9±5.7Kg/m^2 in American such women.[14] Sengpiel et al. (2014) reported similar distribution of normal (68.0%), overweight (24.0%) and obese (8.0%) pregnant women receiving folic acid supplementation in Sweden.[16]

In the present study, preterm delivery occurred in 11(6.5%) patients. A similar frequency of preterm delivery (7.6%) has been reported by Czeizel et al. (2010) in Hungarian pregnant women taking folic acid during 3rd trimester.[9] Shaw et al. reported that preterm delivery occurred in 6.0% of American pregnant women receiving folic acid during third trimester.[14] Similar results have also been reported by Bukowski et al. who reported the frequency of preterm delivery with folic acid intake to be 7.2%.[17] This reported frequency of preterm delivery is much lower as compared to that reported by Badshah et al. (22.8%), Imran et al. (17.9%), Lone et al. (15.7%) and Jaleel et al. (14.5%) in untreated pregnant women from various centres in Pakistan.[18-21]

The present study is first of its kind in local population and has found that preterm delivery occurred in only 6.5% of pregnant women receiving folic acid supplementation during 3rd trimester which is considerably low compared to frequency of preterm labor in untreated population reported in literature and favors routine folic acid supplementation of pregnant women in third trimester to decrease the occurrence of preterm delivery along with associated maternal and neonatal morbidity. In Pakistan, antenatal Iron and Folic acid supplements (elemental iron 60 mg and folic acid 0.5 mg) are distributed free of cost by maternal and child health services through the existing primary healthcare system including health facilities and the community health worker programs. However, the overall level of consumption of antenatal Iron and Folic acid supplements at any stage during pregnancy is currently low in Pakistan (44%), and is even lower for rural women (38%).[22] Keeping in view the significance and potential benefits of folic acid supplementation, it is desirable that folic acid consumption during pregnancy should be encouraged through public awareness and patient education during antenatal visits.

A very important limitation to our study was that we didn't include a control group which would have helped to compare the frequency of preterm delivery with and without folic acid supplementation and could have established the role of folic acid more clearly. Such a randomized controlled trial is imperative and is highly recommended in future research.

CONCLUSION

Our study concluded that preterm delivery occurred in only 6.5% of pregnant women receiving folic acid during 3rd trimester which is considerably low compared to frequency of preterm delivery in untreated population reported in literature. This favors routine

folic acid supplementation of pregnant women in their 3rd trimester to decrease the occurrence of preterm delivery along with associated maternal and neonatal morbidity.

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THE OUTCOME OF A COMPARATIVE STUDY OF LAPAROSCOPIC VERSUS OPEN CHOLECYSTECTOMY IN THE MANAGEMENT OF ACUTE CHOLECYSTITIS

Abdul Majeed,[1] Zain Tayyab,[2] Imran Yousuf,[3] Farooq Ahmed,[4] Aslam Javed[5]

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Abstract

Background: Since the invention of laparoscopy in 1987, it has been a debatable issue whether laparoscopic cholecystectomy/ open cholecystectomy is better and superior in the management of acute cholecystitis;not responding to conservative management.A systematic review and metanalysis is hereby done to find out which one of two interventions is better in management of acute cholecystits when surgicallty intervened. The survey was done by manual performas filling individually considering acute cholecystitis as a pivot of the study.[35,40]

Methods: An approval from hospital ethics committee was attained. A systematic review with meta analysis of trials for comparison of open versus lapaqroscopic cholecystectomy in patients with AC was performed and evaluated . Electronic media searches were performed keeping Pubmed. Cochrane central register of controlled trials (CCTR) & Medline in use. The open hand perform containing open/closed question was distributed among patients as well as surgeons free of restrictions .

Results: The inclusion of 2 trials was brought under consideration with a total of 513 patients by collecting data from various government teaching hospital in Lahore (Pakistan) in last 5 years. 287 in the OC and 213 in the LC groups. 13 patients left the hospital against medical advice after admission. The post operative morbidity was half with LC (OR=0.45). The post operative wound infection & pneumonia rates were by LC (OR=0.50 and 0.51 respectively). The post operative mortality rate wasreduced by LC (OR=0.184). The mean postoperative hospital stay was shortened in the LC group (MD=-4.35 days).

But there were no significant differences in the bile leakages intraoperative blood loss and operative times astonishingly.

Conclusion: Open surgery is the mother of all minimal invasive techniques(MITs) when MITs failed.

Keywords: Acute cholecystitis, laparoscopic, open, surgery, treatment, meta-analysis, mortality, morbidity

In the past few decades, there have been advancements in the management of the acute cholecystitis i.e. laparoscopic cholecystectomy versus open cholecystectomy .The valuable advances include earlier surgery and index admission cholecystectomy.[1-3]

1. Abdul Majeed
2. Zain Tayyab
3. Imran Yousuf
4. Farooq Ahmed
5. Aslam Javed

1-4. Department of Surgery, AIMC/ Jinnah Hospital Lahore.
2. Department of Surgery, Sir Gangaram Hospital Lahore.
3-5. PRCMDC Dina Nath Lahore.

Correspondence:
Dr. Abdul Majeed, *Senior Registrar Surgery, AIMC/ Jinnah Hospital Lahore. E-mail:majeed066@yahoo.com.*

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Actually there are considerable data that favours early surgery instead of delayed cholecystectomy.[1,3] Gurusarny and papi published prospective studies and meta analysis supported respectively either open or laparoscopic surgery in the acute phase was performed. Hospital stay was found shortened when laparoscopic cholecystectomy was compared with open cholecystectomy. Moreover, approximately 18-25% of patients who underwent delayed procedures in some randomized trials had residual disease requiring surgical intervention before their elective operations.[1-11]

There is no single evidence that which one of two techniques is better. My study contains main objective to attain systematic review and analyze the

published data comparing LC and OC in AC in terms of length of hospitalization operation duration and postoperative hemorrhage,mortality.[3]

METHODS

The searches were made electronically by CINHAL, Pubmed and Medi-line etc for published data. The terms used in searching were acute cholecystitis laparoscopy open cholecys-tectomy. No restriction for search was imposed. The concerned references were short listed.

The criteria for diagnosis of AC were = acute RHC tenderness and ultra sonographic evidence of acute cholecystitis (existence of gallstones with disten-ded and oedematous gall bladder wall positive murphys sign and peri cholecystic fluid accumulations) or acute RHC tenderness USG-Conformation of gall stones and one or more of the following: temperature >380 C and/or leukocytosis >11000 /me or C-reactive protein >10mg/L.There was no restriction levied on the language portal used by the patients ..

Acute cholecystitis (AC)-patients= 513

1. Open cholecystectomy-Patients with AC =287
2. Patients who underwent laparoscopic cholecys-tectomy with AC =213 3. patients got LAMA= 13

Study was conducted from November 2015 2020 study setting surgical unit # 1 jinnah Hospital Lahore.

Latest 2021 SPSS Version 1.0.0.1406 was applied

Laparoscopic versus open cholecystectomy

In Acute Cholecystitis

RESULTS

No. of patients converted from LC to OC =61

Astonishingly 10 cases were disclosed of chole-lithiasis along with choledocholithiasis

When all international criteria were consulted ,then my study was found on average scale . But the results are equivocal with the international publications in non-biased studies.

Total Number of Patients =513

No. of Patients undergoing chole (OC)	No. of Patients undergoing Lap chole (LC)
287 Ptients got LAMA=13	213

Laparoscopic Versus Open Cholecystectomy in Acute Cholecystitis Complications=

Sr. #	Variables	Open Cholecys-tectomy n=287	Laparoscopic Chole-cystectomy n=213	p-value for chi-sequence & s-test
1	Intraoperative bleeding > 500ml	10(3.5%)	23(10.8%)	chi-sequence =10.609 P=0.001
2	Biliary leakage	17(5.9%)	33(15.5%)	chi-sequence 12.440 P=0.000
3	Pneumonia	11(3.8%)	7(3.3%)	chi-sequence =0.105 P=746
4	Biliary stricture	8(2.8%)	13(61%)	chi-sequence =3.341 P=0.068
5	Sub-phrenic collection	11(3.8%)	8(61%)	chi-sequence =0.002 P=0..965
6	Mortality rate	3(1.1%)	12(3.7%)	chi-sequence =8.84 P=0.003
7	Patient with Complica-tions	60(20.9%)	96 (45.1%)	chi-sequence 33.259 P=0.000
8	Patients with RHC –drain	188 (65.5%)	198 (93%)	chi-sequence 52.348 P=0.000
9	Operation Tenure Min +SD	70 (+5.34%)	100+(10.58)	chi-sequence T=37.95 P=0.000
10	Hospital stay (days +SD)	6(2.16%)	4.5+1.28)	chi-sequence 9.69 P=0.000

Total Number of Patients =513

No. of patients undergoing OC	No. of patients undergoing LC
No. of patients with RHC drain (OC)=188	No. of patients with RHC drain(LC) =198
No. of patients with RHC drain (OC)=99	No. of patients with RHC drain(LC) =15

	OC	LC
No. of patients with complications	60	96
No. of patients without complications	227	117
No. of patients got LAMA after admission via Emergency	2	7
No. of patients got LAMA after admission via OPD	5	8

12 Patients undergone laparosco-pic cholecystectomy expired & 3 patients undergone open cholecystectomy expired with acute cholecystitis (calculus) after Surgical interventions.

Open cholecystectomy and laparoscopic cholecystectomy were performed in patients admitted for acute cholecystitis in government hospital of (Lahore) Punjab. All data was collected after the fate of the patients. Surgical interventions were performed in patients admitted for > 72 hours whose symptoms were progressive or Persistent.

Morbidity

Operative Time

Open Cholecystectomy (OC)

Mean time= 90 minute,

Lap cholecystectomy (LC)

Mean time= 110 minute,

Open Chole	Lap. Chole
Bleeding >500 ml =10	=25
Intraoperative	
Pneumonia =40	=18
Waind infection =13	=7
Bile leakage =5	=14
Total Morhidity =68(OC)	

Post-Operative Hospital Stay

OC=+4.4 Days

LC=-4.4 Days

DISCUSSION

In complications related to gallstone cholecystitis, there is an accepted consensus that 1-4.5% of patients with gall-stones develop empyema, gangrene and perforation of gallbladder in AC.[30]

In pre-laparoscopic era, there is enough literature in the favour of early OC in acute cholecystitis to avoid above mentioned complications.[37] In the beginning era of laparoscopy,many famous surgeons were confused and adamant which of two: OC/LC should be adopted to treat AC by surgical interventions.[14,15] There is an accelerated rate of urgent (44%) cholecystectomy on same admission (23%) OC and (18%) LC for patients admitted with AC.[31] The laparoscopic cholecystectomy seems to be very safe in first week of acute cholecystitis. It was also confirmed by the interviewing of surgeons manually as well as electronically.[1,32]

Unfortunately, analysis failed to show any clear difference for those patients who undergone operations within 3 or 7 days after onset of symptoms.[32] In panaromic view,it remained non-concluded that at which pet time the patient should be operated by LC in acute exacerbation of cholecystitis. In other view, no convincing material was found on serial searches about superiority of open versus laparoscopic cholecystectomy in the management of AC when surgically intervened. After all, it has been noted that laparoscopic intervention has increased complications in AC because of the hardships faced to perform laparoscopy in such a complicated and fogged operative field already borne. Amazingly high conversion rates and critical events occurring during laparoscopic intervention have usually been the main arguments for postponning early LC in the established AC.[30] The same facts and figures are still arguable factors on the judicious use of LC. Despite of benefits of LC, its safety margin remains questionable due to higher conversion rates (49%) to open surgery. Subgroup analysis of different complications concluded that pneumonia and wound infection were minimized by use of laparoscopy. But it is crystal clear fact that the occurring of bile leakage has no relation with the intrvention whichever used (opon or laparoscopic). These results were evaluated by either RCTs or by analyzing and summation of individual studies. It was supposed that LC had higher mortality and conversion rates butit was concluded there was no significant difference of complication(s) in AC whichever technique (OC vs LC) used in 513 cases of my study.

Bile duct injuries were more prevalent when LC was opted. It was the most significant loopwhole of LC in AC. It was contrary to the predicted merits of laparoscopy as was supposed in its bright background. It reproduced the narrative that more expertise and intensive supervision is needed in LC when treating patients of AC. Conversion rates from LC to OC ranged

from 9 % to 36%. The criteria for conversion inclu-ded symptom's duration > 96h, TCL > 12500 and age > 55 years .It should be remembered that all patients included in study were operated in same admission. The initial management of AC should be recommended with antibiotics, admission with percutaneous cholecystostomy according to international guidelines. Surgery should be reserved in those patients in which conservative treatment has failed to relieve/ remove the symptoms. Indicator should be patients conditions not only AC severity either OC or LC's options adopted. Indication should be based to patients related factor in guidelines.

Key words

AC- acute cholecystitis

OC=open cholecystectomy

RCT= Randomized controlled trials

LC = Laparoscopic cholecystectomy

LAMA=Left against medical advice

CONCLUSION

Cholecystectomy should be first attempted by laparoscopy. But one thing should be kept in mind clearly that open surgery is the mother of all the minimal invasive techniques (MITs) as it mitigates and covers all the complications created during all (MITS)/ endoscopic surgeries .Its significance is unbeatable .So it remained debatable which technique is better in management of AC. More studies are needed.

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FREQUENCY OF VITAMIN D DEFICIENCY AMONG PATIENTS OF EXTRA-PULMONARY TUBERCULOSIS

Muhammad Aftab,[1] Muzammal Aslam Kataria,[2] Rana Muhammad Arif,[3] Farooq Asghar[4] Muhammad Shahid[5]

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Abstract

Background: Tuberculosis is a communicable disease which continues to be a major public health problem. Vitamin D is believed to have an important role in macrophage activation and the subsequent restriction of micro-organism growth.

Objective: To determine the frequency of vitamin D deficiency in patients of extra-pulmonary tuberculosis at a tertiary care hospital.

Methods: A total of 150 patients with extra-pulmonary tuberculosis those fulfilling the selection criteria were approached. An informed consent was taken and after ensuring an overnight fasting, 5 ml of blood samples were taken in the morning and sent to laboratory for serum vitamin D levels the same day. Data was entered and analyzed in SPSS Version 23.0. Cross tabulation was done with independent variable like age, gender, duration of disease and extra pulmonary tuberculosis site involvement. A p value of < .05 was taken as statistical significant. Confidentiality of the data was ensured.

Results: Mean age was 50.2 + 19.8 years and 56% male patients and 44% female patients. Mean duration of disease was 14.14 + 5.29 months. There were 40% patients having site of extra pulmonary tuberculosis as lymphatic, 28% having site of extra pulmonary tuberculosis as meningeal and 32% having site of extra pulmonary tuberculosis as disseminated. Vitamin D deficiency was found in 72% patients. Significant association was found between presence of vitamin D deficiency and age and gender ($p < .005$). Duration of disease was also significantly associated with vitamin D deficiency ($P = 0.001$).

Conclusion: Majority of patients with extra pulmonary tuberculosis had vitamin D deficiency. Effect modifiers like age, gender and duration of disease showed significant influence.

Key words: Extra-Pulmonary Tuberculosis, Calciferol, Deficiency, Vitamin D

The lungs are the major site for Mycobacteriuin tuberculosis infection. Clinical manifestations of tuberculosis (TB) include primary TB, reactivation TB, laryngeal TB, endobronchial TB, lower lung field TB infection. Pulmonary complications of tuberculosis can include hemoptysis, pneumothorax, bronchiectasis and pulmonary dysfunction and chronic pulmonary aspergillosis.[1]

Risk factors for tuberculosis are multifactorial, however, one responsible element may be vitamin D deficiency. Tuberculosis was mainly treated by Vitamin D and sunlight before advent of antituberculosis treatment. Now, there is growing evidence that vitamin D increases anti-mycobacterial protection.[1,2]

Vitamin D, one of many, regulator of macrophage function, can stimulate human anti-mycobacterial activity. Many observations have shown that a higher risk of tuberculosis infection is associated with vitamin D deficiency. In the first place, tuberculosis cases tend

1. Muhammad Aftab
2. Muzammal Aslam Kataria
3. Rana Muhammad Arif
4. Farooq Asghar
5. Muhammad Shahid

1-4. Department of Medicine, Medical Unit 5, Allama Iqbal Medical College/Jinnah Hospital Lahore.

Correspondence:
Dr. Muhammad Aftab, *Department of Medicine, Medical Unit 5, Allama Iqbal Medical College/Jinnah Hospital Lahore.*
Email: maftabm@hotmail.com

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to occur more during the cold seasons at a time when vitamin D synthesis from sunlight in the skin cells is minimized and serum vitamin D levels are lower. In the next step, serum vitamin D levels are lower in untreated TB patients, especially those who live in temperate climates, than healthy individuals. In addition, the prevalence of tuberculosis is higher among people such as the elderly and uremic patients who have lower serum vitamin D levels.[3,4]

The effects of vitamin D on the immune system is due to its role in the innate immunity system.[5] Moreover, CD4+ and CD8+ T cells, by producing chemokines, such as CC and CXC, have protective effects against TB infection.[6] Presence of Vitamin D is needed for the antimicrobial activity of Toll-like receptors (TLRs).[7] Vitamin D works by attaching to its nucleus receptor in the target cell. Therefore, vitamin D deficiency and any structural and functional disorders in its receptor can lead to an impairment of host immunity against bacillus tuberculosis.[8] 25-hydroxyvitamin D is a biomarker for determining the vitamin D levels of the human body.[9]

The aim of our study was to evaluate the level of vitamin D and its confounding factors in patients with extra pulmonary tuberculosis in our population. The objective of the stduy was to determine the frequency of vitamin D defi-ciency in patients of extra-pulmonary tuberculosis.

METHODS

A cross sectional study was conducted at Medical Units of Jinnah hospital Lahore from August, 2019 – March, 2020. A sample of 150 patients with extra-pulmonary tuberculosis was calculated with 95% Confidence interval and 6% margin of error, taking anticipated vitamin D deficiency of 87.0%. Subjects with age range of 20 – 80 years, either gender fulfilling the inclusion criteria of extra-pulmonary tuberculosis were included and patients having chronic liver disease, with immune-deficiency and history of taking drugs affecting vitamin D like Dilantin phenobarbital were excluded. An informed consent was taken and after ensuring an overnight fasting, 5 ml of blood samples were taken in the morning and sent to laboratory for serum vitamin D levels the same day. Data was entered and analyzed in SPSS Version 23.0. Cross tabulation was done with independent variable like age, gender and duration of disease. A p value of < .05 was taken as statistical significant.

RESULTS

Mean age was 50.2 + 19.8 years and 56% male patients and 44% female patients. Mean duration of disease was 14.14 + 5.29 months. There were 40% patients having site of extra pulmonary tuberculosis as lymphatic, 28% having site of extra pulmonary tuberculosis as meningeal and 32% having site of extra pulmonary tuberculosis as disseminated. (Table no:1) Vitamin D deficiency was found in 108 (72%) patients. (Table no:2). 82.1% of subjects age < 50 years and 59.0% of subjects age > 50 years had vitamin D deficiency. (p <.002). 78.7% of female and 63.1% of male had vitamin D deficiency. (p <.047). 95.4% of subjects with duration of disease > 1 year as compared to 55.5% of subjects with duration of disease <1 year had vitamin D deficiency. (p <.001). 85.7% of subjects with meningeal tuberculosis had vitamin D deficiency. (p<.045). Significant association was found between presence of vitamin D deficiency and age, gender, duration of disease (Table no:3).

Table 1: Demographic and Clinical Profile of Subjects

Variables (n=150)	Frequency	Percent
Age (Years) Mean=50.2, SD= 19.8 Min= 20.00, Max=80.00		
< 50 years	84	56.0
> 50 years	66	44.0
Gender		
Male	84	56.0
Female	66	44.0
Duration infection (Months) Mean =14.14, SD= 5.29 Min=7, Max=24		
< 1 year	63	42.0
> 1 year	87	58.0
Distribution of Disease		
Lymphatic	60	40.0
Meningeal	42	28.0
Disseminated	48	32.0

DISCUSSION

The objective of the present study was to determine the frequency of vitamin D deficiency in patients of extra-pulmonary TB at a tertiary care hospital. In this regard the present cross sectional study was conducted in medical units, Jinnah hospital Lahore. So one hundred and fifty cases of extra pulmonary tuberculosis were included by fulfilling the inclusion criteria by using non-probability consecutive sampling.

Table 2: Distribution of Vitamin D Deficiency

Variables (n=150)	Frequency	Percent
Vitamin D Deficiency		
Yes	108	72.0
No	42	28.0

Table 3: Vitamin D Deficiency and Demographic Variables Cross Tabulation

Variables n=150		Vitamin D Deficiency		Total	Chi-square P value
		Yes	No		
Age	< 50 years	69	15	84	P value = .002
		82.1%	17.9%	100.0%	
	> 50 years	39	27	66	
		59.0%	41.0%	100.0%	
Gender	Male	53	31	84	P value =.047
		63.1%	36.9%	100.0%	
	Female	52	14	66	
		78.7%	21.3%	100.0%	
Duration	< 1 year	35	28	63	P value = .001
		55.5%	44.5%	100.0%	
	> 1 year	83	04	87	
		95.4%	4.6%	100.0%	
Extra Pulmonary Site	Lymphatic	42	18	60	P value = .045
		70.0%	30.0%	100.0%	
	Meningeal	36	06	42	
		85.7%	14.3%	100.0%	
	Dissemina -ted	30	18	48	
		62.5%	37.5%	100.0%	

Out of one hundred and fifty patients, it was found that the minimum age was 20 years and maximum age was 80 years with mean standard deviation of age as 50.2 + 19.8 years. The minimum duration of disease was found as 7 months and maximum duration of disease was 24 months with mean standard deviation as 14.14 + 5.29 months.

It is observed in a previous study that the median baseline 25- hydroxyvitamin D (25[OH]D) level in the TB group 9.86 ng/ml (IQR 7.19-14.15) was lower than in controls 16.03 ng/ml (IQR 12.38-20.30, P < 0.001). The prevalence of severe vitamin D deficiency was higher in patients with TB (51.1%) than in controls (8.2%, P=0.001). The median 25(OH)D level increased from 11.40 ng/ml (IQR 7.85-15.73) to 13.18n g/ml (IQR 10.60-19.71) after treatment completion (P = 0.037). On multivariate analysis, presence of TB and history of TB were independently associated with severe vitamin D deficiency. Patients with TB had a higher prevalence of vitamin D deficiency than control subjects in a Korean population. The median 25(DH)D level increased after TB treatment. Further studies are needed to establish a causal relationship.[10]

In this study, there were 56% male patients and 44% female patients. There were 40% patients having site of extra pulmonary tuberculosis as lymphatic, 28% having site of extra pulmonary tuberculosis as meningeal and 32% having site of extra pulmonary tuberculosis as disseminated. Presence of vitamin D deficiency was found in 72% patients while vitamin D deficiency was not found in 28% patients.

Previous research described that the 65 TB notifications were made within the specified time period (male: 52%, female: 48%, median age: 29 years). 62 patients (95.4%) were vitamin D deficient at the time of diagnosis, with a vitamin D level less than 10pg/L. 46 patients (71%) were severely deficient in vitamin D (level < 4pglL). 38 patients (58.5%) were born in the Indian subcontinent (including India, Pakistan, Bangladesh, Nepal and Sri-Lanka), 18 (27.6%) were black- African, 4 (6.2%) were Vietnamese, 4 (6.2%) were white, born in the UK and 1 (1.5%) was white. born outside the UK. All patients were HIV negative at the time of TB diagnosis. Levels of vitamin D were similar between men and women and there was no significant difference in vitamin D levels between patients with pulmonary and those with extra-pulmonary TB.[11]

Studies have shown that vitamin D enhances phagocytosis of macrophages and the production of

Cathelicidin antimicrobial peptide and accelerates Mycobacterium tuberculosis intracellular death.[12] Studies have shown that there is a relationship between the deficiency of vitamin D and TB.[13,14] Also, an anti-microbial pathway depend on INF-γ in macrophages is associated with appropriate serum levels of vitamin D.[15] The vitamin D levels in patients with TB have been controversial in previous studies. Some studies have reported the reduction of vitamin D levels in patient with TB compared to the healthy individuals.[16,17] while others fail to detect these findings.[18] Levels of vitamin D vary among populations are affected by various racial, cultural and geographical causes.[19,20]

After stratification of age, by using chi-square test it was found that presence of vitamin D deficiency was significantly associated with age group having p-value = 0.002. Significant association was found between presence of vitamin D deficiency and gender having p-value = 0.047. Significant association was found between presence of vitamin D deficiency and duration of disease having p-value = 0.001.

Existing literature showed that the mean Vitamin D levels were 23.23 + 6.81 ng/ml in cases, 29.27 + 8.89ng/ml in controls ($p<0.0001$). Vitamin D deficiency was found in 57% of cases and 33% controls ($p < 0.0001$). Mean Vitamin D levels were significantly lower in females with tuberculosis (20.84 ng/ml) as compared to males (25.03 ng/ml, $p = 0.0002$). Mean BMI in patients of tuberculosis with Vitamin D deficiency were 19.51 + 1.77 kg/m^2 and in patients with normal Vitamin D were 21.65+1.79 kg/m^2 ($p < 0.0001$). There is significant deficiency of Vitamin D in patients with tuberculosis as compared to controls. This deficiency is more pronounced in females, individuals with low BMI, extra pulmonary and MDR tuberculosis.[21]

CONCLUSION

The presence of vitamin D deficiency was found in 72% patients of extra pulmonary TB at a tertiary care hospital. Effect modifiers like age. gender, and duration of disease showed significant influence.

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THE IMPACT OF MICRO-ORGANISM GROWTH ON TRACHEAL CULTURES ON DURATION OF ICU STAY IN A CLOSED NEURO-CRITICAL CARE UNIT IN A TERTIARY CARE HOSPITAL

Usman Ahmad Kamboh,[1] Rai Gull Fraz,[2] Aqsa Mughal,[3] Mehwish Manzoor,[4] Manzoor Ahmed[5]

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Abstract

Background: Road traffic accidents are one of the leading causes of morbidity and mortality worldwide. Victims are mostly young and they are in economically productive years of life. Most of them need intensive care unit admissions. Severe traumatic brain injury is a major trauma entity among these patients. In order to combat VAP, intensivists routinely use broad spectrum antibiotics which leads to another health catastrophe in the form of multi-drug resistant microorganisms causing the pneumonia.

Methods: We conducted a prospective study from 1st of July, 2020 to 31st of December 2020 in NCCU of Jinnah Hospital, Lahore. The patients who met the inclusion criteria were enrolled in the study after informed consent from the relatives.

Results: A total of 70 patients were included in the study. The microbial growth obtained from tracheal swabs of these patients showed Acinetobacter as the most common organism isolated from 27 patients (39%). Acinetobacter had a mortality of 47% (13 out of 27), preceded only by cultures showing no growth causing 80% mortality with an incidence of 14% (10). Although, less common organisms [4% (3)] had 0 mortality. Best GOSe for all growths turned out to be 8.

Conclusion: Gram negative organisms have superseded gram positive organisms in ICU. The virulence of Acinetobacter is alarmingly high in severe traumatic brain injury patients in NCCU and the proven fact of high mortality is posing a major threat to the outcome of STBI. Moreover, the outcomes of no growth patients need to be analyzed on individual case basis.

Key words: Severe traumatic brain injury(STBI), neuro critical care unit(NCCU)

Road traffic accidents are one of the leading causes of morbidity and mortality worldwide.[1] Pakistan is a developing country with overpopulated urban areas where traffic rules implementation is lacking and it leads to a grave rise in the incidence of road traffic accidents. Victims are mostly young and they are in economically productive years of life. Most of them need intensive care unit admissions.

Severe traumatic brain injury is a major trauma entity among these patients. Neuro-Critical care unit of Jinnah hospital, Lahore is a unique critical care facility, where specialized neurosurgeons provide state of art critical care to head injury patients in a closed system neurosurgeon driven ICU.

STBI patients are intubated and mechanically ventilated with sedation and paralysis in accordance with the guidelines of Brain Trauma Foundation. Mechanical ventilation modulates cerebral vascular reactivity.[2] Although, ventilation maintains the airway but there is considerable risk of ventilator associated pneumonia; pneumonia that develops after 48-72

1. Usman Ahmad Kamboh
2. Rai Gull Fraz
3. Aqsa Mughal
4. Mehwish Manzoor
5. Manzoor Ahmed

1,3-5: Department of Neurosurgery, Jinnah Hospital Lahore.
2: Department of Pathology, AIMC, Lahore.

Correspondence:
Dr. Usman Ahmad Kamboh, *Department of Neurosurgery, Jinnah Hospital Lahore.*

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hours of intubation.[3] VAP is associated with second highest morbidity and mortality among nosocomial infections.[4]

In order to combat VAP, intensivists routinely use broad spectrum antibiotics which leads to another health catastrophe in the form of multi-drug resistant microorganisms causing the pneumonia.[5] It has been observed that organisms found on tracheal culture growths have multidrug resistant phenotypes[6] leading not only to poor outcome of the patients but also pose a major financial burden. Multidrug resistance can be optimized by appropriate antibiotic prescription, sagacious infection control and continued surveillance.[7]

We conducted this study to find out the impact of bacterial growth on length of ICU stay and outcome of STBI patients in a closed system NCCU.

METHODS

We conducted a prospective study from 1st of July, 2020 to 31st of December 2020 in NCCU of Jinnah Hospital, Lahore. The patients who met the inclusion criteria were enrolled in the study after informed consent from the relatives.

The inclusion criteria were

- Patients of both genders with age above 13 years
- Patients suffering from Severe Traumatic Brain Injury
- Patients who were mechanically ventilated

The exclusion criteria were

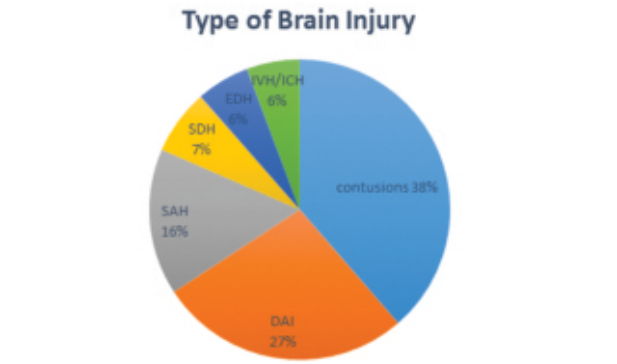
- Polytrauma patients
- Patients who had operative neurosurgical intervention
- Patients having co-morbidities e.g. Diabetes, end organ failure etc.
- Patients who had growth of multiple organisms on cultures

RESULTS

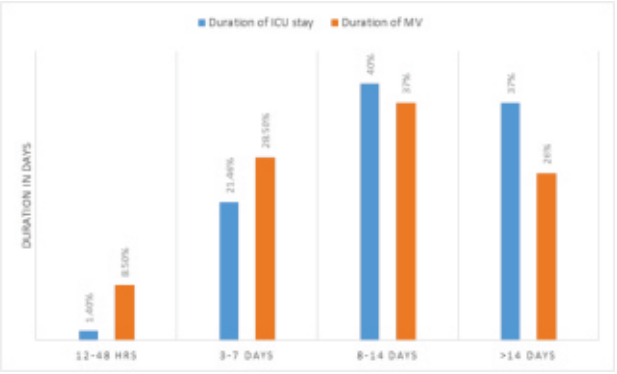
A total of 70 patients were included in the study. Out of these 70 patients, 58 (83%) were males and rest were females. Tracheostomy was done in 55(78.5%) of the patients and 12(17%) of them developed bed sores during their stay. CT scan of a major portion of these patients showed contusion [27(38.5%)] followed by diffused axonal injury [19(27%)] and sub-arachnoid hemorrhage [11(15.7%)]. Subdural, extradural and intra cerebral hemorrhages were less common.

Majority of the patients stayed for 2 weeks [28(40%)], rest had an ICU stay longer than this duration. The minimum ICU stay was less than 48 hours for only one patient. Likewise, 26 out of 70(37%) were on mechanical ventilation for 2 weeks and 18(26%) for more than 2 weeks. Rest were ventilated for less than 48 hours or a week.

Fifty percent (35) of the patients included in the study died within a period of 28 days while 14% (10) had an upper good recovery i.e. a GOSe of 8.



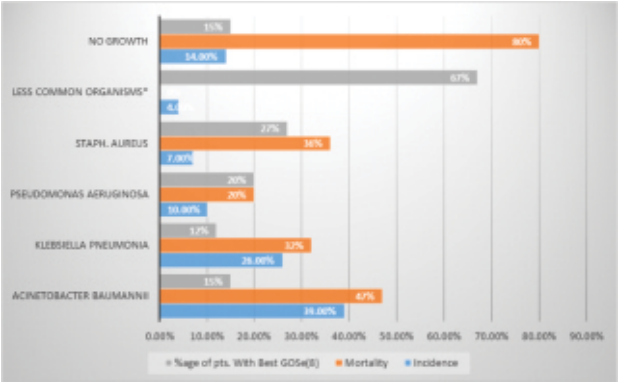
The microbial growth obtained from tracheal swabs of these patients showed Acinetobacter as the most common organism isolated from 27 patients (39%). Acinetobacter had a mortality of 47% (13 out of 27), preceded only by cultures showing no growth causing 80% mortality with an incidence of 14% (10). Although, less common organisms [4% (3)] had 0 mortality. Best GOSe for all growths turned out to be 8.



GOSe on 28th day of admission	Explanation	Patients
1	Dead	50%(35)
2	Vegetative state	5.7%(4)
3	Lower severe disability	12.85%(9)
4	Upper severe disability	4.28%(3)
5	Lower Moderate disability	4.28%(3)
6	Upper Moderate disability	2.85%(2)
7	Lower good recovery	5.7%(4)
8	Upper good recovery	14.28%(10)

Comparing the antimicrobial sensitivity of the micro-organisms, Acinetobacter and klebsiella with highest mortality rates show sensitivity to colistin 82% and 72% respectively.

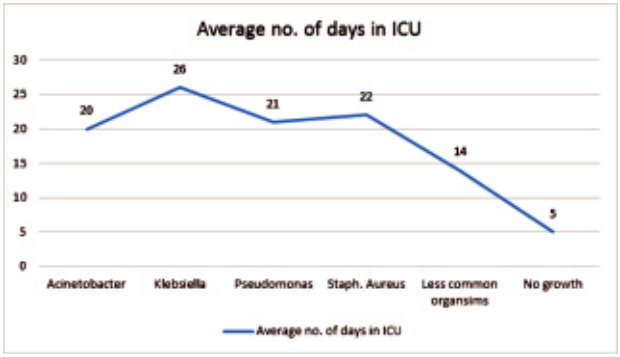
The average ICU stay of a patient for any micro-organism was more than 2 weeks, longest for Klebsiella i.e. 26 days while for cultures showing no growth, patients had an average of 5 days of stay.



DISCUSSION

NCCU of Jinnah Hospital, Lahore is a closed system neurosurgeon driven critical care unit where only traumatic brain injury patients are admitted and offered state of art treatment according to Brain Trauma Foundation guidelines.

Pulmonary infection is the most common infection in NCCU as in any other ICU setting.[8] Trauma patients



are prone to develop infections because of multiple wounds, systemic factors, hypoxia,[9,10] and compromised immunological status.[11,12] Gram positive organisms were the main culprits of ICU mortality and morbidity in late 20th century.[9,13,14] Over passing years, micro-organism growth has changed from gram positive to gram negative pathogens and even fungal growths in few ICU settings.[15,16] Although, Candida species growth is related to higher mortality,[17,18,19,20] there is no candida growth seen in our study.

The positive sample growth in our study was 84% which is comparable with Malik et al i.e 83%[21] and higher than Chandra et al (72.3%)[22] and Gupta et al (53%).[23] Patients with severe traumatic brain injury are received mostly in unconscious state and they have already aspirated which could be a major cause of microbial growth and a higher percentage of positive cultures. Moreover, compared to other wards of the hospital, infection risk in NCCU is higher. [(24)]

Regarding the growth type, it was observed that

	Acinetobacter	Klebsiella	Pseudomonas	Staph. Aureus	Less common organisms
B lactam/lactamase inhibitor combinations	0%	40%	70%	73%	33%
Cephems and cephalosporins	0%	0%	70%	--	33%
Carbapenems	0%	52%	80%	--	33%
Aminoglycosides	59%	56%	80%	55%	67%
Tetracyclins	70.5%	48%	50%	64%	67%
Flouroquinolones	0%	12%	--	36%	33%
Folate pathway inhibitors	14.7%	4%	--	18%	33%
Miscellaneous	--	20%	--	91%	--
Macrolide	--	--	--	18%	--
Vancomycin	--	--	--	64%	--
Colistin	82.3%	72%	--	--	33%

Acinetobacter baumannii was the most prevalent pathogen (39%), followed by Klebsiella pneumonia (26%) and Pseudomonas aeruginosa (10%). Literature review suggests that gram negative organisms have superseded gram positive organisms over the past few decades worldwide. The percentages of A. baumannii, Klebsiella and Pseudomonas vary in different studies but these are the three most prevalent microorganisms.

Malik et al and Chandra et al results showed Klebsiella as the commonest organism, whereas in George et al and Ahmad et al publications Acinetobacter was commonest.[25] In our study, Acinetobacter was the most common isolate. It is a strongly resistant organism[26] and fourth most common nosocomial isolate in China and United states.[27,28]

Mortality rate in patients with Acinetobacter was 47% which was significantly higher than Klebsiella and pseudomonas and it is in accordance with the literature review.[29] Surprisingly, in patients with no growth on cultures, mortality was highest i.e. 80% which needs further analysis of these patients' data on individual case basis.

The best GOSe of 8 was observed in 67% of cases with less common organism isolates and 12% with Klebsiella which is superceded by Acinetobacter i.e. 15%. It showed that top three virulent organisms adversely affect the outcome of severe traumatic brain injury. Anusha et al showed acinetobacter sensitivity to Imipenem and Ciprofloxacin[30] whereas ahmad et al and malik et al rendered tigecycline and sulzone as sensitive regimes while in our study, we found colistin 82.3% and tetracyclines 70.5% sensitive to Acinetobacter isolates. Klebsiella showed sensitivity to colistin and aminoglycosides in our study whereas in ahmad et al and Malik et al, sulzone proved to be best suitable drug. The non-judicious use of broad spectrum antibiotics is changing the spectrum of drug sensitivity and gradually narrowing the number of sensitive drugs for microbial isolates.[31] Pseudomonas on the other hand showed better response to a variety of drugs i.e. carbapenems, aminoglycosides in contrast to literature review while staph. Aureus and less common organisms were found sensitive to numerous routine broad spectrum drugs although outcome of less common organisms was best of all.

CONCLUSION

Gram negative organisms have superseded gram positive organisms in ICU. The virulence of Acinetobacter is alarmingly high in severe traumatic brain injury patients in NCCU and the proven fact of high mortality is posing a major threat to the outcome of STBI. Moreover, the outcomes of no growth patients need to be analyzed on individual case basis.

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AUTOPSY ON PATIENTS WITH ATHEROSCLEROTIC HEART DISEASE UNDER MEDICAL PERSPECTIVE WHO ARE DECLARED UNDER SUDDEN DEATH

Faiza Munir,[1] Zoya Imran,[2] Saima Manzoor,[3] Urooj Husain,[4] Imran Jawaad,[5] Zubia Iqbal[6]

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Abstract

Background: One of the leading causes of death in Pakistani population is atherosclerosis and coronary heart disease and is emerging as an epidemic which needs immediate action. The incidence of heart disease has increased many folds in the last couple of decades and if proper measures on emergency bases are not taken effectively it shall be the leading cause of death widening the gap between other causes of death.

Methods: During medico legal autopsy those cases that had previous history of heart disease were selected at District Head Quarter Hospital Sheikhupura during a period of 06 months from 1st January to 30th June 2021. Only those cases that had previous history of heart disease and were using some medication were included in the study. All the three major coronary arteries were examined grossly, dissected and sectioned. Microscopic examination was carried out to rule out myocardial infarction, ischemic heart disease or atheroma. The criterion which was followed was based on American Heart Association for atherosclerotic plaque. All these steps were followed by medical department.

Results: During the period of 06 months 57 cases were short listed to be included in the study.
Atherosclerosis at various age groups which is observed in both sexes. Atheroma makes its appearance around the age of 20 years and becomes significantly prominent after 30 years and grossly is observed between 40 to 60 years. Coronary arteries showed calcification in 17.5% case, 13.9% had capillary defects. 22.8% cases showed gross atheroma ranging from luminal surface which have lipid core covered by intima which is normal to prominent calcification. 12% of these cases had a single vessel disease whereas 41.9% had two vessel diseases and 45% had triple vessel disease. Involvement of right coronary artery was 78.3%, left coronary artery in 81%, left anterior descending artery in 73% cases. The average age of patients who had myocardial infarction in this study is 51±12 years between 30 to 75 years.

Conclusion: The study concludes that clinical complains of the patient are quite close to the expected finding in the coronary vessels as observed at the time of autopsy. It is further supported by the microscopic finding in the vessels.

Key words: : Coronary artery, atherosclerosis, autopsy, myocardial infarction

One of the leading cause of death in Pakistani population is atherosclerosis and coronary heart disease and is emerging as an epidemic which needs immediate action. The incidence of heart disease has increased many folds in the last couple of decades and if proper measures on emergency bases are not taken effectively it shall be the leading cause of death widening the gap between other causes of death.

The reported number of cases in the last year were more than 2.5 million and deaths reported among this group is more than half million. The expected deaths from coronary heart disease by 2022 is 01 million and the alarming situation is that 13% will be <30 years,

1. Faiza Munir
2. Zoya Imran
3. Saima Manzoor
4. Urooj Husain
5. Imran Jawaad
6. Zobia Iqbal

1. Forensic Medicine & Technology, Allama Iqbal Medical College, Lahore.
2. 4th Year Student SMC.
3-5. University College of Medicine & Dentistry, Lahore.

Correspondence:
Faiza Munir, *Demonstrator Forensic Medicine & Technology. Allama Iqbal Medical Colelge, Lahore*

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29% will be <40 years.

With the introduction of latest technologies and gadgets in medical science which have benefited the medical community directly and indirectly and thus have enhanced the quality of the patient life, resulting in prolong life of the patient. If good quality management is added with latest medication it shall not only increase in the expected life of the patient but also improve the quality of life which was beyond imagination a few decades ago.

Despite all these efforts there is an increase in overall incidence in coronary heart disease cases and increase in the mortality of heart cases.

Table 1: Sex and age distribution of cases on which autopsy was performed

Age	Male	Female	Total	%age
Less than 20	1	1	2	3.5%
20-29	9	4	13	22.8%
30-39	7	3	10	17.5%
40-49	8	0	8	14%
50-59	13	6	19	33.3%
60-69	3	0	3	5.2%
More than 70	2	0	2	3.5%
	0.9%	19.1%		

A study was conducted by performing autopsy of dead bodies of those corpse who had history of heart disease or was taking heart medication. This study was conducted in collaboration with medicine department. In Pakistan there is no law to conduct medical autopsy, so autopsy was performed in medicolegal cases with known heart disease, consent was taken from blood relation of cases undergoing medicolegal autopsy and they were briefed about the nature of study and its benefit for future. This study was conducted at District Head Quarter Hospital Shekhupura in collaboration with medical unit. Autopsy is the only procedure which provides the exact prevalence, grading and detailed atherosclerotic lesion of the coronary vessels which is the main objective of the study.

METHODS

During medicolegal autopsy those cases that had previous history of heart disease were selected at District Head Quarter Hospital Sheikhupura during a period of 06 months from 1st January to 30th June 2021. Only that cases who had previous history of heart disease and were using some medication were

Table 3: Atheroma distribution among major coronary arteries

Grade	Right coronary artery		Left coronary artery		Left anterior descending	
	N	%	N	%	n	%
Minimal change	2	5.4%	3	8.1%	1	2.7%
Fatty streak	2	5.4%	1	2.7%	4	10.8%
Intermediate lesion	4	10.8%	3	8.1%	5	13.5%
Atheroma	5	13.5%	6	16.2%	7	18.9%
Fibo-atheroma	8	21.6%	7	18.9%	5	13.5%
Fibo-atheroma with thromsosis	7	18.9%	9	24.3%	8	21.6%
Calcification	9	24.3%	8	21.6%	7	18.9%
Atheroma to calcification	29	78.3%	30	81%	27	73%
Total	37		37		37	

Table 2: Atherosclerosis encountered at different age group in relation to gender

Age	Minimal change			Fatty streak			Intermediat lesion			Atheroma			Fibo-atheroma			Fibo-atheroma with thromsosis			Calcification			Total			Significant atheroma	
	M	F	=	M	F	=	M	F	=	M	F	=	M	F	=	M	F	=	M	F	=	M	F	=	n	%
Less than 20	2	0	2			0			0			0			0			0			0	2		2	0	
20-29	2	1	3	3	1	4	1	1	2	1	1	2	2	0	2			0			0	9	4	13	0	
30-39	1	0	1	2	0	2			0	3	1	4	1	1	2	1	0	1			0	8	2	10	1	10%
40-49			0			0			0	1	1	2	1	1	2	2	1	3	1	0	1	5	3	8	2	20%
50-59			0			0	1	2	3	2	1	3	2	1	3	3	1	4	4	2	6	12	7	19	3	30%
60-69			0			0			0			0	0	1	1			0	1	1	2	2	1	3	3	30%
More than 70			0			0			0			0			0	1	0	1	1	0	1	2	0	2	4	40%
Total	5	1	6	5	1	6	2	3	5	7	4	11	6	4	10	7	2	9	7	3	10	40	17	57	13	22.8%

included in the study. Those cases whose relatives consented for the study were also included in the study.

During autopsy heart was taken along with its vessels and fixed in 10% formalin, immediately after removal of the heart its weight was done and gross examination was done to observe any infarct. Valvular circumferences was measured for all the four valves.

All the three major coronary arteries were examined grossly, dissected and sectioned. After dissecting examination of the arteries was done to observe its thickness, plaque, calcification or yellow streaks. The ventricles were also sectioned at an interval of 10 mm for any gross abnormality.

In the next step microscopic examination was carried out to rule out myocardial infarction, ischemic heart disease or atheroma. The criteria which was followed was based on American Heart Association for atherosclerotic plaque. All these steps were followed by medical department.

RESULTS

During the period of 06 months 57 cases were short listed to be included in the study. 81% were males, the average weight of male heart was 290±69 gm and that of female was 270±72 gm. Age of various cases were recorded and tabulated in Table-I

Table-2 highlights atherosclerosis at various age group which is observed in both sexes. Atheroma makes its appearance around the age of 20 years and becomes significantly prominent after 30 years and grossly is observed between 40 to 60 years. The most common type of atherosclerosis observed is pre atheroma or fibo atheroma and fibo-atheroma with thrombosis along with calcification in which there is pool of lipid which is extracellular in nature with core not properly defined.

Coronary arteries showed calcification in 17.5% case, 13.9% had capillary defects. 22.8% cases showed gross atheroma ranging from luminal surface which have lipid core covered by intima which is normal to prominent calcification.

12% of these cases had a single vessel disease whereas 41.9% had two vessel disease and 45% had triple vessel disease. With increasing age, the number of vessels involved and plaque formation increase.

Table-3 shows involvement of right coronary artery 78.3%, left coronary artery in 81%, left anterior descending artery in 73% cases.

At autopsy 29% cases showed gross myocardial infarction among these cases 5 had acute myocardial infarction whereas 21 showed chronic ischemic changes. The average age of patients who had myocardial infarction in this study is 51±12 years between 30 to 75 years.

DISCUSSION

Coronary artery disease has emerged as an alarming threat in the morbidity and mortality of causalities reported in the last decade, a study conducted in 2019 by Nowbar AN, Gitto M, Howard JP, Francis DP, Al-Lamee R and a similar study conducted by Ralapanawa U, Sivakanesan R in a narrative review in 2021 shows similar finding as found out in the present study (1, 2). The concern about the whole scnerio is the rapid increase in the cases and in the coming decade could be one of the leading cause of death a study with low atherosclerosis among physically active people in 2017 by Merghani A, Maestrini V, Rosmini S, Cox AT, Dhutia H, Bastiaenan R, et al and another study conducted in the Netherlands which was cross sectional in nature conducted by Kendir C, van den Akker M, Vos R, Metsemakers J in 2018 shows similar finding as seen in the present study.[3,4]

Different studies have shown that the occurrence of atherosclerosis is fluctuating among different races and is also affecting different age groups depending upon their dietary habits and living style, a study conducted in 2018 by Ardeshna DR, Bob-Manuel T, Nanda A, Sharma A, Skelton IV WP, Skelton M, et al and another study conducted by Sharma K, Shah K, Brahmbhatt P, Kandre Y in 2018 along with study on western dietary pattern by Oikonomou E, Psaltopoulou T, Georgiopoulos G, Siasos G, Kokkou E, Antonopoulos A, et al in 2018 supports our study(5-7). This study has shown that the development of atherosclerosis starts at quite an early age when there is no physical

complain of any symptoms which makes concern about the underlying disease, a study conducted on old age athlete with low profile coronary artery disease in 2020 by Dores H, de Araujo Gongalves P, Monge J, Costa R, Tata L, Malhotra A, et al shows finding similar as in the current study.[8] With advance in age disease also progresses and become significantly prominent with gross symptoms which ultimately presents as coronary heart disease a study conducted by Smilowitz NR, Mahajan AM, Roe MT, Hellkamp AS, Chiswell K, Gulati M, et al about mortality due to myocardial infarction by gender, age, and coronary artery disease which is obstructive in nature in 2017 shows similar finding as in the present study.[9]

The present study shows that majority of the reported cases are dominated by males as compared to that of female gender due to multiple reasons, a study conducted in 2017 by Reiner Z is in favor of our study.[10] The dominance of males is highlighted by the fact that they are exposed to more stress, unhealthy dietary habits such as smoking, alcoholism a study conducted in 2017 by Pathak LA, Shirodkar S, Ruparelia R, Rajebahadur J on Indian women shows similar results as in the current study.[11] Due to long working hours they find less time for exercise which makes them more vulnerable to coronary heart disease, in a cross sectional study conducted in 2017 by Sugiura T, Dohi Y, Takase H, Yamashita S, Fujii S, Ohte N highlighting the close association of oxidative stress with stiffning of coronary arteries, especially in old age males who are smokers without previous history of cardiovascular events is in close association with our study.[12]

American Heart Association have not only classified coronary heart disease on the bases of atherosclerotic lesions but suggest that all these lesions progress from one stage to next ultimately leading to coronary heart disease.

The most significant factor contributing in thrombus formation is dislodging of plaque which lead to acute coronary heart disease, a study conducted in 2020 by Fox KA, Metra M, Morais J, Atar D supports our study.[13] Autopsy finding in this study have shown that fibo-atheroma, fibo- atheroma with thrombosis leading to calcification are the major contributors in heart disease a study conducted in 2019 by Gupta N, Zhao Y-Y, Evans CE is in favour of our study.[14] These autopsy finding are also correlating with the clinical finding of the patient.

Those individuals developing coronary heart disease, it has been observed that in all such patient's atherosclerosis develops at an early age, in the present study the gross examination at autopsy, such changes were observed before the age of 20 years a study conducted in 2017 on correlation between ratio of platelet with lymphocyte and its possible link to coronary artery disease by Trakarnwijitr I, Li B, Adams H, Layland J, Garlick J, Wilson A and another similar study conducted by Andersson C, Vasan RS on the prevalence of coronary artery disease disease among youngsters in 2018 shows similar finding as in our study.[15,16] We passing age the changes also progress and become quite threatening around the age of 30 years onward.

Autopsy revealed that atheroma with calcification in right coronary artery was observed in 78.3%. Similar finding was observed in the left coronary artery in 81% of the cases and in the left anterior descending artery in 73% of the cases.

The incidence of thrombosis in the right coronary artery was 18.9%, in the left coronary artery was 24.3% and in the left anterior descending artery was 21.6%.

The study concludes that clinical complains of the patient are quite close to the expected finding in the coronary vessels as observed at the time of autopsy. It is further supported by the microscopic finding in the vessels.

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EFFICACY OF CORTICOSTEROID INJECTION IN DE QUERVAIN'S DISEASE

Muhammad Zafar Iqbal Shahid,[1] Faizan Majeed,[2] Tanveer Haider[3]

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Abstract

Objective: To assess the long term effectiveness of corticosteroid injection for pain relief in De Quervain's disease with the hypothesis that steroid injection have long term lasting effect.

Methods: This prospective case series study was carried out at department of Orthopedic Surgery Services Hospital, Lahore from Feb, 2019 to Jan, 2020 on OPD basis. A total number of sixty patients were included in the study. After approval from hospital ethical committee each patient was injected with 40mg Triamcinolone with 2% lignocaine. These patients were followed up at interval of 1st, 4th, 6th, 8th week and thereafter at 6months and then at 1 year. Each patient was assessed by VAS score and Finkelstein test. Data analysis was done through SPSS version 20. Chi Square test was used for Finkelstein test and t test was used to compare VAS score among patients with positive and negative Finkelstein test. A p-value of <0.005 was considered as significant.

Results: Among these 60 patients there were 83.3% were females and 16.7% were males with a male to female ratio of 1:5. Mean age was 37 + 8.7 years with age range was 25 years to 50 years. Right hand was involved in 73.3% patients while the remaining 26.7% patients had left hand involved. These patients were having symptoms for the last 4-6 weeks. Diagnosis of the De Quervain's disease was based upon the history and positive Finkelstein test. At 4th week 91.6% were symptom free and only 5 patients (8.4%) had recurrence. At the end of final follow up 90.0% patients were symptom free and 10.0% did not respond to the corticosteroid injection and they required surgery. No adverse effects were noted except in 15.0% patients there was hypopigmentation at the site of injection which resolved after 6 weeks without any medication.

Conclusion: In our study corticosteroid injection has success rate of 90% as initial treatment modality. It is recommended as treatment of choice for this disease. One or two injections of corticosteroids results in significant improvement in sign and symptoms of de Quervain's disease.

Keywords: De Quervain's disease, Tenosynovitis, Corticosteroid injection

De Quervain's disease was first described by Swiss surgeon Fritz De Quervain in 1895 in a number of cases. In 1930 Finkelstein is credited with detailed review of literature and presented 24 cases[1] of De Quervain's Tenosynovitis and described a physical examination test called Finkelstein test.[2,11] In 1936 Peterson described the De Quervain's Disease in detailed. Multiple names have been attributed to the De Quervain's Disease like stenosing Tenosynovitis, stenosing tendinitis, peritendinitis, styloid tenovaginitis, stenosing tenovaginitis and stenosing tendovaginitis. But all these terms are misleading as De Quervain's Disease is a non inflammatory condition and represent an attritional and degenerative process of the compartment. It is tenosynovitis of abductor pollicis longus and extensor pollicis brevis tendon sheath because of its stenosing effects. It is also known as gamer's thumb, mother's thumb, black berry thumb, mummy thumb or designer thumb. Because of its

1. Muhammad Zafar Iqbal Shahid 2. Faizan Majeed
3. Tanveer Haider
1-3. Department of Orthopedic Surgery, Services Hospital/SIMS, Lahore.

Correspondence:
Dr. Muhammad Zafar Iqbal,*Services Institute of Medical Sciences / Services Hospital, Lahore. E-mail: drzafar2014@gmail.com*

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superficial location it can lead to injury to these tendons and its sheath.

Knowledge of anatomy of dorsal compartments of wrist is central to understanding of pathophysiology of De Quervain's Disease. First dorsal compartment is approximately is 2cm long and it is located at the radial styloid process proximal to the radio carpal joint.

Tendons of abductor pollicis longus and extensor pollicis brevis passes through the first dorsal compartment of wrist. Abductor pollicis longus is multi stranded while extensor pollicis brevis is much smaller than abductor pollicis longus. Extensor pollicis brevis may be congenitally absent. A small septum separates the abductor pollicis longus from extensor pollicis brevis.

When there is repetitive radial or ulnar deviation of wrist combined with flexion of the thumb, it results in thickening of the abductor pollicis longus and extensor pollicis brevis tendon sheath. This thickening of tendon sheath causes pain where the tendon crosses the distal radial styloid process. It is primarily a non-inflammatory condition with pathology of tendon sheath and accumulation of muco-polysaccharides.[6] First dorsal compartment becomes thicken and tender to touch on superficial and deep palpation. The compartment thickening results in fusiform mass at the radial aspect of wrist. Although thickened first dorsal compartment shows the fusiform thickening, x-rays of the wrist should be done to exclude the tenosynovitis from the osteoarthritis of the trapezo-metacarpel joints. Further it results in difficulty in making the grip and holding the objects. Tendon sheaths are not only stenosed and fibrosed but there is also nodularity. Female between 30-50 years of age are more common sufferers than the males, especially in case of pregnant and peri-menopausal females and is linked to the repetitive overuse of the wrist. It also occurs in patients who have occupation that involves the repetitive gripping with thumb for example racquet players, disc throwing, golf playing and smart phone users. The professions that involve the repetitive use of wrist cause the trauma and strain that result in insufficient gliding of the tendon through the sheath. On examination there is tenderness at the distal radial styloid process, positive Finkelstein's test i.e., pain at radial styloid when the patient make the fist with the thumb tucked in with the wrist in ulnar deviation. The thickened tendon sheath causes the impingement and mechanical obstruction between the gliding tendon and the wall of first dorsal compartment leading to pain and restriction of thumb moments.

Although the exact cause of De Quervain's tenosynovitis is unknown, any activity that relies on the repetitive hand or wrist motion such as sports activity like golf, racket sports can make it worse. Females between 30-50 years have higher chance to develop this disease. Other factors are pregnancy, lifting the child that repeatedly involves using thumb as leverage especially in case of lactating mothers.

A lot of treatment options are available to treat de Quervain's disease.[4,5,6] These include physiotherapy,[14] modification of wrist activity, NSAIDs, thumb spica splintage,[8,18] acupuncture ozone therapy hyaluronic acid injections, ultrasound guided percutaneous needle tenotomy,[13] PRP injections and prolotheraphy.[3,12] But NSAIDs and splinting are effective only with minimal symptoms. Majority of the patients continue to have the problems on resuming the initial activity. Next treatment option is local Corticosteroids injections and surgical decompression.[9] The intra sheath steroid injections are quite effective in number of patients.[24,25,26] Corticosteroids are more commonly uses to treat the de Quervain's disease with reported rate of success of 70-93%.[19,20,21,22,23] The steroid injections are given into tendon sheath of extensor pollicis brevis and abductor pollicis longus tendons. 40mg of triamcinolone is given with 1% lignocaine[b]. If pain persists one can repeat the injection at interval of 4-6 weeks. The complications of steroid injection are skin de pigmentation at the site of injection,[7] thinning of the sheath due to fat necrosis, tendon attrition and rupture with repeated injections.[17]

In resistant cases the surgical release of first dorsal compartment is done taking care to protect the radial sensory nerve and identifying all the accessary compart-

ments.[15] Repair of extensor retinaculum by step cut lengthening are other techniques are rarely required.

METHODS

This prospective study was conducted on OPD basis at department of Orthopaedic Surgery, Services Hospital, Lahore, from Feb 1st, 2019 to Jan 31st 2020. A total No. of 60 patients with diagnosed De Quervain's Disease included in the study. The approval of this study was obtained from hospital ethical and research committee. Before start of the treatment each patient was counseled regarding the procedure and a written consent was obtained. Each patient underwent X-Rays of the involved wrist and hand both AP LAT views to rule out the osteoarthritis and other disorders of trapezometacarpal joint. The age range was 25-50 years. There were 50 females and 10 males in the study.

After complete aseptic measures to prepare the injection site, each patient was injected 1ml of 2% Xylocaine and 40mg of triamcinolone into the sheet on the dorsal aspect of tendon about 1cm proximal to the tip of radial styloid process. Needle confirmation was done by observing the feeling of tendon sheet distal to the annular ligament of the first dorsal compartment. Patients were instructed to avoid the activities that aggravate the pain for one week.

Each patient was followed for a period of one year after the injection at interval of one week, after 04 weeks, after 08 weeks, after 06 months and thereafter at 01 year. Each patient was assessed for pain by VAS score, tenderness at the radial aspect of wrist and for negative Finkelstein test.

Statistical assessment was done by using SPSS version 20. Chi square test and student t-tests were used for statistical test significance. A p value of < 0.05 was considered as significance.

RESULTS

A total no. of 60 patients with De Quervain's Disease was included in the study. Among these 60 patients there were 50 females and 10 males with a male to female ratio of 1:5. The age range was 25 years to 50 years. (Average 37 years). Right hand was involved in 44 patients while the remaining 16 patients had left hand involved. These patients were having symptoms for the last 4-6 weeks. Diagnosis of the De Quervain's disease was based upon the history and positive Finkelstein test.

Most of these patients were teachers (30 patients) followed by house wife (20 patients) and after that 10 patients were manual workers.

Before start of treatment the Finkelstein test was positive in all patients and VAS score range was from 30-90mm in all patients. At the end of first week Finkelstein test remained positive in 40 patients while it was negative in 20 patients after the injection. The VAS score range was from 30-60mm with a mean of 27.2mm. After four weeks Finkelstein test was negative in 55 patients, VAS score was zero. In the remaining 05 patients Finkelstein test was positive and VAS score was 22-30mm. After 08 weeks Finkelstein test was negative in all the patients except in six patients who had positive Finkelstein test. While the 54 patients had VAS score of zero and in 06 patients it was 10mm and 20mm respectively. These 06 patients required the second injection. (Table no: 1)

After 06 months nine more patients had recurrence of symptoms and they required the second injection and these patients remained symptoms free. The mean symptom free interval was 16.4 weeks after the first injection. The recurrence of De Quervain's disease was correlated with initial severe pain than patients with mild and moderate pain intensity. ($p< 0.001$). The recurrence was also related to the duration of the symptoms which were present for more than 03 months in these patients (4 patients). (Table no: 2)

Moreover, in the lactating females (5 patients) the recurrence rate was higher (30%) as compared to the other females (10%). At the end of final follow up after one year 54 patients were symptoms free. The remaining 06 patients didn't get any beneficial effect from the injection and these patients required the surgery.

15 patients got localized skin hypo pigmentation at the injection site which resolved 06 weeks after the injection in all these patients without any medication.

DISCUSSION

De Quervain's disease is one of the most common tendinopathy of hand. It is a strain and stenosing condition that involves the 1st dorsal compartment of wrist. The usual presenting symptom is pain which is aggravated with flexion, pinching of thumb and abduction.[10] The most common patients are females with age between 30-60 years with mean age of 25.5 years.

Table 1: *Comparison of Finkelstein Test and Duration of Treatment*

Duration	Finkelstein test		Chi square test p value
	Positive	Negative	
01 WEEK	40 (66.6%)	20 (33.4%)	-
04 WEEK	5 (8.4%)	55 (91.6%)	X^2 = 43.193 P = 0.000
08 WEEK	6 (10.0%)	54 (90.0%)	X^2 = 40.412 P = 0.000
1 YEAR	6 (10.0%)	54 (90.0%)	X^2 = 40.412 P = 0.000

Table 2: *Comparison of Mean VAS Score Among Patient with Positive and Negative Finkelstein Test.*

Duration	Frequency (%age)	Mean (mm)	T test p value
01 WEEK	40 (66.6%)	70 (± 12.56)	t = 8.80
	20 (33.4%)	5 (± 2.41)	P = 0.000
04 WEEK	5 (8.4%)	50 (± 8.96)	t = 45.49
	55 (91.6%)	0 (± 0.0)	P = 0.000
08 WEEK	6 (10.0%)	15 (± 2.17)	t = 54.71
	54 (90.0%)	0 (± 0.0)	P = 0.000
1 YEAR	6 (10.0%)	15 (± 2.98)	t = 9.45
	54 (90.0%)	0 (± 0.0)	P = 0.000

A lot of treatment options are available to treat this disease.[4,5,6,8,9,12,16] Corticosteroid injections are the most effective mode of treatment in this disease. Lot of studies shows high success rate with intra sheath injection of corticosteroid with this problem. The efficacy rate of corticosteroids injection in our study was 90% (54). The remaining 6 patients out of 12 patients who has recurrence of disease also improved with corticosteroid injection. Only 6 patients in our study did not responded to corticosteroid treatment and they required the surgical intervention.[13,15] patients developed skin hypo pigmentation that resolved without any medication.[7]

Lot of studies has proved the efficacy of steroid injection in De Quervain's disease with 80–90% success rate.[14,15] The study conducted by Jeyapalan et al on intra-sheath injection of corticosteroid in De Quervain's stenosing tenosynovitis reveals that corticosteroids injections are safe and useful in controlling the symptoms of this stenosing tenosynovitis. They have reported the success rate of 89% in their patients.[25]

Similar study was conducted by W.U Ashok et al.[26] They noted excellent (83.33%) results with steroid injection in De Quervain's disease. They concluded that steroid injection in De Quervain's is superior to any form of local ointments and NSAIDs.

In the study conducted by Omoke et al in clinical outcome of non-operative treatment of De Quervain's disease with local steroid injection in Nigerian setting.[20] They concluded that local steroid injection as a treatment modality have 90% success rate. They also came to the conclusion that this mode of treatment is rarely associated with adverse side effects.

In his study Rowland et al[19] also confirms that corticosteroid injection in De Quervain's disease have significant increase in patient symptom resolution, pain relief and improved function of wrist and thumb.

On the basis of study conducted by Dr. Rohan et al, they confirmed that intra-sheath injection of Triamcinolone is effective in treatment of De Quervain's disease.[21] Corticosteroid injection in De Quervain's disease results in statistically significant increase in pain relief and improved function of wrist.

Similar study was conducted by Methew et al. they came to the conclusion that corticosteroid injection are very effective for the treatment of De Quervain's disease.[22]

In his study SA Gulzar in 2013 deduced that one or two injection of corticosteroid in De Quervain's disease leads to early improvement in patients with the Stenosing tenosynovitis.

All these studies confirm the effectiveness of corticosteroid injections in controlling the sign and symptoms of De Quervain's disease. It does not lead to serious adverse effects and should be the preferred initial treatment.[23,24]

Limitations of Study

In our study the sample size was small. A large multicentric study with large sample size should be conducted. Furthermore the study should be better designed randomized control trial of longer duration to establish the full benefits of this mode of treatment.

Conflict of Interest: None

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ROLE OF SITE OF OSTEOTOMY IN TIBIAL LENGTHENING SURGERY USING NA EXTERNAL FIXATOR

Usman Zafar Dar,[1] Muhammad Ali,[2] Syed Asif Ali,[3] Rashid Hussain,[4] Shahzad Anjum,[5] Tayyab Shoaib[6]

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Abstract

Objectives: To determine the role of the site of osteotomy in tibial lengthening surgery using NA external fixator, and to compare the two different osteotomy sites in term of different qualitative and quantitative parameters in our patients at GMC, Gujranwala, Pakistan.

Methods: This cross-sectional analysis include patients having short tibia who underwent tibial lengthening procedure using NA external fixator. These patients were categorized int two groups: Proximal tibial osteotomy group and middle tibial osteotomy group. Statistical analysis was done using SPSS version 25. Independent sample T test and Chi-square test for independence were used for quantitative and qualitative variables respectively to determine their significant association with the site of tibial osteotomy used during lengthening procedure. The p-values were taken statistically significant if < 0.05.

Results: Amongst 100 patients, osteotomy site was proximal metaphysis in 74% and mid-tibia in 26% patients. The mean age of these two group patients was 18.19 + 7.59 years and 17.85 + 10.34 years respectively. The mean number of pins inserted during tibial lengthening procedure when site of osteotomy was proximal metaphysis was 7.08 + 0.92, while the mean number of pins inserted during tibial lengthening procedure when site of osteotomy was mid-tibia was 5.62 + 1.77. Significantly greater number of pins had to be inserted when osteotomy site was proximal metaphysis ($p<0.01$). There was insignificant association of the site of osteotomy with duration of hospitalization (4.95 + 3.76 days vs 5.92 + 4.11days, p=0.268), duration of external fixation (255.11 + 97.66days vs 299.92 + 181.14days, p=0.117), and time of healing (315.43 + 121.54days vs 317.54 + 212.99days, p=0.951). The rate of skin reaction to fixator pins was significantly more in mid-tibial osteotomy patients as compared to proximal metaphyseal osteotomy patients (69.2% vs 45.9%, p=0.034). Similarly, the rate of post-healing pain /discomfort was significantly more in mid-tibial osteotomy patients as compared to proximal metaphyseal osteotomy patients (84.6% vs 64.9%, p=0.047). There was statistically insignificant association of the site of osteotomy with the gender of the patients (p=0.582), cause of shortening of leg (p=0.504), side of affected limb (p=0.240), bone grafting during lengthening procedure (p=0.119), and complications of external fixator (p=0.230)

Conclusion: Proximal metaphysis was the site of osteotomy among majority patients who underwent tibial lengthening procedure at our institute. Significantly greater number of pins had to be inserted when osteotomy site was proximal metaphysis as compared to mid-tibia. Similarly, Skin reaction to fixator pins as well as post-healing pain were significantly more common in mid-tibial osteotomy patients. There was statistically insignificant association of the site of osteotomy with the gender of the patients, duration of hospitalization, duration of external fixation, time of healing, cause of shortening of leg, side of affected limb, bone grafting during lengthening procedure, and complications of external fixator.

Keywords: Osteotomy site, Tibial lengthening surgery, NA external fixator, SPSS

1. Usman Zafar Dar
2. Muhammad Ali
3. Syed Asif Ali
4. Rashid Hussain
5. Shahzad Anjum
6. Tayyab Shoaib

1,3-4,6: *Gujranwala Medical College/Teaching Hospital, Gujranwala, Pakistan*
2. *Rawalpindi Medical University / DHQ, Pakistan*
5. *Rawalpindi Medical University / Benazir Bhutto Hospital, Rawalpindi, Pakistan*

Correspondence:
Dr. Usman Zafar Dar, *Gujranwala Medical College/Teaching Hospital, Gujranwala, Pakistan.* Email: mdrshahidm@gmail.com

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Tibial osteotomy[1] is an orthopaedic surgical procedure in which tibial bone is broken to lengthen, shorten or straighten the leg of knee joint. After osteotomy, surgeon fix it internally or externally for a period of time.[2,3] Tibial osteotomies are performed for numerous purposes including medial compartement arthrosis of knee joint,[4] short leg syndrome,[5] and congenital tibial bowing like blount disease.[6] High osteogenic potential is a pre-requisite for the better site for osteotomy.[7] The osteotomy site can be proximal metaphysis, distal metaphysis, middle of the shaft or any area of diaphysis. Some studies have shown that better bone healing is obtained by an osteotomy in the metaphysis than in the diaphysis,[8,9] and other studies have shown no difference between the 2 procedures.[10,11] The high tibial osteotomy is the hot favorite due to super osteogenesis potential according to the current literature.[12,13] The national data on the topic of the site of osteotomy for tibial lengthening surgery followed by external fixation is deficient. That is why the author selected this topioc, so the objective of our study is to determine the role of the site of osteotomy in tibial lengthening surgery using NA external fixator, and to compare the two different osteotomy sites in term of different qualitative and quantitative parameters in our patients at GMC, Gujranwala, and KEMU, Lahore, Pakistan.

METHODS

It was a cross-sectional analysis.[14] It was carried out from June 2001 to May 2021 at the Department of Orthopaedics, GMC Teaching hospital, Gujranwala and KEMU, Lahore. The patients having short tibia of all age groups, belonging to both genders, who underwent tibial lengthening procedure using NA external fixator were included. The data was collected by purposive sampling. Informed consent was received. After aseptic measures, NA external fixator was applied under fluoroscopy control, then osteotomy/ corticotomy was performed through proximal metaphyseal/ middle diaphyseal region and compression was given at osteotomy site. Lengthening was started at day 10, 1mm daily incremental till the required length was achieved. In those cases, in which the lengthened bone was weak, the plaster was applied. The plaster was removed after one month. These patients were categorized based on osteotomy site into two groups: Proximal tibial osteotomy group and middle tibial osteotomy group.

Statistical analysis was performed using the Statistical Package for Social Science (SPSS), version 25. Age of the patients, number of pins inserted during procedure, duration of hospitalization, duration of external fixation, and time of healing were the quantitative variable, while gender, cause of shortening of leg, side of affected limb, site of tibial osteotomy, complications of external fixator, skin reaction to pins, bone grafting during procedure, and post-healing discomfort were the qualitative variables. Independent sample T test[15] and Chi-square test for independence[16] were used for quantitative and qualitative variables respectively to determine their significant association with the two different sites of osteotomy. The p-values were taken statistically significant if < 0.05.

RESULTS

Amongst 100 patients who underwent tibial lengthening procedure using NA external fixator, the site of osteotomy was proximal metaphysis in 74% patients and mid-tibia in 26% patients (Picture 1). The mean age of the patients in which proximal metaphysis was osteotomy site was 18.19 + 7.59 years while the mean age of the patients in which mid-tibia was osteotomy site was 17.85 + 10.34 years. The age difference was statistically insignificant (p=0.854). The mean number of pins inserted during tibial lengthening procedure when site of osteotomy was proximal metaphysis was 7.08 + 0.92, while the mean number of pins inserted during tibial lengthening procedure when site of osteotomy was mid-tibia was 5.62+1.77. Significantly greater number of pins had to be inserted when osteotomy site was proximal metaphysis ($p<0.01$). There was insignificant association of the site of osteotomy with duration of hospitalization (4.95 + 3.76 days vs 5.92+4.11days, p=0.268), duration of external fixation (255.11+97.66days vs 299.92+181.14days, p= 0.117), and time of healing (315.43 + 121.54days vs 317.54 + 212.99days, p=0.951) (Table 1).

The skin reaction to fixator pins occurred in 45.9% (34 out of 74) patients in which site of osteotomy was proximal metaphysis, while the skin reaction to fixator pins occurred in 69.2% (18 out of 26) patients in which site of osteotomy was mid-tibia. Skin reaction to fixator pins was significantly more common in mid-tibial osteotomy patients (p=0.034). The post-healing pain/ discomfort occurred in 64.9% (48 out of 74) patients in which site of osteotomy was proximal metaphysis, while the post-healing pain /discomfort occurred in 84.6% (22 out of 26) patients in which site of osteotomy was mid-tibia. post-healing pain /discomfort was significantly more in mid-tibial osteotomy patients as compared to proximal metaphyseal osteotomy patients (p=0.047). There was statistically insignificant association of the site of osteotomy with the gender of the patients (p=0.582), cause of shortening of leg (p= 0.504), side of affected limb (p=0.240), bone grafting during lengthening procedure (p=0.119), and complications of external fixator (p=0.230) (Table 2).

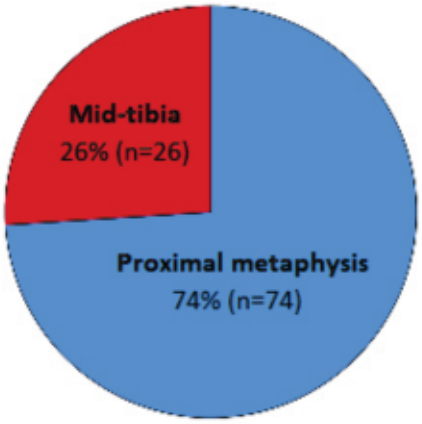

Fig 1: *Site of Osteotomy in Tibial lengthening surgery using NA external fixator (n=100).*

DISCUSSION

We had a pool of one hundred patients suffering short leg syndrome, majority consequence of neurological disorder, poliomyelitis. The lengthenig procedure included external fixation using Naseer Awais (NA) fixator. We compared the two groups of different tibial osteotomies and found significant more number of pins utilization (p<0.01), more skin reactions to pins (p=0.034) as well as more proroption of cases

Table 1: *Associations of Site of Osteotomy with Quantitative Variables in Patients who Underwent Tibial Lengthening Procedure using NA External Fixator (n = 100) **

Quantitative variables	Site of Osteotomy		Mean difference	p-value
	Proximal metaphysis (mean + SD)	Middle tibia (mean + SD)		
Age (years)	18.19 ± 7.59	17.85± 10.34	0.343	0.858
No. of pins inserted during procedure	7.08 ± 0.92	5.62 ± 01.77	1.466	<0.01
Duration of hospitalization (days)	4.95 ± 3.76	5.92 ± 4.11	- 0.977	0.268
Duration of external fixation (days)	255.11 ± 97.66	299.92± 181.14	- 44.815	0.117
Time of healing (days)	315.43 ± 121.54	317.54 ± 212.99	- 2.106	0.951

*Independent sample T-test was used

Table 2: *Associations of Site of Osteotomy with Qualitative Variables in Patients who Underwent Tibial Lengthening Procedure using NA External Fixator (n = 100)*

Predictors / Factors	Site of Osteotomy		Total	p-value
	Proximal metaphysis	Middle tibia		
Gender:				
Male	40 (74.1%)	14 (25.9%)	54 (54.0%)	
Female	34 (73.9%)	12 (26.1%)	46 (46.0%)	0.582
Cause of shortening of leg:				
Polio	66(75.0%)	22 (25.0%)	88 (88.0%)	0.504
Orthopaedic	08 67.7%)	04 (33.3%)	12 (12.0%)	
Trauma				
Side of affected limb:				
Right	50 (78.1%)	14 (21.9%)	64 (64.0%)	0.240
Left	24 (66.7%)	12 (33.3%)	36 (36.0%)	
Complications of external fixator:				
Yes	28 (82.4%)	06 (17.6%)	34 (0.0%)	0.230
No	46 (69.7%)	20 (30.3%)	66 (0.0%)	
Skin reaction to pins:				
Yes	34 (65.4%)	18 (34.6%)	52 (52.0%)	0.034
No	40 (83.3%)	08 (16.7%)	48 (48.0%)	
Bone grafting during lengthening procedure:				
Yes	04 (50.0%)	04 (50.0%)	08 (08.0%)	0.119
No	70 (76.1%)	22 (23.9%)	92 (92.0%)	
Post-healing pain /discomfort:				
hurts	48 (68.6%)	22 (31.4%)	70 (70.0%)	
No hurt	26(86.7%)	04(13.3%)	30 (30.0%)	0.047

*Chi-square test for independence was used

with post-healing pain (p=0.047) associated with proximal metaphyseal osteotomy. Osteotomy can be used for leg lengthening17 or shortening18 purpose.

The diaphyseal osteotomy for tibial lengthing has been used rarely. According to the available literature, very few orthopaedic surgeons had utilized this technique. In 1914, Daniele Santoro19 used diaphyseal osteotomy for correction of post-traumatic malalignment. In 2020, Bjorn Vogt and colleagues20 discussed high tibia metaphyseal osteotomy in leg lengthening techanique. In 1913, Khalilollah Nazem, Arash Fouladi, and Mozhdeh Chinigarzadeh[21] used double tibial osteotomy. We used proximal metaphyseal osteotomy among majority patients (74%); and middle tibia diaphyseal osteotomy in 26 patients. Comparison of these two types of osteotomies is present in literature wit variable view and conclusions. J Fischgrund, D Paley, and C Suter[8] compared metaphyseal, diaphyseal, double levels and concluded that metaphyseal lengthening healed faster than diaphyseal and double-level lengthening. Similarly, J Aronson and X Shen[9] proved metaphyseal osteotomy better for tibial lengthening surgery than diaphyseal site in term of non-union rate (6.2% vs 18.7%) and new bone consolidation (22 + 7.6 days per cm VS 26.5 + 6.5 days per cm). On the other side, Lokietek and colleagues[b] concluded that neither the type of external fixator nor the location or shape of osteotomy had any specific influence on healing after tibial lengthening surgery. Similarly, H Sheen and TO Fjeld[11] found no inferioriy among metaphyseal and diaphyseal osteotomies for tibial lengthenig procedure. In our research, we studied different complications of the NA external fixator like loosening of pin, breaking of pin, loosening of clamp and breaking of clamp etc., and found both groups (i.e proximal metaphyseal osteotomy group and middle tibia osteotomy group) comparable, and non had statistically-proved inferiority (p=0.230). Similarly, duration of the hospitalization (p=0.117) and time of healing (p= 0.951) were also comparable between proximal metaphyseal osteotomy group and middle tibia osteotomy group. Inspite that high metaphyseal osteotomy is favorite according to current literature, few advantages of middle tibia osteotomy has been observed in our study in term of less number of pins utilization for external fixation as well as less skin reaction to the pins and less post-healing discomfort. However, further studies with large sample size may be required to elboate the significance of the findings in detaile.

CONCLUSION

Proximal metaphysis was the site of osteotomy among majority patients who underwent tibial lengthening procedure at our institute. Significantly greater number of pins had to be inserted when osteotomy site was proximal metaphysis as compared to mid-tibia. Similarly, Skin reaction to fixator pins as well as post-healing pain were significantly more common in mid-tibial osteotomy patients. There was statistically insignificant association of the site of osteotomy with the gender of the patients, duration of hospitalization, duration of external fixation, time of healing, cause of shortening of leg, side of affected limb, bone grafting during lengthening procedure, and complications of external fixator.

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ETIOLOGY OF SHORTENED LEG AND ITS ASSOCIATIONS IN PATIENTS WHO UNDERWENT TIBIAL LENGTHENING SURGERY USING NA EXTERNAL FIXATOR

Tayyab Shoaib,[1] Usman Zafar Dar,[2] Syed Asif Ali,[3] Muhammad Ali[4], Yasir Iqbal,[5] Rashid Hussain[6]

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Abstract

Objectives: To determine the etiologies of leg shortening in our patients at GMC, Gujranwala, and and KEMU, Lahore, Pakistan. In addition, this study will also find significant factors of NA fixator-assisted lengthening surgery associated with the etiology of leg shortening in the studied population.

Methods: A cross-sectional analysis of the patients having short leg who underwent tibial lengthening procedure using NA external fixator was performed. These patients were categorized into two etiological groups: post-polio and post-trauma. Statistical analysis was done using SPSS version 25. Independent sample T test and Chi-square test for independence were used for quantitative and qualitative variables respectively to determine their significant association with the etiology of shortened leg. The p-values were taken statistically significant if < 0.05.

Results: Out of the total of 100 short leg patients, etiology was neurological in 88% and post-trauma in 12% patients. The mean age of the post-polio patients was 17.59 + 6.50 years while the mean age of post-trauma patients was 21.83 + 16.55 years. The post-polio patients were young as compared to post-trauma patients (p=0.048). Significantly a greater number of pins had to be inserted during lengthening procedure in post-trauma patients as compared to post-polio patients. (8.00 + 1.35 vs 6.52 + 1.26, p<0.01). In 83.33% (10 out of 12) post-trauma patients, plaster had to be applied on fixator removal while in 56.81% (50 out of 88) post-polio patients, plaster had to be applied on fixator removal. The etiology of shortened leg in patients who underwent tibial lengthening procedure using NA external fixator had insignificant association with the gender of the patients (p=0.539), duration of hospitalization (p=0.975), the duration of external fixation (p=0.975), healing time (p=0.304), side of affected limb (0.555), site of tibial osteotomy (p=0.504), complications of external fixator (p=0.617), skin reaction to pins (p=0.617), type of bone healing (p=0.455), and post-healing discomfort (p=0.502).

Conclusion: The commonest etiology of shortened leg was neurological especially poliomyelitis in our studied population. The post-polio patients were young as compared to post-trauma patients. Significantly a greater number of pins had to be inserted during lengthening procedure in post-trauma patients as compared to post-polio patients. The plaster had to be applied on fixator removal more likely in post-trauma patients as compared to post-polio patients. The etiology of shortened leg in patients who underwent tibial lengthening procedure using NA external fixator had insignificant association with the gender of the patients, duration of hospitalization, the duration of external fixation, healing time, side of affected limb, site of tibial osteotomy, complications of external fixator, skin reaction to pins, type of bone healing, and post-healing discomfort.

Keywords: Short Tibia, Tibial lengthening surgery, NA external fixator, etiology, SPSS

1. Tayyab Shoaib
2. Usman Zafar Dar
3. Syed Asif Ali
4. Muhammad Ali
5. Yasir Iqbal
6. Rashid Hussain

1-3,6: *Gujranwala Medical College/Teaching Hospital, Gujranwala, Pakistan*
4. *Rawalpindi Medical University / DHQ, Pakistan*
5. *Swat Medical College / Swat Medical Complex Teaching Hospital, Swat, Pakistan*

Correspondence:
Tayyab Shoaib, *Gujranwala Medical College/Teaching Hospital, Gujranwala, Pakistan. Email: mdrshahidm@gmail.com*

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Leg length discrepancy (LLD)[1] is a prevailing disorder with a variety of etiologies. It usually occurs due to shortening of one leg[2] and very occasionally as consequence of leg elongation seen in partial gigantism[3] and hemihyperplasia.[4] According to Swedish and USA researchers, one third of the population has upto 1 to 1.5cm of LLD normally.[5,6] It is greater than 2cm LLD that requires surgical correction.[7] The prevalence of this more than 2cm LLD is about 0.1% (i.e. one case per 1000 population).[8] LLD can be congenital or acquired.[9,10] In congenital cases, affected leg grows continuously slower than normal leg. Leg shortening can be acquired as a result of traumatic, surgical or infectious bone loss or epiphyseal plate injury during growing period. Sometimes, bone tumors result in short leg.[11] If untreated, various risks and complications are associated with LLD, among which painful muscular asymmetries and spine, hip joint and knee joint degenerative disorders are significant.[12,13,14] Hence, lengthening surgeries for these patients are of particular importance. In Pakistan where poliomyelitis[15] still exists, etiologies of leg shortening are different. The local literature on this topic is also scarce. Hence, the auther decided to study the etiologies of leg shortening in our population. The objective of our study is to determine the etiologies of leg shortening in our patients at GMC, Gujranwala, Pakistan. In addition, this study will also find significant factors of NA fixator-assisted lengthening surgery associated with the etiology of leg shortening in the studied population.

METHODS

This cross-sectional analysis was carried out from June 2001 to May 2021 at the Department of Orthopaedics, GMC Teaching hospital, Gujranwala. The data of the patients having short tibia was collected by purposive sampling. Informed consent was taken. These patients underwent tibial lengthening procedure using NA external fixator. After aseptic measures, NA external fixator was applied with or without fluoroscopic control, then osteotomy / corticotomy was done through proximal metaphyseal/ middle diaphyseal region and compression was given at osteotomy site. Lengthening was started at day 10, 1mm daily incremental till the required length was achieved. In those cases, in which the lengthened bone was weak, the plaster was applied after removal of external fixator. The plaster was removed after one month. These patients were categorized int two groups depending on the etiology of short leg: Post-polio patient's group and post-trauma patient's group.

Statistical Package for Social Science (SPSS), version 25 was used for statistical analysis. Age of the patients, number of pins inserted during procedure, duration of hospitalization, duration of external fixation, and time of healing were the quantitative variable, while gender, cause of shortening of leg, side of affected limb, site of tibial osteotomy, apply of plaster, complications of external fixator, skin reaction to pins, bone grafting during procedure, type of bone healing and post-healing discomfort were the qualitative variables. Independent sample T test[16] and Chi-square test for independence[17] were used for quantitative and qualitative variables respectively to determine their significant association with the etiology of shortened leg. The p-values were taken statistically significant if < 0.05.

RESULTS

Out of the total of 100 short leg patients, etiology of 88% (n=88) was neurological, mostly poliomyelitis while of 12% (n=12) was orthopaedic trauma (Picture 1). The mean age of the post-polio patients was 17.59 + 6.50 years while the mean age of post-trauma patients was 21.83+16.55 years. The post-polio patients were young as compared to post-trauma patients (p= 0.048). Significantly a greater number of pins had to be inserted during lengthening procedure in post-trauma patients as compared to post-polio patients. (8.00 + 1.35 vs 6.52 + 1.26, $p<0.01$). The duration of hospitalization (p=0.975), the duration of external fixation (p= 0.975), and healing time (p=0.304) had no statistically significant association with the etiology of shortened leg in patients who underwent tibial lengthening procedure using NA external fixator (Table 1).

Amongst 100 total patients, 54% were male while

46% were female. 85.2% (n=46) male had post-polio shortened leg while 91.3% (n=42) female had post-polio shortened leg. 14.8% (n=8) male had post-trauma shortened leg while 8.7% (n=4) female had post-trauma shortened leg. There was statistically insignificant association of the gender of the patients with the etiology of shortened leg in patients who underwent tibial lengthening procedure using NA external fixator. In 83.33% (10 out of 12) post-trauma patients, plaster had to be applied on external fixator removal for a period of time while in 56.81% (50 out of 88) post-polio patients, plaster had to be applied on fixator removal. Post-trauma short leg required more plaster on fixator removal as compared to post-polio short leg; however, association was statistically insignificant (p=070). Similarly, the etiology of shortened leg in patients who underwent tibial lengthening procedure using NA external fixator had insignificant association with the side of affected limb (0.555), site of tibial osteotomy (p=0.504), complications of external fixator (p=0.617), skin reaction to pins (p=0.617), type of bone healing (p=0.455), and post-healing discomfort (p=0.502). (Table 2).

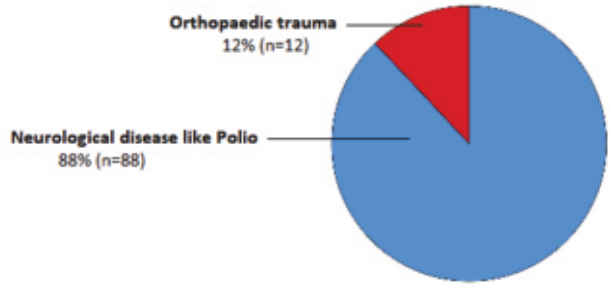

Fig. 1: *Etiology of Leg Shortening Among Patients who Underwent Tibial Lengthening Procedure (n=100)*

DISCUSSION

There are a variety of causes for LLD worldwide.[18] In our patients, we found 88% patients suffering short leg after poliomyelitis while 12% patients suffering short leg after road side accident trauma. Poliomyelitis is still a common condition in developing countries like Pakistan, and leg-length discrepancy is exceedingly common in polio survivors.[19]

Our research topic was odd in terms that we tried to find some significant difference in the management of

Table 1: *Associations of Etiology of Shortened Leg with Quantitative Variables in Patients who Underwent Tibial Lengthening Procedure using NA External Fixator (n = 100) **

Quantitative variables	Etiology of shortened leg		Mean difference	p-value
	Neurological (mean + SD)	Orthopaedic trauma (mean + SD)		
Age (years)	17.59 ± 6.50	21.83 ± 16.55	- 1.47	0.048
No. of pins inserted during procedure	6.52 ± 1.26	8.00 ± 1.35	- 1.47	<0.01
Duration of hospitalization (days)	5.20 ± 3.89	5.17 ± 3.74	0.038	0.975
Duration of external fixation (days)	268.07 ± 126.73	257.17 ± 119.32	10.90	0.779
Time of healing (days)	310.27 ± 150.39	357.83 ± 141.73	-47.56	0.304

*Independent sample T-test was used

Table 2: *Associations of Etiology of Shortened Leg with Qualitative Variables in Patients who Underwent Tibial Lengthening Procedure using NA External Fixator (n = 100) **

Predictors / Factors	Etiology of shortened leg		Total	p-value
	Neuro-logical	Orthopaedic trauma		
Gender:				
Male	46 (85.2%)	08 (14.8%)	54 (54.0%)	0.539
Female	42 (91.3%)	04 (8.7%)	46 (46.0%)	
Side of affected limb:				
Right	56 (87.5%)	08 (12.5%)	64 (64.0%)	
Left	32 (88.9%)	04 (11.1%)	36 (36.0%)	0.555
Site of Tibial Osteotomy:				
Proximal metaphysis	66 (89.2%)	08 (10.8%)	74 (74.0%)	
Middle Tibia	22 (84.6%)	04 (15.4%)	26 (26.0%)	0.504
Plaster applied on fixator removal:				
Yes	50 (83.3%)	10 (16.7%)	60 (60.0%)	0.070
No	38 (95.0%)	02 (5.0%)	40 (40.0%)	
Complications of external fixator:				
Yes	30 (88.2%)	04 (11.8%)	34 (34.0%)	0.617
No	58 (87.9%)	08 (12.1%)	66 (66.0%)	
Skin reaction to pins:				
Yes	44 (84.6%)	08 (15.4%)	52 (52.0%)	0.362
No	44 (91.7%)	04 (8.3%)	48 (48.0%)	
Type of bone healing:				
Distraction healing	82 (87.2%)	12 (12.8%)	94 (94.0%)	0.455
Atrophic nonunion	06 (100%)	0 (0.0%)	06 (06.0%)	
Post-healing pain /discomfort:				
hurts	60 (85.7%)	10 (14.3%)	70 (70.0%)	0.502
No hurt	28 (93.3%)	02 (6.7%)	30 (30.0%)	

*Chi-square test for independence was used

both groups. However, no significant difference was seen and both these groups i.e. post-poliomyelitis and post-trauma LLD had comparable duration of hospitalization (p=0.975), duration of external fixator (p=p=0.779), and time of healing (p=0.304). Only statistically significant difference was in number of pins inserted during the procedure. Significant more number of pins were inserted in the patients suffering LLD after orthopaedic trauma. Tibial lengthening as a means of correcting certain discrepancies in lower limb length has become a well-accepted, though rarely indicated, procedure. Success depends upon knowledgeable evaluation of all factors involved in the problem, upon adherence to the indications and prerequisites, and upon strict attention to all details of the operation. External fixators are frequently used during tibial lengthening procedures. This external fixation is connected with a variety of complications like pin-site infection, aseptic loosening of pin, deep vein thrombosis, pulmonary embolism, loss of reduction, and non-union of fractures.[20,21] Meta-analysis[22] suggests 23.6% oveall complication rate associated with external fixators. We studied different complications of NA external fixator in our study including loosening of pin, breaking of pin, loosening of clamp, and breaking of clamp. We also compared the occurence of these complications in our two cohorts, and found that there was no significant difference of complications among patients suffering post-poliomyelitis LLD from the patients suffering LLD after trauma (p=0.617). Post healing pain or discomfort after leg lengthening surgery is also a problem for majority of the patients.[23] It was seen in our 70% patients in some degree or intensity. However, its presence was comparable for both etiologic groups of the patients (p=0.502). Similary, limb affected by poliomyelitis and orthopaedic trauma has no favourite side of the limb to be affected (p=0.555). There are lot of things to be studied in orthopaedics in the field of external fixator assisted leg lengthening techniques. Vast studies with alrge sample size are required to document management differences in these two major etiological groups of LLD, post-poliomyelitis and post trauma patients.

CONCLUSION

The commonest etiology of shortened leg was neurological especially poliomyelitis in our studied population. The post-polio patients were young as compared to post-trauma patients. Significantly a greater number of pins had to be inserted during lengthening procedure in post-trauma patients as compared to post-polio patients. The plaster had to be applied on fixator removal more likely in post-trauma patients as compared to post-polio patients. The etiology of shortened leg in patients who underwent tibial lengthening procedure using NA external fixator had insignificant association with the gender of the patients, duration of hospitalization, the duration of external fixation, healing time, side of affected limb, site of tibial osteotomy, complications of external fixator, skin reaction to pins, type of bone healing, and post-healing discomfort.

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SIDE OF SHORTENED LEG AND TIBIAL LENGTHENING SURGERY USING NA EXTERNAL FIXATOR

Syed Asif Ali,[1] Tayyab Shoaib,[2] Rashid Hussain,[3] Muhammad Ali,[4] Yasir Iqbal,[5] Muhammad Ikramullah Khan[6]

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Abstract

Objectives: To determine the side of shortened leg in our patients who underwent tibial lengthening procedure using NA external fixator at GMC, Gujranwala, and KEMU, Lahore, Pakistan. In addition, this study will also compare the significant differences between two legs in term of management, procedural and post-procedural complications in the studied people.

Methods: This was a cross-sectional study of patients having short tibia who underwent tibial lengthening procedure using NA external fixator. These were categorized into affected left leg and affected right leg patients. SPSS version 25 was used for statistical analysis. Independent sample T test and Chi-square test for independence were used for quantitative and qualitative variables respectively to determine their significant association with the side of affected leg. The p-values were taken statistically significant if < 0.05.

Results: Amongst 100 patients, 64% (n=64) had right leg while 36% (n=36) had left leg involved. The mean age of right shortened leg patients was significantly more than left shortened leg patients (19.66 + 9.05 years vs 15.33 + 6.07 years, p=0.012). Similarly, the healing time in right leg affected patients was significantly less than the healing time in left leg affected patients (295.53 + 134.12 days, 352.33 + 169.45 days, p=0.048). The left leg required significantly more bone grafting as compared to right leg (16.6% vs 3.1%, p=0.024). The left leg faced more complication rate as compared to right leg; however, the association was statistically insignificant (64.7% vs 28.1%, p=0.076). There was no statistically significant association of side of the affected leg with gender of the patients (p=0.304), cause of shortening of leg (p=0.555), site of tibial osteotomy (p=0.240), skin reaction to pins (p=0.123), type of bone healing (p=0.121), post-healing discomfort (p=0.449), number of pins inserted during procedure (6.75 + 1.45, 6.61 + 1.18, p=0.624), duration of hospitalization (4.75 + 3.46 days, 6.00 + 4.41days, p=0.120), and duration of external fixation (252.63 + 107.69days, 291.89 + 150.14days, p=0.133).

Conclusion: Right leg was shortened more commonly than left leg in our studied population. The age was significantly more of the patients whose right leg was shortened as compared to the patients whose left leg was shortened. The left leg faced higher complication rate, more healing time, and required more bone grafting as compared to right leg. There was statistically insignificant association of the side of the affected leg with gender of the patients, cause of shortening of leg, site of tibial osteotomy, skin reaction to pins, type of bone healing, post-healing discomfort, number of pins inserted during procedure, duration of hospitalization, and duration of external fixation.

Keywords: Short Tibia, Tibial lengthening surgery, NA external fixator, Side of short leg, SPSS

1. Syed Asif Ali
2. Tayyab Shoaib
3. Rashid Hussain
4. Muhammad Alib
5. Yasir Iqbal
6. Muhammad Ikramullah Khan

1-3,6: *Gujranwala Medical College/Teaching Hospital, Gujranwala, Pakistan*
4. *Rawalpindi Medical University / DHQ, Pakistan*
5. *Swat Medical College / Swat Medical Complex Teaching Hospital, Swat, Pakistan*

Correspondence:
Dr. Syed Asif Ali, *Gujranwala Medical College/Teaching Hospital, Gujranwala, Pakistan. Email: mdrshahidm@gmail.com*

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Leg lengthening surgery[1] is used to correct discrepancy of lower limb. It may involve either elongation of femur or tibia; however tibial lengtheing is commonly performed procedure for leg length discrepancy (LLD).[2] It is always followed by internal or external fixation[3] for a duration of period required for proper healing. Each centimeter of lengthening takes 36 days of healing.[4] The tibial lengthening procedures have an aim to enhance the functional mobility of the patients suffering LLD and prevent long term comp-

lications like lower back pain,[5] degenerative joint disease,[6] and stress fractures,[7] in them. A variety of external fixators are applied after lengthening procedure world-wide. Naseer Awais (NA) external fixator[8] is an exquisite creation by well-repuited Pakistani Orthopaedic surgeon and educationist, Professor Dr. Muhammad Awais. It is commonly utilized in our hospitals now a days. LLD can be anatomical or functional.[9] A significant proportion of the population has a LLD of upto 1.5cm normally.[10,11] The prevalence of lengthening-requiring LLD of 2cm is about one per 1000 people.12 LLD may involve either right or left leg depending upon the involvement by the disease process or trauma. The knowledge about the differences in the management of right leg from left leg in term of duration of external fixator[13] and hospitalization, healing time[14] and complications[15] of fixators is scarce. This made the author keen to choose this topic for research. Hence, the objective of our study was to determine the side of shortened leg in our patients who underwent tibial lengthening procedure using NA external fixator at GMC, Gujranwala, and KEMU, Lahore, Pakistan. In addition, this study will also compare the significant differences between two legs in term of management, procedural and post-procedural complications in the studied people.

METHODS

A cross-sectional analysis of the patients who underwent tibial lengthening procedure using NA external fixator was carried out from June 2001 to May 2021 at the Department of Orthopaedics, GMC Teaching hospital, Gujranwala and KEMU, Lahore. The data was collected by purposive sampling. Informed consent was received. The patients having short tibia of all age groups, belonging to both genders, who underwent lengthening surgery were included. After aseptic measures, NA external fixator was applied under fluoroscopy control, then osteotomy / corticotomy was performed through proximal metaphyseal/ middle diaphyseal region and compression was given at osteotomy site. Lengthening was started at day 10, 1mm daily incremental till the required length was achieved. In those cases, in which the lengthened bone was weak, the plaster was applied. The plaster was removed after one month. Depending upon side of the leg involved by shortening, the patients were categorized int two groups: Right leg involved, left leg involved.

Statistical analysis was performed using the Statistical Package for Social Science (SPSS), version 25. Age of the patients, number of pins inserted during procedure, duration of hospitalization, duration of external fixation, and time of healing were the quantitative variable, while gender, cause of shortening of leg, side of affected limb, site of tibial osteotomy, complications of external fixator, skin reaction to pins, bone grafting during procedure, and post-healing discomfort were the qualitative variables. Independent sample T test[16] and Chi-square test for independence[17] were used for quantitative and qualitative variables respectively to determine their significant association of the side of involvement by LLD. The p-values were taken statistically significant if < 0.05.

RESULTS

Amongst 100 patients suffering leg length discrepancy, 64% (n=64) had right leg involved while 36% (n=36) had left leg involved (Picture 1).

The mean age of the patients in which right leg got affected was 19.66 + 9.05 years while the mean age of the patients in which left leg got affected was 15.33 + 6.07 years. The difference was statistically significant (p=0.012). Similarly, the healing time in right leg affected patients was 295.53 + 134.12 days while the healing time in left leg affected patients was 352.33 + 169.45 days. The healing time was 56.80 days more for left leg patients , and the difference was also statistically significant (p= 0.048). There was insignificant association between the side of the shortened leg and number of pins inserted during procedure (6.75+1.45, 6.61+1.18, p=0.624), duration of hospitalization (4.75 + 3.46 days, 6.00 + 4.41days, p=0.120), and duration of external fixation (252.63 + 107.69 days, 291.89 + 150.14days, p=0.133) (Table 1).

Among 3.1% (2 out of 64) patients in which

right leg was short, bone grafting had to be done during tibial lengthening procedure. While among 16.6% (6 out of 36) patients in which left leg was short, bone grafting had to be done during tibial lengthening procedure. The left leg required significantly more bone grafting as compared to right leg (p=0.024).

Similarly, the rate of complications of external fixator in case of right short leg was 28.1% (in 18 patients out of 64) while the rate of complications of external fixator in case of left short leg was 64.7% (in 22 patients out of 36). The left leg faced more complication rate as compared to right leg; however, the association was statistically insignificant (p=0.076).

There was no statistically significant correlation of side of the affected leg with gender of the patients (p=0.304), cause of shortening of leg (p=0.555), site of tibial osteotomy (p=0.240), skin reaction to pins (p=0.123), type of bone healing (p=0.121), and post-healing discomfort (p=0.449). (Table 2).

Table 1: *Associations of Side of Shortened Leg with Quantitative Variables in Patients who Underwent Tibial Lengthening Procedure using NA External fixator with (n = 100) **

Quantitative variables	Side of shortened leg		Mean difference	p-value
	Right (mean+SD)	**Left** (mean+SD)		
1. Age (years)	19.66 ± 9.05	15.33 ± 6.07	- 4.32	0.012
2. No. of pins inserted during procedure	6.75 ± 1.45	6.61 ± 1.18	- 0.14	0.624
3. Duration of hospitalization (days)	4.75 ± 3.46	6.00±4.41	1.25	0.120
4. Duration of external fixation (days)	252.63 ± 107.69	291.89 ± 150.14	39.26	0.133
5. Time of healing (days)	295.53 ± 134.12	352.33 ± 169.45	56.80	0.048

*Independent sample T-test was used

Table 2: *Associations of Side of Shortened Leg with Qualitative Variables in Patients Who Underwent Tibial Lengthening Procedure using NA External Fixator with (n = 100) **

Predictors / Factors	Side of shortened leg		Total	p-value
	Right	**Left**		
Gender:				
Male	32 (59.3%)	22 (40.7%)	54 (54.0%)	0.304
Female	32 (69.6%)	14 (30.4%)	46 (46.0%)	
Cause of shortening of leg:				
Polio	56 (63.6%)	32 (36.4%)	88 (88.0%)	0.555
Orthopaedic Trauma	08 (66.7%)	04 (33.3%)	12 (12.0%)	
Site of Tibial Osteotomy:				
Proximal metaphysis	50 (67.6%)	24 (32.4%)	74 (74.0%)	0.240
Middle Tibia	14 (53.8%)	12 (46.2%)	26 (26.0%)	
Complications of external fixator:				
Yes	18 (52.9%)	16 (47.1%)	34 (34.0%)	0.076
No	46 (69.7%)	20 (30.3%)	66 (66.0%)	
Skin reaction to pins:				
Yes	30 (57.7%)	22 (42.3%)	52 (52.0%)	0.123
No	34 (70.8%)	14 (29.2%)	48 (48.0%)	
Bone grafting during lengthening procedure:				
Yes	02 (25.0%)	06 (75.0%)	08 (08.0%)	0.024
No	62 (67.4%)	30 (32.6%)	92 (92.0%)	
Type of bone healing:				
Distraction healing	62 (66.0%)	32 (34.0%)	94 (94.0%)	0.121
Atrophic nonunion	02 (33.3%)	04 (66.7%)	06 (06.0%)	
Post-healing pain /discomfort:				
hurts	44 (62.9%)	26 (37.9%)	70 (70.0%)	0.449
No hurt	20 (67.7%)	10 (33.3%)	30 (30.0%)	

*Chi-square test for independence was used

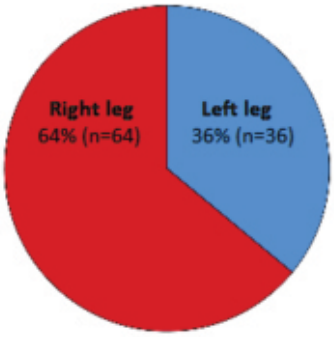

Fig. 1: *Sides of Shortened Leg Among Patients who Underwent Tibial Lengthening Procedure (n=100)*

DISCUSSION

Limb length discrepancy (LLD) is a condition in which one leg or arm is longer than other one. The discrepancy in leg lengths is more likely to be noticed and to affect activities of daily living. Depending on the degree of difference, leg-length disparities can lead to a variety of problems, such as functional scoliosis, and hip, knee, and ankle problems.[18] A systemic review evaluating the prevalence of LLD by radiographic measurements revealed that 90% of the normal population had some type of variance in bony leg length, with 20% exhibiting a difference of >9 mm.[19] The disease or trauma leading to LLD can involve either of the legs. In our study, LLD of right leg was found more than left leg (64% vs 36%) and the age of the affected persons who had involved right leg was significantly more than persons who had involved left leg (19.66 + 9.05 years vs 15.33 + 6.07 years, p=0.012). There are many different reasons to have a leg length discrepancy, but we received two types of patients; one with neurological etiology and second who had orthopaedic trauma. The affected leg by LLD either right or left had no correlation with etiology of the LLD (p=0.555). Similarly, our study also found that gender had no association with the side of affected leg (p=0.304). According to literature, upto 23.6% complication rate is associated with external fixators.[20] Among these complications, pin-track, beaking or loosening of pins, thromboembolic events, loss of reduction, delayed union, and non-union of fractures are common.[21,22] We corelated the occurence of the complications of the external fixator with the side of leg affected by LLD. The complication rate was more in left leg disease as compared to right leg disease (44% vs 28%); however the association was statistically insignificant (p=0.076). After leg lengthening procedure, external fixators are kept for a long duration of the time. On recovary, fixators are removed and patients are followed for post-healing pain or discomfort. Orthopaedics categorizes this post-healing pain broadly into two gropus: one whether it hurts the daily activity of the patients or no. The rate of the post-healing pain hurting daily activity was 62.5% in group of patients affected right leg while rate of the post-healing pain hurting daily activity was 72.2% in group of patients affected left leg (p=0.449). The overall rate of the post-healing pain that hurts was 70% in our studied population. In leg lengthening procedures, osteotomy is followed by fixation. Sometimes, osteotomy gap requires bone graft. We also studied that need of bone grafting during lengthening procedure and found that bone grafting during tibial lengthening procedure had to be performed significantly in more number of patients with affected left leg in comparison to number of patients with affected right leg. (25% vs 75%, p= 0.024). Healing time is the period from date of osteotomy to the date when distraction or atrophic healing had occured. We also compared the healing time for both legs and found that time of healing after tibial lengthening procedure was significantly less for right leg as compared to left leg in our patients. (295.53 + 134.12 days vs 352.33 + 169.45 days, p=0.048). This was a good prognostic clue for left leg affected people. Which factors contributed in this fast recovary had to be ascertain. Larger studies with adequate sample size has to be conducted to prove these findings.

CONCLUSION

Right leg was shortened more commonly than left leg in our studied population. The age was significantly more of the patients whose right leg was shortened as compared to the patients whose left leg was shortened. The left leg faced higher complication rate, more healing time, and required more bone grafting

as compared to right leg. There was statistically insignificant association of the side of the affected leg with gender of the patients, cause of shortening of leg, site of tibial osteotomy, skin reaction to pins, type of bone healing, post-healing discomfort, number of pins inserted during procedure, duration of hospitalization, and duration of external fixation.

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DIAGNOSTIC ACCURACY OF ULTRASOUND GUIDED FINE NEEDLE ASPIRATION CYTOLOGY OF AXILLA IN STAGING OF BREAST CANCER

Shahzad Aslam,[1] Rashid Mehmood,[2] Sana Afroze,[3] Ali Akbar,[4] Samreen Mushtaq,[5] Humayun Siddique,[6] Ameer Afzal,[7] Khalid Masood Gondal[8]

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Abstract

Objective: To determine the diagnostic accuracy of ultrasound guided fine needle aspiration cytology of axilla in staging of breast cancer taking histopathology as gold standard

Methods: 160 patients fulfilling inclusion criteria were enrolled in the study from the outpatient department (OPD) of Surgery, Mayo Hospital, Lahore. All female patient diagnosed with carcinoma breast underwent ultrasound-guided fine needle aspiration cytology by a senior consultant radiologist under local anesthesia with assistance of researcher. Fine needle aspiration cytology samples were sent to the pathology department of the hospital. Reports were obtained and patients were labeled as positive or negative. Meanwhile, all patients underwent surgical intervention of primary tumor and Axillary lymph node dissection under general anesthesia by a consultant surgeon with assistance of researcher.

Results: The mean age of patients was 49.53 ± 11.02 years with minimum and maximum age as 25 and 70 years. On ultrasound-guided fine needle aspiration cytology of axillary lymph nodes,95(59.38%) females had positive axillary lymph node involvement nodes while 65(40.62%) females had negative axillary lymph node involvement. On histopathology 91(56.88%) females had axillary lymph node metastasis and 69(43.12%) females had no evidence of axillary lymph node metastasis. There were 85 cases who had positive axillary lymph node involvement both on histopathology and ultrasound-guided fine needle aspiration cytology, 59 cases had negative axillary lymph node involvement on both histopathology. The Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value and Diagnostic Accuracy of ultrasound guided fine needle aspiration cytology was 93.41%, 85.51%, 89.47%, 90.77% and 90.00% respectively.

Conclusion: It is concluded that ultrasound guided fine needle aspiration cytology of axilla has very good diagnostic accuracy (Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value and Diagnostic Accuracy of ultrasound guided fine needle aspiration cytology was 93.41%, 85.51%, 89.47%, 90.77% and 90.00% respectively) in staging of breast cancer taking histopathology as gold standard. Hence this cheap, easily available, patient compliant and minimally-invasive method can be used to stage the axilla in breast cancer. Moreover, by quick and early detection of the stage the appropriate treatment can be initiated timely for good prognosis.

Key Words: Ultrasound guided, histopathology, Fine needle aspiration cytology, axilla, breast cancer.

1. Shahzad Aslam
2. Rashid Mehmood
3. Sana Afroze
4. Ali Akbar
5. Samreen Mushtaq
6. Humayun Siiddique
7. Ameer Afzal
8. Khalid Masood Gondal

1-8. Department of North Surgical Ward, King Edward Medical University, Mayo Hospital, Lahore.
3. Department of Pathology, Allama Iqbal Medical College, Lahore.

Correspondence:
Dr. Ali Akbar, *Mayo Hospital, Lahore.*
Email: dr.aliakbar81@gmail.com,

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Malignant breast neoplasia is the main cause of deaths caused by cancer in women worldwide. The introduction of new techniques has allowed the diagnosis of early-stage lesions and more conservative treatments.[1] Currently, the histopathological diagnosis of breast cancer is carried out by means of minimally invasive methods, whenever possible by means of imaging-guided percutaneous biopsy.[2] In a study, out of 3471 patients of breast cancer, and 53.0% had

axillary lymph node metastases at diagnosis.[3] The locoregional lymph node involvement is a key element in the staging of patients with invasive breast cancer, representing a major prognostic factor and contributing to an optimal therapeutic management.[4]

Axillary ultrasonography should be included in the preoperative staging of all patients with invasive breast cancer. The addition of USG-FNA in cases of lymph nodes suspicious for malignancy may prevent more than 50% of sentinel lymphadenectomies, significantly shortening the time interval to definitive therapy.[5] Preoperative staging of the axilla in women with invasive breast cancer using ultrasound-guided needle biopsy identifies approximately 50% of patients with axillary nodal metastases prior to surgical intervention. Although moderately sensitive, it is a highly specific staging strategy that is rarely falsely- positive, hence a positive ultrasound-guided needle biopsy allows patients to be triaged to axillary lymph-node dissection avoiding potentially unnecessary sentinel node biopsy.[6]

Sensitivity of USG-FNAC was 78.95%, specificity was 100%, PPV was 100%, NPV was 55.56% and diagnostic accuracy was 83.33% for staging of breast cancer.[7] Another study showed that For the US-FNAC, the respective values were 68%, 100%, 100% and 65% for staging of breast cancer.[8] However, one study found that For the US-FNAC, the respective values were 92.2%, 87.8%, 94.6% and 82.7% for staging of breast cancer.[9]

METHODS

This study was conducted on 160 patients in north surgical ward of Mayo Hospital, Lahore in 6 months duration from march 2019 to September 2019. It was a cross sectional study by design and patient selection was Non-probability, consecutive sampling. Female patients of age 25-70 years presenting with invasive breast cancer of size T1-T2, clinically negative axilla for lymph nodes but having suspicious nodes on ultrasound were included. Features of suspicion for malignancy in axillary lymph nodes on ultrasound are; size more than 10 mm, absence of fatty hilum, hypoechoic internal echo, circular shape, sharply demarcated border compared with surrounding fatty tissue, cortical thickening with eccentric lobulation of hypoechoic cortical rim. Patients with history of diabetes mellitus (BSR> 186 mg/dl), INR>2, surgical excision of adjacent breast due to malignancy and metastasis were excluded. 160 patients fulfilling inclusion criteria were enrolled in the study from the Outpatient Department (OPD) of Surgery, Mayo Hospital, Lahore. A written informed consent was taken. Demographic information (name, age, marital status, duration of diagnosis, history of breast feeding) were recorded. Then all females underwent USG-FNAC by a senior consultant radiologist under local anesthesia with assistance of researcher. FNAC samples were sent to the pathology department of the hospital for assessment of axillary lymph node involvement. Reports were obtained and patients were labelled as positive if there was axillary lymph node involvement and were labeled as negative if there was no axillary lymph node involvement. Meanwhile, all patients underwent surgical intervention for primary tumor and axillary lymph node dissection under general anesthesia by consultant surgeon with the assistance of researcher. On histopathology, it was labeled as positive if there were cancer cells present in lymph nodes of axilla and was labeled as negative if there were no cancer cells in lymph nodes. All this information was recorded on proforma.

All the collected information was entered into SPSS version 21. Quantitative variables like age and duration of diagnosis was presented as mean and standard deviation. Qualitative variables like positive or negative (on USG-FNAC and histopathology) were presented as frequency and percentage. Results of USG-FNA were tabulated in the form of tables to calculate the sensitivity, specificity, PPV, NPV and diagnostic accuracy of USG-FNAC taking histopathology as gold standard.

RESULTS

The mean age of patients was 49.53 ± 11.02 years with minimum and maximum age as 25 and 70 years. Table -1 On USG-FNAC 95(59.38%) females had

positive axillary lymph node involvement and 65 (40.62%) females had negative axillary lymph node involvement. Table -2 On histopathology 91(56.88%) females had axillary lymph node metastasis and 69 (43.12%) females had no evidence of axillary lymph node metastasis. Table-3 When compared USG-FANC with histopathology findings, 85 case were true positive, 59 cases were true negative,10 false positive cases and 06 false negative cases. The Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value and Diagnostic Accuracy of USG-FNAC was 93.41%, 85.51%, 89.47%, 90.77% and 90.00% respectively. Table-5.

DISCUSSION

Axillary nodal status is a major prognostic indicator in early breast cancer. Evaluation of the axillary lymph nodes remains an integral part of staging, prognostication and selection of patients for adjuvant systemic therapy. In the past decade, axillary staging for breast cancer has undergone a paradigm shift towards less invasive methods of assessment and surgical management, and preoperative axillary imaging is now an integral component of pretreatment investigation[10]. Patients with clinically and radiologically negative axillary nodes proceed to sentinel node biopsy (SNB); however, if morphologically abnormal lymph nodes are identified, ultrasound-guided lymph node sampling is recommended.[11]

Patients confirmed to have axillary nodal disease proceed directly to axillary lymph node dissection (ALND) as they are considered likely to have a high nodal disease burden, or may alternatively proceed to neoadjuvant chemotherapy (NACT). Publication of the American College of Surgeons Oncology Group (ACOSOG) Z0011 trial and the rapid adoption of its results into clinical practice have raised questions about the value of preoperative axillary imaging in the era of minimally invasive and less aggressive axillary surgery.[12]

Results from the Z0011 trial are not applicable to all patients and current practice guidelines continue to recommend preoperative axillary ultrasonography as standard practice in patients with malignant breast lesions. It has been reported that ultrasound-guided percutaneous lymph node sampling/biopsy improves selection of patients with a high axillary nodal burden who will benefit from direct ALND. If there is no evidence of lymph node metastasis on ultrasound-guided percutaneous sampling, SNB remains a necessary component of initial surgical management owing to the low negative predictive values reported for techniques used in percutaneous biopsies of axillary lymph nodes[13]. Ultrasound-guided fine-needle aspiration (USG-FNAC) is the preferred approach to the preoperative assessment of axillary lymph node status as it is a low-risk procedure with minimal complications. This technique is not without limitations as USG-

Table 1: Descriptive Statistics of Age

Age(years)	
Mean	49.53
S.D	11.02
Range	45.00
Minimum	25.00
Maximum	70.00

Table 2: Findings on USG-FNAC

USG-FNAC	Patients	Percentage
Positive	95	59.38%
Negative	65	40.62%
Total	160	100%

Table 3: Findings on Histopathology

Histopathology	Patients	Percentage
Positive	91	56.88%
Negative	69	43.12%
Total	160	100%

Table 5: Comparison of USG-FNAC with Histopathology

		Histopathology		Total
		Positive	Negative	
USG-FNAC	**Positive**	85	10	95
	Negative	6	59	65
Total		91	69	160

Sensitivity	93.41%
Specificity	85.51%
Positive Predictive Value	89.47%
Negative Predictive Value	90.77%
Diagnostic Accuracy	90.00%

FNA is largely operator-dependent, with accuracy depending on a skilled radiologist and cytopathologist. Recent reports suggest that ultrasound-guided core needle biopsy (USG- CNB) may be superior to US-FNA in this setting, providing a more accurate determination of axillary nodal status before surgery. There are, however, few published studies directly comparing the two techniques.[14]

Reported complication rates were significantly higher for US-CNB compared with US-FNA (7•1 versus 1•3 per cent; P < 0•001). Conversely, the requirement for repeat diagnostic procedures was significantly greater for US-FNA (4•0 versus 0•5 per cent; P < 0•001). Hence, it can be concluded that USG-CNB is a superior diagnostic technique to USG-FNAC for axillary staging in breast cancer.[15]

Hu X, et al carried out a study to evaluate the sensitivity, specificity and accuracy of axillary ultrasound (US) and fine needle aspiration biopsy (FNAB) in the diagnosis of axillary metastases in patients with early breast cancer. The results of Ultrasound and cytology were compared to histopathological results to determine their sensitivity, specificity, positive and negative predictive value and accuracy. A total of 76 out of 214 patients (35.5%) had axillary lymph node metastases at final histology. The sensitivity and specificity of axillary US alone were 59.2% (45/76) and 78.3% (108/138), respectively. Axillary US with FNAB identified 32 patients with positive lymph node metastases, and increased the sensitivity and specificity to 71.1% (32/45) and 100.0% (30/30). Combined with FNAB, the positive and negative predictive values were 100.0% (32/32) and 69.8% (30/43), respectively. Axillary US-alone or combined US/FNAB had a high accuracy rate and a satisfactory result as they cost less and it is easy to assess the status of axillary lymph nodes. Thus, axillary US with FNAB may avoid unnecessary SLNB in a significant number of patients.[16]

Cardoso-Coelho LP, et al conducted a study in which USG-FNAC was performed in 27 patients with early-stage breast cancer for comparison with SLNB. Tumor subtypes included invasive ductal carcinoma (85%), invasive lobular carcinoma (7%), and tubular and metaplastic carcinoma (4%). FNA had a sensitivity of 45%, specificity of 100%, positive predictive value of 100% and a negative predictive value of 73%. Axillary lymph node cytology obtained by ultrasound guided-FNA in patients with breast cancer had a specificity similar to that of sentinel lymph node histopathology in the presence of axillary node metastases. However, when lymph node cytology is negative, it does not exclude the existence of metastatic implants, due to its low sensitivity in comparison to sentinel lymph node histopathology.[17]

Another study was conducted by Diaz-Ruiz MJ et al to determine the stage of disease at diagnosis. Patients with negative USG-FNAC and breast tumors of 30 mm in size were candidates for selective sentinel lymph node biopsy (SLNB). The anatomopathological results of AD or SLNB were used as reference tests. The result has demonstrated that Lymph nodes were detected by US in 207 (50.8%) axillae. Of these, USG-FNAC was performed on 180 (86.9%). 94 axillae (52.2%) were positive for carcinoma and 79 women received AD. US-FNA had 77.5% sensitivity, 100% specificity, 100% positive predictive value, 69.3% negative predictive value, and 85.1% diagnostic accuracy. US-FNA avoided SLNB in 18.1% of patients who underwent AD. So, Axillary USG-FNAC is an accurate technique in the staging of patients with BC. It allows reducing the number of SLNB and, when positive, offers a fast and useful tool.[18]

Houssami and colleagues have previously reported on the accuracy of preoperative ultrasound-guided needle sampling techniques for diagnosing nodal metastasis in invasive breast cancer. They described sensitivity, specificity and positive predictive values of 79·6%, 98·3% and 97·1% respectively. The diagnostic accuracies of these techniques were not compared. Core needle biopsy has been shown to be more accurate in assessing breast masses, but there is no clear consensus in the literature regarding its superior diagnostic accuracy in preoperative percutaneous axillary lymph node staging. It is important to determine which sampling method provides a more accurate

preoperative diagnosis to streamline patients for definite surgery without unnecessary additional procedures, or to provide information in relation to patient selection for NACT.[19]

CONCLUSION

It is concluded that ultrasound guided fine needle aspiration cytology of axilla has very good diagnostic accuracy (Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value and Diagnostic Accuracy of UG-FNAC was 93.41%, 85.51%, 89.47%, 90.77% and 90.00% respectively) in staging of breast cancer taking histopathology as gold standard. Hence this cheap, patient compliant easily available and minimally-invasive method can be used to determine the stage the cancer of breast. Moreover, by quick and early detection of the stage the appropriate treatment can be initiated timely for good prognosis.

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THE FREQUENCY OF HYPOCALCEMIA IN PATIENTS UNDERGOING TOTAL THYROIDECTOMY ON FIRST POSTOPERATIVE DAY

Wajahat Amir,[1] Ali Akbar,[2] Sana Afroze,[3] Rashid Mehmood,[4] Samreen Mushtaq,[5] Humayun Siddique,[6] Ameer Afzal,[7] Khalid Masood Gondal[8]

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Abstract

Objective: To assess the frequency of hypocalcemia in patients undergoing total thyroidectomy on the first postoperative day

Methods: 100 patients fulfilling inclusion criteria were enrolled in the study from the outpatient department (OPD) of General Surgery, CMH, Lahore. The non-probability purposive sampling technique was used in this study. Informed consent was taken from all the patients. Their demographics like name, age, gender, and address were noted. All surgeries were done under general anesthesia. After one day of surgery, the blood sample was obtained under aseptic measures. All samples were sent to the laboratory of the hospital for assessment of calcium level. Reports were assessed and calcium levels were noted. If calcium level was <8mg/dl, then hypocalcemia was labeled. All this information was recorded on proforma. Data were analyzed using SPSS 20.0

Results: The mean age of patients was 46.00±15.64years. There were 36 (36%) males and 64 (64%) females. The mean calcium level after thyroidectomy was 8.26±1.38mg/dl. There were 33 (33%) patients who developed hypocalcemia after thyroidectomy while 67 (67%) had normal calcium levels.

Conclusion: Thus, the frequency of hypocalcemia was high after total thyroidectomy. Optimization of the surgical technique (parathyroid preservation) could prevent the occurrence of hypocalcemia after total thyroidectomy in some cases; in other cases, identification of risk factors of hypocalcemia pre-operatively could permit early detection and effective treatment of these patients.

Key Words: Hypocalcemia, total thyroidectomy, first postoperative day,

The thyroid gland is an endocrine gland that is a site of several common diseases susceptible to medical or surgical treatments, or a combination of both.[1] Thyroidectomy is a routine procedure with very low mortality and an acceptable morbidity rate at high volume centers. Total thyroidectomy has become a mainstay of treatment used today for thyroid diseases.[2]

One of the most common early complications of thyroid surgery is hypocalcemia which occurs in about 20–30% of cases.[3] One study showed that the frequency of hypocalcemia was 24% in patients who underwent total thyroidectomy.[4] Another study showed that the frequency of hypocalcemia was 24.14% in patients who underwent total thyroidectomy[5] Karim et al. showed yet a higher frequency as compared to the above-mentioned studies i.e. 37.5% on 1st post-operative day of total thyroidectomy.[6]

The rationale of the study is to assess the frequency of hypocalcemia in patients undergoing total thyroidectomy on the first postoperative day. Literature has shown that the frequency of hypocalcemia was high

1. Wajahat Amir
2. Ali Akbar
3. Sana Afroze
4. Rashid Mehmood
5. Samreen Mushtaq
6. Humayun Siiddique
7. Ameer Afzal
8. Khalid Masood Gondal

1-8: Department of North Surgical Ward, King Edward Medical University, Mayo Hospital, Lahore

3. Department of Pathology, Allama Iqbal Medical College, Jinnah Hospital Lahore.

Correspondence:
Ali Akbar, *Mayo Hospital, Lahore.*
Email: dr.aliakbar81@gmail.com

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in patients who underwent total thyroidectomy. But variable results have been noticed in the literature. Moreover, not enough data is available in local literature regarding hypocalcemia after total thyroidectomy.

METHODS

This study was conducted on 100 patients in the Department of General Surgery, CMH, Lahore from December 2017 to June 2018. It was a Cross-Sectional study by design and patient selection was done by non-probability purposive sampling. Patients of age range 18-70 years of either gender undergoing elective total thyroidectomy under general anesthesia for benign diseases of the thyroid were included in the study.

Patients with malnutrition(BMI<18kg/m^2) or taking calcium supplements, Previous history of any parathyroid disease, medical renal disease (creatinine >1.2mg/dl), and hypocalcemia before surgery (<8mg/dl on medical record) were not included in the study. 100 patients who fulfilled selection criteria were enrolled in the study. Informed consent was obtained. Demographics including name, age, gender, BMI, and duration of diagnosis were also recorded. All surgeries were done by a single senior consultant surgeon with the assistance of a researcher. All surgeries were done under general anesthesia. After surgery, patients were shifted to post-surgical wards and were followed-up there. After one day of surgery, the blood sample was obtained under aseptic measures. All samples were sent to the laboratory of the hospital for assessment of calcium level. Reports were assessed and calcium level was noted. If calcium level <8mg/dl, then hypocalcemia was labeled All this information was recorded on proforma. Data were analyzed using SPSS Version 20.0. Mean ± SD was given for quantitative variables like age, BMI, calcium level, and duration of diagnosis. Frequency and percentage were given for qualitative variables like gender and hypocalcemia. Data was stratified for age, gender, BMI, and duration of diagnosis. Post-stratification, the chi square test was applied with P-value ≤ 0.05 taken as significant.

RESULTS

The mean age of patients was 46.00±15.64 years. There were 36 (36%) males and 64 (64%) females. The mean BMI of patients was 25.24 ± 5.37kg/m^2. The mean duration of symptoms was 7.17±3.53years. The mean calcium level after thyroidectomy was 8.26±1.38mg/dl. There were 33 (33%) patients who developed hypoca-lcemia after thyroidectomy while 67 (67%) had normal calcium levels. Data was stratified for the age of patients. In patients aged 18-30years, hypocalcemia developed in 9 (42.9%) cases. In patients aged 31-50 years, hypocalcemia developed in 11 (30.6%) cases. In patients aged 51-70years, hypocalcemia developed in 13 (30.2%) cases. The difference was insignificant (p>0.05). Data was stratified for the gender of patients. In male patients, hypocalcemia developed in 14 (38.9%) cases. In female patients, hypocalcemia developed in 19 (29.7%) cases. The difference was insignificant (p>0.05). Data was stratified for the duration of diagnosis of thyroid disease. In patients having the disease for ≤ 5years, hypocalcemia developed in 12 (34.3%) cases. In patients having disease from >5years, hypocalcemia developed in 21(32.3%) cases. The difference was insignificant (p> 0.05).

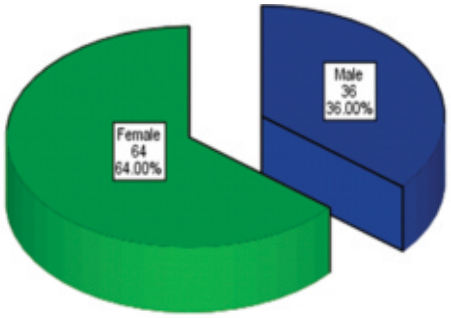

Fig 1: *Distribution of Gender of Patients*

Table 1: *Descriptive Statistics of the age of patients*

Age (years)	**n**	100
	Mean	46.00
	SD	15.64
	Minimum	18
	Maximum	70

Table 2: *Descriptive Statistics of BMI of patients*

BMI (kg/m^2)	**N**	100
	Mean	25.24
	SD	5.37
	Minimum	16.20
	Maximum	34.67

Table 3: Descriptive Statistics of the Duration of Diagnosis

Duration (years)	**N**	100
	Mean	7.17
	SD	3.53
	Minimum	1
	Maximum	12

Table 4: Descriptive Statistics of Calcium Level

Calcium (mg/dl)	**N**	100
	Mean	8.26
	SD	1.38
	Minimum	5.3
	Maximum	10.2

Table 5: Comparison of Hypocalcemia in Age Groups

		Age (years)			Total
		18-30	31-50	51-70	
Hypo-calcemia	Yes	9	11	13	33
		42.9%	30.6%	30.2%	33.0%
	No	12	25	30	67
		57.1%	69.4%	69.8%	67.0%
Total		21	36	43	100
		100%	100%	100%	100%

p-value = 0.557 (Insignificant)

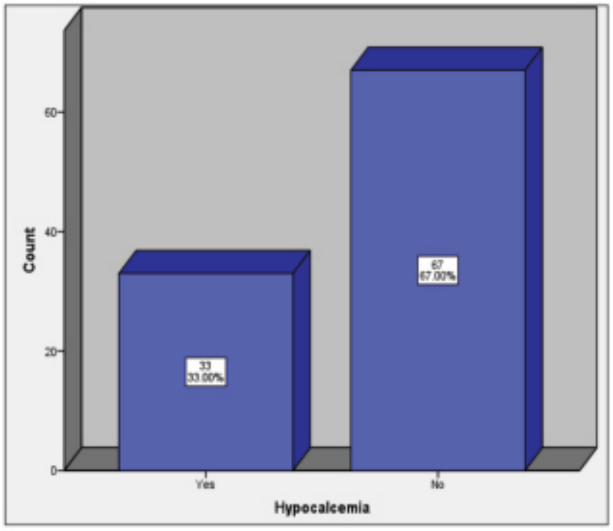

Fig 2: *Distribution of Hypocalcemi*

DISCUSSION

Hypocalcemia following thyroid surgery is more commonly associated with total thyroidectomy particularly for malignant lesions, thyroidectomy along with laryngectomy, and thyroidectomy in younger patients.[7,8]

Table 6: Comparison of Hypocalcemia in Gender Strata

		Gender		Total
		Male	**Female**	
Hypocalcemia	Yes	14	19	33
		38.9%	29.7%	33.0%
	No	22	45	67
		61.1%	70.3%	67.0%
Total		36	64	100
		100%	100%	100%

p-value = 0.348 (Insignificant)

Table 7: Comparison of Hypocalcemia in the Duration of Diagnosis Strata

		Duration		Total
		⩽ 5years	>5years	
Hypocalcemia	Yes	12	21	33
		34.3%	32.3%	33.0%
	No	23	44	67
		65.7%	67.7%	67.0%
Total		35	65	100
		100%	100%	100%

p-value = 0.841 (Insignificant)

Post-thyroidectomy hypocalcemia arises because of para-thyroid removal, devascularization and damage. vitamin D deficiency, an acute increase in calcitonin serum levels (because of gland handling during surgery) or "hungry bone syndrome" are believed to contribute to this process. Other causes include post-operative alkalosis-induced hypocalcemia resulting from hyper ventilation triggered by postoperative pain, and dilution hypocalcemia. Early postoperative hypocalcemia was detected in 3.5% patients with bilateral subtotal thyroidectomy, in 18.7% patients with near-total thyroidectomy and in 28.76% patients with total thyroidectomy.[9,10]

In our study, the mean calcium level after total thyroidectomy was 8.26±1.38mg/dl. There were 33 (33%) patients who developed hypocalcemia after thyroidectomy while 67 (67%) had normal calcium levels.

In some studies, conducted by Mali et al., in 2011, by Christou and Mathonnet in 2013 and by Viswanathan et al. in 2014, hypocalcemia was reported in 24.14%[5] 20–30% (3) and 24%(4 of cases respectively. But Faizi et al., conducted a study in 2015 and showed higher

frequency as compared to above these studies i.e. 37.5% on 1st postoperative day of total thyroidectomy[6]. The findings of this study are much higher than our study. Iqbal J et al. reported asymptomatic hypocalcemia in 18.8% of patients in his study after total thyroidectomy.)[11] Findings of these study are comparable with the present study.

In one study by Erbil et al, total thyroidectomy was performed in 130 patients with multinodular goiter and asymptomatic hypocalcemia was found in 31.2% of patients.[12] In another study by Lankarani et al, subtotal thyroidectomy was performed in 102 patients with multinodular goiter and asymptomatic hypocalcemia was found in 19.6% of patients.[13] In another study by Gentileschi et al., asymptomatic hypocalcemia was reported as 19.27%.[14]

Previous studies also give various other risk factors like age, basic pathology, and duration of surgery as reasons for an increased incidence of hypocalcemia. All patients with low calcium levels were symptomatic on day one. 99% of patients with low calcium levels were symptomatic on the second and again on the third day, all patients with low calcium levels were symptomatic ultimately if not treated.[15]

Surgeon's ability to predict the onset of post-thyroidectomy hypocalcemia is very important for post-operative management. Early detection of any risk of developing hypocalcemia will reduce the hospital stay length and eliminate unnecessary laboratory examinations. When hypocalcemia is predicted, treatment with prophylactic calcium and vitamin D supplements can prevent the development of hypocalcemia symptoms and premature discharge of patients.[9]

CONCLUSION

In our study, the frequency of hypocalcemia was high after total thyroidectomy. Optimization of the surgical technique (parathyroid preservation) could prevent the occurrence of hypocalcemia after total thyroidectomy in some cases; in other cases, identification of risk factors of hypocalcemia pre-operatively could permit early detection and effective treatment of these patients.

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COMPARISON OF TREATMENT OUTCOME OF HEMORRHOIDS USING ELECTRO CAUTERIZATION VERSUS INJECTION SCLEROTHERAPY

Abdul Majeed,[1] Farooq Ahmed,[2] Hina Khan,[3] Aslam Javed,[4] Muhammad Kamran Chaudhary[5]

How to cite the article :Majeed A, Ahmed F, Khan H, Javed A, Chaudhary MK. Comparison of treatment outcome of hemorrhoids using electro cauterization versus injection sclerotherapy. JAIMC. 2021; 19(4):914-16.

Abstract

Objective: To compare the efficacy of electro cauterization versus injection sclerotherapy in first degree harmorthhoids in respect of pain and necurrence meterials and methods.

Methods: A total of 130 patients were included in my study at Jinnah Hospital, Lahore from September 2017 to September 2021.The history in detail was taken from the patients and proctoscopic examination was done . Patients were dinded into 2 groups one groups was treated with electrocuteriztion and the other group was treated with injection scolero therapy (IS) The outcome was measured.

Results: The mean age of he patients was 45 years to patients were females. P value of injection sclerotherapy was 0.001. it mean the injection sclew therapy was not so much effective p value for EC was 0.045 also higher number of patients were compared to is.

Conclusion: Although EC is more painful to the patients with a hemorrhoids but its effectiveness was high in treating its degree hermorhoid.

Key Words: Hemorrhoids, electro cautrization, sclerotherapy

Many number of the people among the human population suffers from haernorhoids at any stage of the age, haemorrhoides is a treated disease but more challenging in surgical management when detec-ted earlier. Unfortunately many patients with haemorr-hoids seek medical advice with delayed presentation.[1]

Haemorrhoids are the most widely to he one of the most widely distributed of human ailments ranking first among diseases of rectum and anal canal.[2]

Treatment modalities include:

1. Abdul Majeed
2. Farooq Ahmed
3. Hina Khan
4. Aslam Javed
5. Muhammad Kamran Chaudhary

1,2,5. Department of Surgery, Jinnah Hospital, Lahore.
3. Department of Surgery, FJMU, Lahore.
4. PRCMDC, Dina Nath, Lahore.

Correspondence:
Dr. Abdul Majeed, *Surgical Unit-I Jinnah Hospital, Lahore*

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1. Electrocuterization
2. Injection sclerotherapy

IS is preferable to EC for the end patient treatment of piles, due to the neasons that it is quicker less tedious and relatively comfortable with equally effective results.[3]

Nonetheless, large dose single session IS provides only short term efficacy with symptoms relief. Complications using both conservative and surgical treatment of piles are rare. Dithering is simple technique and may be appropriate treatment in suitable cases.[4] Both direct current and bipolar diathermy probes are effective. For control of chronic bleeding however direct current cautery has less complications. The presented study was targeted for comparing two methods in terms of bleeding per rectu, pain score and patient satisfac-tion score.

METHODS

Between September 2017 and September 2021 130 patients were selected by using criteria of virgin

1'st and 2nd degree haemorruids non recurrent and age between 25 years to 65 years taking 45 years as diverge age. After recruitment to trial they were randomized to two groups and were called one by one on the assigned date to outdoor patient departments (OPD) for the procedure. For stronger follow up only those patients who were registered for the free treatment at Jinnah Hospital,Lahore were in cluded in the study. Patients of aboth the genders having 1st degree and 2nd degree piles were included. Patients with pregnancy local infections immune deficiency 3rd and 4th degree piles and bleeding disorders were excluded patients of total 130 70 males and 60 females ranging from 25 years to 65 years were included patients were divided into 2 equal group. 65 patients underwent IS and 65 patients under went EC. IS or EC procedures were performed on outdoor patient basis. Injection sckrotherapy was applied by 1-2 ml of 5 % phenol in almond oil by injection into the submucosa of each pile above the dentate line. Whereas, electro eauterization (EC) was applied by EC machine (wieda china made) direct current of 10-20 Ma was applied with a bipolar probe in the submucosal plance of each haemorrhod above the dentate line. The current was applied for 45-70 seconds for each pile core.

An appropriate pain scale was applied ranging from 0 to 10 in which patient had to mark the intensity of pain felt by him/her. On this score to meant the worst pain ever felt in the life of the patient. Patients of the both groups were given a treatment with metronidazole 400mg. thrice daily for two days and bulk forming laxative (skilax 10 drops) in water daily twice for one week daily twice for one week were given to all patients.

Follow-up at 1st, 3rd and 8th week was done to both groups. History and proctoscopic examination were done on every follow up of the all patient.

On proctoscopy , following findings were noted:

1. No effect
2. Reduced bleeding
3. Regressed pile
4. Fully cured

At the 8th week of follow up

Overall patient's satisfaction

Score was measured

0- Means not satisfied

1- Means modercetely satisfied.

2- Means highly satisfied

The statistical analysis was done using SPSS version.

21 Chi square test and Fischer's test were applicable and were applied for assessing the importance of difference in the outcomes of the two above mentioned procedures. i.e (IS versus EC).

The outcome was measured in terms of reduction in bleeding per rectum, reduction in pain and overall patients own satisfaction.

RESULTS

A total of 130 patients included in study the mean age of the patient was 45 years with STD of 16 years. 70 were males and 60 were females. Most of the patients (n = 76, 58%) symptoms for more than 6 months. N=35 (26.9%) had symptoms for 1–2 months and n=19, 14.6% had symptoms for 1 week to 1 month about 30% of the patients had associated symptoms of pain other had no associated symtoms. All the patients had complain of bleeding per rectum. 78 patients told this bleeding in the form of drops during or after defection. 29 patients had bloody splash. 23 patients had also mucus discharge .

History of constipation was present in 88 patients. Most of the times. 30 patients had occasional constipation on 10 patients denied any complaint of constipation. Only 2 patients had complaint of weight loss who were found CA rectum on digital rectal examination. Only 30 patients had positive history of piles. Dietary history was taken from all patients. 88 patients had history of vegetable usage. 42 patients had history of fibreless diet and taking more meat and pulses. Proctoscopy was done in all patients. Most patients had 3 or more piles comes. 28 patients had 2 piles 12 patients had a single pile of first degree. Patients were into 2 groups and were subjected to EC or IS. 65 patients received EC and 65

patients received IS. These both groups patients were suffering from 1st degree or 2nd degree haemorrhoids. The pain experienced by the patients with EC was compared with patients undergone IS. Pain was less in IS. Pain was more in patient undergone EC. Reduction in bleeding PR was seen more promi-nent 83% in EC at 8 week followup as compared to IS 46%. Patients satisfaction was more prevalent in EC as compared to IS. 15 (11%) patients in IS were not satisfied as compared to EC 2 not satisfied. This difference in overall patients satisfaction score was statistically significant (p=0.04)

DISCUSSION

Piles are common problem. Haemorriadectomy is procedure of choice. Males were more in numbers than females in our study. This could be done to the reason that haemorr-hoidal disease affects males more than females as supported by another study.

		Pain	Bleeding P/R	Satisfaction
IS	65	13 (10%)	23 (17.69%)	50(38.4%)
EC	65	38 (29%)	14 (10.76%)	63 (48.46)

Most of the patients in our study had constipation thus relating etiopathogenesis. However this association has been argued. Recently by some of the global studies. This conflict may be due to the difference in the race and ethinicity to our population. Injection selerotherapy is an older method of treating piles non surgically. It is very effective, less tedious procedure but is not devoid of complications. Cure rate was 67% overall.

In comparison to 67% fully cured of parental bleeding who were induced IS. Verma et. Al from hong kong have found early cure rate of 84% with IS. Aftab has observed 63% cure rate. Saleem observed 95% cure rate in 1st degree piles. Electro cauterization on the other hand has been found more effective than injection sclerotherapy. 88% was cure rate seen EC). EC of biopare and dired current were qually effective, although earlier hs less complication rate.

CONCLUSION

EC is a recent technique for curing piles as compared to IS. EC is more safe, acceptable and accurate technique in treating patients of 1st & 2nd degree piles as compared to injection sclerotherapy. But 2st only drawback (EC) experienced by the patient occasionally.

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FREQUENCY OF RECURRENT LARYNGEAL NERVE INJURY IN SUBTOTAL THYROIDECTOMY IN BENIGN DISEASES OF THYROID

Abdul Majeed,[1] Muhammad Kamran Chaudhary,[2] Farooq Ahmed,[3] Aslam Javed[4]

How to cite the article :Majeed A, Chaudhary MK, Ahmed F, Javed A. Frequency of recurrent nerve injury in subtotal thyroidectomy in benign diseases of thyroid. JAIMC. 2021; 19(4):917-19.

Abstract

Background: To evaluate the frequency of recurrent laryngeal nerve damage in subtotal thyroidectomy versus total thyroidectomy in benign diseases of thyroid.

Methods: Methodology: This comparative study was conducted at Jinnah Hospital, Lahore Pakistan. Patients date comprised from September 2017 to September 2021 who underwear subtotal or total thyroidectomy. A self-generated proforma was used to documents per operative findings and post-operative complications. The visits for follow up were also highlighted at the discharge cards. Patients who could not come for follow-up were inter nerved on phone. Date was analysed using SPSS 20.

Results: Of the 94 patients 78 (82.97%) were females and 16 (17%) were males. 47 patients under went subtotal thyroidectomy under went total thyroidectomy all the patients had benign disease of thyroid contirmed by Pre-operative FNAC. Recurrent laryngeal nerve unilateral in 2 patients 2.12%) and 1 (1.06%) in bilateral recurrent nerve injury were seen in subtotal thyroidectomy.

Recurrent laryngeal nerve injury was seen in 4 (4.25 %) as unilateral and (2.1%) seen as bilateral recurrent laryngeal nerve injury when total thyroidectomy was opted (these injury were permanent.

Conclusion: Simple multinodular was sufficiently cured with total thyroidectomy although recurrent laryngeal nerve injury incidence was higher in this technique as compared to subtotal thyroidectomy.

Keywords: total /subtotal thyroidectomy recurrent laryngeal nerve.

First successful thyroidectomy in the history of surgery was performed in 1902 by Theodore kocher of Switzerland.

Since then, surgery has brought revolution over the past century with advances in technology and surgical expertise.

Surgical complications made thyroidectomy an adventurous endeavor . although complications are accepted by legal definitions by following the standard treatment (surgery) but serious complications can interfere with the quality of life. One of complications following thyroidectomy is recurrent laryngeal nerve (RLN) injury either temporary or permanent. Here permanent RLN injury will be discussed in my study. RLN injury causes horseness in case unilateral one. RLN injury cases airway obstruction in many researches have favored the total thyroidectomy for benign diseases whereas others have favoural subtotal thyroidectomy in light of the RLN safeguarding. The present study was planned with intension to asses the frequency of RLN injury following total or subtotal thyroidectomy in benign diseases of thyroid at tertiary care hospital.

1. Abdul Majeed
2. Muhammad Kamran Chaudhary
3. Farooq Ahmed
4. Aslam Javed

1-3: Department of Surgery, Allama Iqbal Medical College/Jinnah Hospital, Lahore.
4. PRCMDC, Dina Nath, Lahore

Correspondence:
Dr. Abdul Majeed, Registrar, Department of Surgery, Allama Iqbal Medical College/Jinnah Hospital, Lahore.

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METHODS

My study was prospective one that was conducted at Jinnah Hospital/Allam Iqbal Medical College, Lahore. It lasted from September 2017 to September 2021. It included all patients of multimnodular goiter

with unferlying benign pathology confirmed an FNAC. Since the hospital, turnover of igoitre was slow due to Covid -19 sampling of the patients was done by strict scrutiny with dead –sure of benign disease and using SLOVIN formula. n=N/1+ne2) patients of age 20-55 years were included. A self generated performa was used to documents operative findings and post-operative complications especially RLN injury. The patients with RLN neuropraxia were excluded at end. Total sample size was 94. 78 were females (82.97%). 16 were males (17%).

Patients were contacted via phone for giving consent for inclusion. Pre operative assessment for vocal cards was done by ENT deptt using telemetry. After gaining medical fitness.

All patients undergone generat anaesthesia half by the patients i.e 47 undergone half by the patients i.e 47 undergone half of patients i.e 47 undergone total thyroidectomy. Vocal coards were checked immediately by the anaesthetist by using tarygoscope while extubating the patient from endotracheal tube. Immediate documentation about mobility of vocal cords was registered in the file of the patients, also the vocal cards were evaluated by post-operative conversation with the patients when he /she became fully conscious. Patients with hoarseness were followed for 3 months post-operatively. The patients with horseness were re-evaluated by the 8 and 12 weeks 0,2,4,8 and 12 weeks of only one patient reverted from horseness to normal speech after 8 months follow-up. P value was <0.05 as already mentioned SLOVIN formula was applied where n = number of samples, N = Total number of population and e = error margine. The sampling technique was nonprobability convenience. Also hypocalcemia was excluded by repeated serum calcium sampling in patients with horseness of voice. SPSS version was applied.

RESULTS

Of the 94 patients 47 underwent total thyroidectomy. Remaining 47 patients underwent subtotal thyroidectomy. RLN neuropraxia /hyprcalcemia sequence were excluded from the study at the end of the task.

Table 1:

Sample Size	94
Subtotal thyroidectomy	47
Total Thyroidectomy	47

Table 2:

Sr.No	RLN unilateral Injury	RLN Bilteral injury
Subtotal Thyroidectomy	2 (2.12%)	1(1.06%)
Total Thyroidectomy	4 (4.25%)	2 (2.12%)

15 cases of recurrent goiter were included in the study. As seen by the results the incidence of RLN injury twice as compared to the subtotal thyroidectomy. However speech therapy was advised to unilateral RLN injury where as the bilateral RLN injury was managed by tracheostomy done in 3(3.19%) patients.

DISCUSSION

As the RLN injury ranges from 3 % to 11% so 3.19% bilateral RLN, 638% UNILATERAL RLN and 9.57% of the overall RLN injuries are acceptable. The reasons for these injuries were i.e extensive fibrosis, tedious thyroid follicular adenomas multicentric and hashimoto's thyroiditis in some patients. The only plus point of total thyroidectomy was extremely low also thyroidectomies were performed by various to exclude the base in this study.

Fortunately, mortality rate was 0% upto the end of my study. The ligation of branches of inferior thyroid artery was performed the highly qualified surgeons. There is a variable prevalence of RLN injury in literature ranging 0-14%. Some studies reflect intermediate rates of permanent RLN palsy. Certain studies reported higher permanent RLN palsy rates. This reflected variation in type of operation (SST OR TT), Surgical expertise and number of surgeries done at that particular centre and recurrent benign goiter.

CONCLUSION

As compared with the international ratios, results are acceptable. However one inference dawns from the horizon of this study that subtotal thyroidectomy is superior technique as compared to the total thyroi-

dectomy when seen RLN injury (storm among horizon)

Conflict of Interest None

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EXTRAPOLATIVE FACTORS AND OXIDATIVE PROFILE IN YOUNG PREGNANT FEMALES SUFFERING FROM PREECLAMPSIA

Ahmad Saleem,[1] Noreen Akmal,[2] Nuzhat Malik,[3] Amna Akmal,[4] Arif Malik,[5] Mukhtar Ahmad[6]

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Abstract

Background: Preeclampsia is a life threatening complication of pregnancy that starts at 20th week of gestation and is typically related to widespread vascular endothelial malfunction and vasospasm. .Clinically it is defined as raised blood pressure (HTN), either equal to or higher than 140/90 mmHg and proteinuria (albumins in urine, 300mg/24H or more). Or a proteinuria of 1+ or more on repeated measures on dipstick method with a systolic blood pressure of more than 140 mmHg or a diastolic blood pressure of more than 90 mmHg on repeated readings, after 20th week of gestation (Hubel, 1999). Hereditary predisposition is also an important factor. Its prevalence in different relations is, Sisters 37%, Daughter 26%, and Grand daughters 16%.

Methods: Pregnant females diagnosed as having preeclamsia at the Jinnah hospital Lahore and Sir Ganga Ram Hospital, Lahore were selected. Total of one hundred (100) females were taken for present study, fifty (50) as control and remaining fifty (50) were included in the patient group. Informed consent was obtained before being included in this study.

Results: Highly significant (p=0.0l4) difference of malondialdehyde level was observed between women suffering from preeclampsia and normal subjects (5.26±01.23 Vs. 0.93±0.065 umol/L). Level of antioxidants such as SOD, GSH, CAT and GPx was decreased (0.l09±0.016 U/ml, 4.26±l.44 umol/L, 2.99±0.923 U/L and4.26±l.44 umol/L respectively) in preeclatnpsia patients as compared to controls (0.66±0.023 U/l, 9.66±2.55 umol/L,6.35±1.88 U/L and 8.89±3.26 umol/L respectively).

Conclusion: The study concludes that increase in oxidative stress and pro-inflammatory cytokines are not only involved in endothelial cell dysfunction but can also be considered as one of the potential source for preeclampsia. Enhanced inflammatory response could be seen due to the increased pro-inflammatory cytokines, neutrophil activation, leukocyte activation and acute phase proteins in preeclampsia Out of all cytokines, IL-6 and TNF alpha are considered to play primary role in the immune activation.

Key Board: Pregnant, pre-eclampsia, oxidative profile

1. Ahmad Saleem
2. Noreen Akmal
3. Nuzhat Malik
4. Amna Akmal
5. Arif Malik
6. Mukhtar Ahmad

1. *Department of Physiology, Allama Iqbal Medical College/Jinnah Hospital,Lahore*
2,3. *Department of Gynaecology and Obstetrics. Fatima Jinnah Medical University/Sir Ganga Ram Hospital,Lahore*
4. *Punjab Thalassemia and Other Genetic Disorders Prevention and Research Institute.*
5. *Institute of Molecular Biology and Biotechnology, University of Lahore.*
6. *Jinnah Hospital, Lahore.*

Correspondence:
Dr Ahmad Saleem, *Senior Demonstrator, Department of Physiology, Allama Iqbal Medical College/Jinnah Hospital,Lahore*
Email: docahmad786@gmail.com

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Preeclampsia is a life threatening complication of pregnancy that starts at 20th week of gestation and is typically related to raised blood pressure with a BP either high or equal to 140/90 mmHg and proteinuria (albumins in urine, 300mg/24H). Or an albumin concentration of 1+ or more, on repeated measures by dipstick method along with HTN, starting at 20th week of gestation (Hubel, 1999). Hereditary predisposition is also important factor. Its prevalence in different relation is; Sisters 37%, Daughter 26%, and Grand daughters 16%.

Besides the hemodynamic changes in maternal blood, one of its main features is utero-placental circulation insufficiency and this leads to IUGR i.e; intrauterine growth restriction (reduced amniotic fluid, and abnormal oxygenation) (Hubel, 1999). Inadequate trophoblastic migration and lack of physiologic transformation of spiral artery with its arterioles persisting up to end of pregnancy results is narrowing of artery and arterioles. Their walls are sensitive to vasoconstrictive factors, as platelets aggregation causes narrowing of the lumen. This results as HELLP syndrome. Hemolysis, elevated liver enzymes and low platelet count (Maarten et al., 2004). Signs and symptoms of HELLP include upper right quadrant or epigastric pain, nausea, vomiting, 30-60% have headache, 20% have visual symptoms, HTN, proteinuria, some have malaise (general feeling of illness or discomfort) before PE (Preeclampsia). Some have conception without fetus called as hydatidiform mole (placenta contains grape like vesicles). Placenta is the main organ to connect the blood supply of the mother to her unborn baby. It with its blood vessels is not well developed, and as a result the uteroplacental insuffiency develops (Asha and Varghese, 2015).

An abnormal placement of placenta may also lead to placental ischemia. In such cases reperfusion may cause placental injury and an increase in the oxidative stress, resulting in the generation of free radicals of oxidative stress. This patho-physiology may cause abortion, preeclampsia,complication of delivery due to acidemia and intrauterine growth retardation (IUGR). Generation of free radicals increases the ROS production. Lipid hydroperoxides are formed which bind to lipoproteins and are transported to distant sites via maternal blood circulation causing injury. Primigravida are more prone to be affected with abnormalities of coagulation system, disturbed liver function, renal failure and even cerebral ischemia (Badland et al., 2007). Limited sperm exposure increases risk of PE, and extended intercourse reduces the risk of PE. While one abortion with same partner reduce the risk of PE, women having one abortion with new partner increase risk of PE, like primigravida.(Veison, 2006).

Twin pregnancy or multiple pregnancies have a 2-3 times higher risk of PE than a single pregnancy. It is due to the soluble FMS like tyrosine kinase-1, which is a circulating antiangiogenic molecule of placental origin and it plays a major role in PE by antagonizing the vascular endothelial growth factor (VEGF) and placental growth factor. High altitude may also be a predisposing factor in development of PE. Chronic hypoxia is an important predisposing factor for PE, and at high altitudes lack of oxygen causes placental hypoxia or ischemia, resulting in release of some products in the maternal circulation and this initiates the pathophysiological changes which cause post hypoxic placental perfusion leading to PE with oxidative damage to placenta and its vessels (Badland et al., 2007) .

Altered lipid profile, increase of PUFA (polyunsaturated fatty acid) in cell membranes, lipoproteins, synthesis of free radicals and placenta are the chief source of ROS(reactive oxygen species) production. Other causes of ROS production are maternal leukocyte activation and endothelium damage. Inflammatory state is also a cause of oxidative stress leading to preeclampsia. PUFA get oxidized by free oxygen radicals, decrease antioxidants (VITAMIN A,C, & E), SOD (superoxide dismutase) and glutathione per oxidase, neutrophil activation with NADPH oxidase, increased cyclooxigenase-2 and lipooxygenase. Increase in LPO (lipoxygenase)leads to atherosclerosis and PE (Hubel, 1999).Leukocytes are usually observed in inflammation and when got activated, release the sL-selection from their surface, responsible for leukocyte adhesion along the endothelial cells. Leukocytes are also observed in vascular cell adhesion molecules (VCAM), crucial for the interaction between leukocytes and endothelial cells (Atamer et al., 2005).

Enhanced inflammatory response occurs due to increase in proinflamatory cytokines. TNF-alpha and IL6 play an important role in immune activation in PE. Acute-phase proteins(CRP) and leukocyte activation also enhance the inflammatory response. Oxidative stress in maternal circulation, and/or hypoperfused placenta is the major source of ROS production and

pro-inflammatory cytokines, which may induce the oxidative stress (Bayhan et al., 2005). Increased level of cytokines (TNF-alpha and IL-6), may trigger the activation of neutrophils, causing the release of some chemo attractants in the process of inflammation. Increase in levels of platelet cell adhesion molecule (PCAM) plays an important role for leukocytes in transmigration across the endothelial layer of blood vessels. Neutrophil activation; increase in metabolic activation causes release of their granules in circulation and tissues leading to increase in the inflammatory response and oxidative stress in PE.

Increased level of cytokines, also plays an important role in activation of immune system in PE, specifically by TNF-alpha and IL6 cytokines. These inflammatory stimuli lead to increased production, and hence increased levels of CRP and alpha -1-antitrypsine. Increased maternal oxygen level increases the ROS production which leads to signal transduction, various regulatory pathways activation and increased platelets activation resulting in PE (Schafer et al., 2001).

Increased level of thiols and ceruloplasmine, cause the ROS production, and endothelial dysfunction leading to hypoperfusion of placenta resulting in PE. Increase level of endothelial-derived nitric oxide (NO), with decreased SOD activity leads to reaction of NO with superoxide and formation peroxynitrite (ONOO-), which is a strong oxidizing agent and has the capacity to develop LPO, which leads to endothelial dysfunction resulting in PE. Increased level of peroxynitrite (ONOO-) also causes increased inflammation, increased nitration of tyrosine residues of protein, increase in prostaglandin synthesis, subsequently causing blockage of vascular relaxation with increase in smooth muscle contraction which results in hypertension (Xeu and Zhang, 2009). Endothelial cell dysfunctioning in preeclampsia is primarily caused by decrease in trophoblast invasion of endothelial arteries leading to placental ischemic reperfusion and resulting in formation of free radicals. These free radicals attack free fatty acids in cell membrane and form lipid hydroperoxide. It also causes increase of vasopressors in PE. Imbalance in peroxidants and antioxidants leads to increase in per oxidants, which cause the cell and tissue damage in PE.

Ca+2 ATPase activity is decreased in tissues plasma membranes in PE, with an increase in lipid per oxidation and it causes failure of protective mechanism against oxidative stress (OD). Increase level of lipid inhibits the membrane bound enzymes and Ca+2 ATPase is one of them. Oxidation of LDL impairs the endothelial dysfunctioning by release of nitric oxide (NO), which interferes with leucocytes; and platelet adhesion results in the vasospasm in PE (Symonds et al., 2007). Oxidized LDL and TNF-alpha bind with their receptors LOX-1 and TNFR. Both LOX-1 and TNFR after activation generate superoxide radicals with NADPH oxidase. NO produced by NO-synthase reacts with oxygen radicals producing ONOO- which causes the activation of NFkB. ONOO- also reacts with MMP-2, which adds up with cleavage of ET-1which causes the activation of ET-1, leading to iNOS production in bulk along with NO which forms ONOO- and decreased PGI-2. NO and PGI-2 are vasodilators but ONOO- and decrease PGI-2 cause vasoconstriction and result in endothelial dysfunction and consequently results in preeclampsia. Increase in biological oxidation and reduced antioxidants are the fundamental cause of endothelial cell damage in tissues of placenta in pregnant young ladies suffering from PE. Changes in Oxidative stress in preeclampsia at the level of placenta are developed by xanthine oxidase and NADPH oxidase and this causes increase in the lipid peroxidase in placenta, increase in F2-prostances, increased oxidative protein damage, increase in oxidative potential and decreased antioxidant activity in placenta (Ziech et al., 2011).

Due to decrease in vitamin E concentration, decrease in glutathione level, decrease in glutathione peroxidase enzyme, decrease in SOD, decrease in catalase enzyme, increase in transcription of genes mediated by free radicals permeate into maternal circulation. Due to oxidative stress added to maternal circulation, the generation of radicals starts along with the syncytiotrophoblast debris shedding and activates maternal neutrophils. Neutrophils are also locally

activated when blood passes through placental circulation and vascular cell adhesion molecule(VCAM), release of lipid peroxide in maternal circulation & cytokine synthesis occurs from activated neutrophils. It cause further neutrophil activation and may cause the maternal endothelial cell activation et al., 2009).

All of these factors subsequently cause leukocyte adhesion. In preeclampsia fatty acids (FA), triglycerides (TGs), very low density lipoprteins (VLDL) concentration is increased and high density lipo-protein (HDL) is decreased . Cholesterol and other lipoproteins remain unchanged. It increases the lipid per oxidation and the first biomarker of LPO, which is found in serum of women with preeclampsia, is Malondialdehyde (MDA). It is the major metabolite of LPO break down which is the result of formation of prostaglandin-(PF2) antibodies against modified (LDL), F2 Isoprostane. In short the preeclampsia is potentially dangerous complication of pregnancy which increases the risk of vascular disease, increases risk of cardio-vascular accidents (CVA), renal disease, liver disease, diabetes and hypertension (HTN). (Tong and Zhang, 2012).

METHODS

The study was designed to evaluate the important role of oxidative variables in the development of pre-eclampsia in young pregnant women. All the selected patients were diagnosed at the Jinnah hospital Lahore and Sir Ganga Ram Hospital, Lahore. Total One hundred (100) age and sex-matched individuals were selected in present study, fifty (50) as control and remaining fifty (50) were included into patient groups. Informed consent was obtained before being included in this study. The experimental protocol was approved by the Research Ethical Committee of The Institute of Molecular Biology and Biotechnology, The University of Lahore.

Five ml of venous blood sample were taken from the anticubital vein of each participant. The sample bottles were centrifuged within one hour of collection, after which the serum was separated and stored at -70°C until assayed.

The diagnosis of preeclampsia in pregnant women (20-30 years of age).

The subjects with the history of taking drugs (including alcohol and cigarette), pre-diagnosis medications (e.g. Anti-Parkinsonsian,Anti-psycotics) were excluded from this study. All chemical reagents of analytical grades were purchased from Sigma/Invitrogen Chemical (St. Louis, USA). Complete blood count of the selected subjects was performed on the automated hematology blood analyzer by Sysmex (version. XE-2100).

Lipid peroxidation in sample was estimated calorimetrically by using the method of Ohkawa et al., (1979). The estimation of Superoxide dismutase was done through Kakkar method that was established in 1984. The activities of Catalase were evaluated through Aebi method that was introduced in 1974, by using the spectrophotometer and the absorbance were taken at 230nm. According to above mentioned anti-oxidants the activity of GSH was also determined by Moron method, established in 1979, by using the spectrophotometer with absorbance taken at 412nm.

The activities of Glutathione reductase was determine through spectrophotometer method by following the David and Richard method that was established in 1983. The gutathione peroxidase was determined with the help of buffer/ enzyme reagent wendel, 1980, by the method of spectrophotometer. Witko-Sarsat and its colleagues (1996) established the method to evaluate the role of Advanced oxidation protein products (AOPPs). The same protocol was followed. The levels of NO were determine by using Grease's reagent (Buries and Bories, 1995). The levels of TNF alpha was determined by commercially available human ELISA kit method (by Affimatrix). The levels of inflammatory biomarkers like IL6 was evaluated by using commercially available human ELISA kit assay (R &D Systems, MN USA). Human sL-Selectin is a glycoprotein and was evaluated by the ELISA kit assay (by Human Diag-nostics)

For the analysis T-test was performed on SPSS version 16.

RESULTS

Highly significant (p=0.0l4) difference of malondialdehyde level was observed between women suffering from preeclampsia and normal subjects (5.26± 01.23 Vs. 0.93±0.065 umol/L). Level of antioxidants such as SOD, GSH, CAT and GPx was decreased (0.l09±0.016 U/ml, 4.26±l.44 umol/L, 2.99±0.923 U/L and 4.26±l.44 umol/L respectively) in preeclatnpsia patients as compared to controls (0.66±0.023 U/ml, 9.66±2.55 umol/L, 6.35±1.88 U/L and 8.89±3.26 umol/L respectively). Whereas the level of GR was elevated (17.19±2.47umol/L) in women with preeclatnpsia than that of healthy controls (3.29±0.956 umol/L). Proinflarnrnatory cytokines such as TNF alpha and IL-6 were significantly raised (p=0.0l4 and p=0.0l7) in diseased group (37.26±6.35 pg/ml and 19.36 ± 2.88 pg/ml) as compared to control ones (l9.36 ± 4.74pg/ml and 6.28±l.15). Marked increased in the level of other circulating variables including homocysteine, NO and inhibin-B was observed in women suffering from preeclarnpsia (7.56±3.77 umol/L, 39.35±2.07umol/L and 70.26±4.28 ppm) as compared to normal individuals (7.06±2.07 umol/L, l8.26±2.65 umol/L and 25.23±l.88 ppm respectively).

DISCUSSION

Preeclampsia is enhanced inflammatory processes in maternal circulation. There are levels of phase proteins, antitrypsin and proinflamatory cytokines. Increased level of CRP starts being to produce at the 16 weeks of gestation in first Trimester (Myatt, 2010). The increase level of CRP accompanied with pro-proinflamatory entitites (TNF a,IL-6) were observed in PE in previous studies. In these cases the placenta is the major source of cytokines in pregnancy and these are disturbed in preeclampsia. This added with higher concentrations of proinflammatory cytokines in maternal circulation are without doubt important factors in inflammatory processes leading to PE (Bogdarina et al., 2010). A higher count of leukocytes and neutrophils is observed in patients of PE than in normotensive pregnant ladies. Cellular adhesion molecules in placenta and in maternal circulation are also increased in preeclampsia (Bames and Ozzane, 2011). There is also increased expression of platelet endothelial adhesion molecules PECAM-I, intracellular adhesion molecules ICAM-I and vascular cellular adhesion molecules in normotensive and preeclampsia. These are the member of Ig family (Gluckman et al., 2008).

The increase in sVCAM-I causes the adhesion of leukocytes to the endothelium and PECAM-I plays an important role in transmigration of leukocytes and results in endothelial dysfunction. It is observed that sL-selectin is increased in acute inflammatory conditions and it is decreased in chronic inflammatory conditions (Cambonie et al., 2007). The increase in leukocyte and decrease in sL-selectin favors the leukocyte endothelial adhesion in preeclampsia (Maarten et al., 2004). Inflammatory state is also one of the causes of oxidative stress leading to preeclampsia. PUFA gets oxidized by free oxygen radicals; decreased antioxidants, SOD and glutathione per oxidase, neutrophil activation with NADPH oxidase, increased cyclooxigenase-2 and lipooxigenase, increase in LPO leading to atherosclerosis and PE (Hubel, I999). Leukocyte activation, is usually observed in inflammation and when activated, there is a release the SL-seletin from the surface of the almost all leukocytes which is respon-

Table 1: *Levels of Circulating Biochemical Markers of Medical Importance in Women Suffering from Preeclampsia*

Variables	Controls	Patients	P-values
MDA(umol/L)	0.93±0.065	5.26±1.23	0.014
SOD(U/ml)	0.66±0.023	0.109±0.016	0.000
GSH(umol/L)	9.66±2.55	4.26±1.44	0.032
CAT(U/L)	6.35±1.88	2.99±0.923	0.046
IL-6(pg/ml)	6.28±1.75	19.36±2.88	0.017
TNF-alpha(pg/ml)	19.36±4.74	37.26±6.35	0.014
Homocysteine(umol/l)	7.06±2.07	17.56±3.77	0.000
NO(umol/l)	18.26±2.65	39.35±2.07	0.012
GPx(umol/L)	8.89±3.26	4.26±1.44	0.000
GR(umol/L)	3.29±0.956	7.19±2.47	0.065
Inhibin-B(ppm)	25.23±1.88	70.26±4.28	0.012

MDA=Malondialdehyde
SOD=Superoxide dimutase
GSH=Reduced glutathione
CAT=Common antioxidant enzyme
NO=Nitric oxide
GPx=Glutathione peroxidase
GR=Glutathione reductase

sible for cell adhesion along the endothelial cells (Nuyt and Alexander, 2009). It is also observed that in vascular cell adhesion molecule (VCAM), are crucial for the interaction between leukocytes and endothelial cells (Casasco et al., 1997). Enhanced inflammatory response; In this increase in proinflamatory cytokines TNF-alpha and and IL-6 plays an important role in immune activation in PE, acute-phase proteins(CRP) and leukocyte activation also enhance the inflammatory response (Cerda and Weitzman, 1997). Increase in alpha-1 antitrypsin masks the activity of elastase due to the inhibition of the elastase by antitrypsin. TNF-alpha and IL-6 also activate the neutrophils and their small granules are released in maternal circulation and it increases the inflammation (Castagne et al., 1999). Hereditary predisposition is also important factor. Its prevalence in different relation is, Sisters 37% Daughter 26%, and Grand daughters 16%. Besides the hemodynamic changes in maternal blood, one of its main features is uteroplacental circulation insuffiency and this leads to IUGR-intrauterine growth restriction (reduced amniotic fluid, and abnormal oxygenation) (Hubel, 1999). Inadequate trophoblastic migration and lack of physiologic transformations of spiral artery with its arterioles persisting up to end of pregnancy results is narrowing of artery and arterioles. Their walls are sensitive to vasoconstrictive factors, as platelets aggregation cause narrowing of the lumen. This result as HELLP syndrome. Hemolysis elevated liver enzymes and low platelet count (Maarten et al., 2004). Elastase and lactoferrin are the tests to see the activation of neutrophils in the blood. Elastase is stored in azurophilic granules in neutrophils and has the functions of proteolytic activity, induction of cytokines, bactericidal action, platelet activation and leukocyte activation (Erickson et al., 2003). There is the correlation in between the elastase/ antitrypsin (inhibition by antitrypsin), elastase/neutrophil ratio, which indicates the association with PE (Gheorghe et al., 2010).

It has been observed that there are higher level of TBARS, thin barbituric acid reactive substances, in PE than the normal pregnancy, but there is no difference in total antioxidant stress TAS (Park et al., 2008). Different molecules may contribute to TAS as Vitamin E & C, bilirubin, uric acid and albumin are the main features of PE and may disturb the Pathophysiology of PE (Elmes et al., 2007). TBARS are the biomarkers of lipid per oxidation and effective in increased level of oxidative stress in maternal circulation. Higher levels of uric acid is the characteristic property of PE and may contribute to pathogenesis of preeclampsia. Higher levels of uric acid may also contribute to the total anti-oxidant stress (Cristina et al., 2012). It has been reported that there is decrease in anti-oxidant or increased oxidative stress in pregnant ladies due to increase in lipid peroxidation and MDA. Uric acid and placenta play the protective role in removing the MDA, while anti- oxidative capacity may remain unchanged (Asha and Anju, 2015; Curhan et al., 1996).

CONCLUSION

The study concludes that increase in oxidative stress and proinflammatory cytokines may be considered as one of the potential source for preeclampsia. The same is also involved in endothelial cell dysfunction. Enhanced inflammatory response could be seen due to the increased pro-Inflammatory cytokines, neutrophil activation, leukocyte activation and acute phase proteins in preeclampsia Out of all cytokines (IL-6, TNF alpha) are considered to play primary role in the immune activation.

Conflict of Interest None

Contribution of Authors

1. Ahmad Saleem; Collection of data, Analysing data and writing the manuscript.
2. Noreen Akmal; Collection of data and guidance.
3. Nuzhat Malik; Collection of data and guidance.
4. Amna Akmal & Eeman Ahmad; Literature review.
5. Prof Arif Malik; Chemical Analysis and qualitative and quantitative tests were performed in Research Laboratory of IMBB, UOL, under his guidance.

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INTERFERON INDUCED OXIDATIVE STRESS IN CHRONIC HEPATITIS C PATIENTS

Fariha Muzammil,[1] Zobia Mushtaq,[2] Hamza Muzammil,[3] Zareen Amjad,[4] Abdul Wassae[5]

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Abstract

Objective: Objective of our study was to asses oxidant status of patients with chronic hepatitis C and the effect of pegylated interferon alpha plus ribavirin combination treatment on oxidative stress.

Methods: This cross-sectional study was done in Sahiwal medical college and allied hospitals from May2021 to September 2021. Serum and saliva samples of thirty patients of HCV on IFN therapy and thirty age and sex matched controls were selected for the current study. MDA and Isoprostanes were assayed to assess oxidative stress caused by therapy.

Results: The samples obtained from HCV patients showed statistically Significant (P=0.014) higher level of MDA in serum (3.29±0.465nmol/ml) and saliva (0.182±00065nmol/ml) of patients in comparison with normal individual's serum (0.91±0.027nmol/ml) and saliva (0.0215±0.005nmol/ml). An overall highly significant increasing trend was also observed between HCV patients and controls (p=0.000, p=0.011) as the mean levels of isoprostanes and 8-OHdG in control's serum (0.79±0.036pg/ml, 0.034±0.001ng/ml) and saliva (0.001±0.0005pg/ml, 0.0013±0.0004ng/ml) and patient's serum (4.319±3.09pg/ml, 1.06±0.046ng/ml) and saliva (0.29±0.019pg/ml, 0.026±0.0014ng/ml) were observed respectively.

Conclusion: Patients of HCV who received the IFN therapy show increased lipid peroxidation and oxidative stress. Levels of MDA, 8-OHdG and Isoprostanes in serum and saliva of subjects were higher when they were compared with the controls which helped us to bring about a conclusion that IFN may serve as a reason for increased lipid peroxidation and oxidative stress in hepatitis C patients under treatment.

Keywords: HCV, IFN, Isoprostanes, Lipid peroxidation, MDA.

HCV is a blood - borne enveloped positive-stranded RNA virus and belongs to the Flavi viridae family. It causes the inflammation of liver which is the major organ of our body. Hepatitis C virus (HCV) infection is a global health problem.[1,2] World Health Organization (WHO) highlights the burden from acute HCV infection. Hepatitis C Virus (HCV) affects around 150 million people. Mostly infections caused by HCV are chronic and disease can progress from steatosis and fibrosis to cirrhosis and hepatocellular carcinoma. About 80% of HCV infection leads to chronic infection that can result into cirrhosis and hepatocellular carcinoma. The combination of pegylated interferon (IFN)-A and ribavirin is the main treatment. Unfortunately, this therapeutic strategy results in a low sustained virological response (SVR), defined as an absence of detectable serum HCV-RNA at six months after antiviral therapy; SVR obtained in less than 50% of treated patients that have HCV genotype 1 and a high viral load.

Generally IFN-a in combination with ribavirin is not very well tolerated, and the side effects experienced by patients may result in cessation of therapy. The major adverse effects are anemia, fatigue, hair loss, depression, insomnia, vertigo, anorexia, nausea, nasal congestion, cough, dyspnea, pruritus, and growth

1. Fariha Muzammil
2. Zobia Mushtaq
3. Hamza Muzammil
4. Zareen Amjad
5. Abdul Wassae

1,3-5. Sahiwal Medical College, Sahiwal.
2. Department of Pharmacology, Faisalabad Medical University, Faisalabad.

Correspondence:
Dr. Fariha Muzammil, *Assistant Professor Biochemistry SLMC.*
Email: Dr.farihaniaz@yahoo.com

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delay.[3] HCV infection is associated with elevated levels of circulating reactive oxygen species (ROS) in patients,[4] which are normal products of cell metabolism but increases during inflammation. Increased fat deposit in the liver is prone to attack by reactive oxygen species (ROS), results into lipid peroxidation.[5] The oxidized lipids formed during lipid peroxidation are malondialdehyde (MDA), 4-hydroxynonenal (4-HNE) and isoprostanes (IsoPs) . Lipid peroxidation is main reason for hepatocyte damage[6] and shown as increase level of malondialdehyde (MDA). Standard treatment of chronic HCV infection is pegylated interferon and ribavirin. Ribavirin alone is not effective for inducing sustained virologic response. Currently we have two formulations of pegylated interferon that are approved for HCV therapy: cessation of treatment because of side effects is common. Around 50 to 60 percent of patients may experience influenza-like symptoms. Patients should be monitored closely for hematologic, renal, and thyroid abnormalities. Approximately 30% of patients undergoing treatment experience depression, emotional lability or anger. So treatment of HCV infection is contra indicated in persons with uncontrolled major depression. A recent study showed that the overall adverse effects of pegylated inter-feron alfa-2b plus ribavirin (8.6 percent) and pegylated interferon alfa-2a plus ribavirin (11.7 percent) were similar.

METHODS

The present study was designed to investigate the key metabolites or predispositional variables in thirty (30) HCV patients receiving interferon. Patients taken from march 2021 to October 2021.Thirty (30) age and sex matched subjects in the age group of 25-35 years served as control. Informed consent was obtained before being included in this study. The experimental protocol was approved by the Research Ethical Committee of Sahiwal medical college SAHIWAL.

Five ml of serum and saliva were taken and centrifuged within one hour of collection and stored at -70°C until assayed. The subjects with the history of taking drugs (including alcohol and cigarette), pre-diagnosis medications (e.g.antiparkinsonian/antipsychotic), were excluded from this study. None of the controls were on any medication, history of chronic infections, malnutrition syndrome, metabolic dysfunction (Such as diabetes mellitus, liver diseases, cancer) that could interfere with their oxidative metabolites status. Lipid peroxidation in sample was estimated by using the method of Ohkawa et al.,[7] The measurements of isoprostanes (IsP) and 8-OHdG (8-Hydroxyguanosine) were assessed by commercial kits (ENZO) using Eliza.

Males and females having age ranging from 18-40. HCV RNA level > 10000 IU/ml. The subjects with history of any drugs (including smoking and alcohol) and diag-nosis medication and without history of any chronic infection were excluded out of the study. All chemical reagents of analytical grades were purchased from sigma/Invitrogen chemical Cooperation.

Serum were separated by centrifugation for 10 minutes at 3000 rpm and stored at -70°C until any further analysis is done. MDA was estimated by the simple method devised by Ohkawa et al,[4] For which about 200 microlitre sample was taken in the test tube then about same amount of 8.1% SDS along with 1.5ml Acetic acid (20%) and 1.5ml of TBA was added and then tubes were allowed to heat for an hour. At last, it was cooled down and 4ml of n-butanol was added and then centrifuged at 300 rpm for 10 mins. Upper layer was then separated and absorbance was taken at 532nm against blank. The levels of isoprostanes were estimated by using commercial ELIZA kit . Levels of 8OHdG were determined by the help of commercial ELIZA kit .

RESULTS

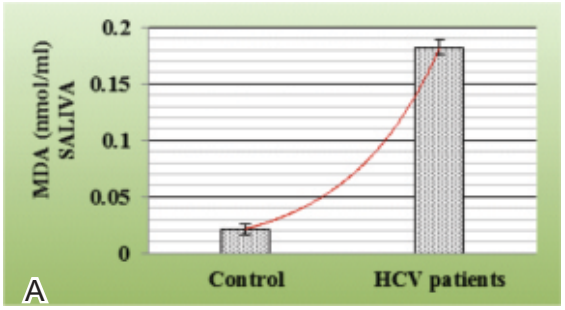
Circulating oxidative stress biomarkers were measured. The samples obtained from patients showed statistically Significant ($p \leq 0.014$) higher level of MDA in serum (3.29±0.465nmol/ml) and saliva (0.182 ± 0.0065nmol/ml) in patients in comparison with normal individual's serum (0.91 ± 0.027 nmol/ml) and saliva (0.0215±0.005nmol/ml). On the other hand, the mean levels of isoprostanes in serum and saliva

of controls are 0.79±0.036pg/ml and 0.01±0.005pg/ml and patients are 4.319±1.46pg/ml and 0.29±0.019 respectively. An overall highly significant increasing

Table 1: Prognostic Variables Of Oxidative Stress Inhcv Patients Receiving Ifn-α

Variables	n=30	Saliva	Serum	P-value
Malondialdehyde (MDA nmol/ml)	Control	0.0215±0.005	0.91±0.027	0.014
	Subjects	0.182±0.0065	3.29±0.465	
Isoprostanes (pg/ml)	Control	0.01±0.005	0.79±0.036	0.000
	Subjects	0.29±0.019	4.319±1.46	
8-Hydroxy guanosine (ng/ml)	Control	0.0013±0.0004	0.034±0.01	0.011
	Subjects	0.026±0.0014	1.06±0.046	

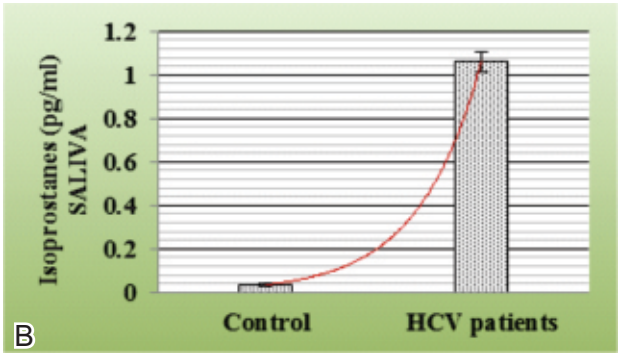
trend was also observed between HCV patients and controls (p=0.000). As far as levels of 8-Hydroxyguanosine is concerned, a persistent higher significant (p=0.011) pattern was observed in patients serum (1.06±0.046ng/ml) and saliva (0.026±0.0014ng/ml) as compared to control group's serum (0.034±0.01 ng/ml) and saliva (0.0013±0.0004ng/ml) respectively.

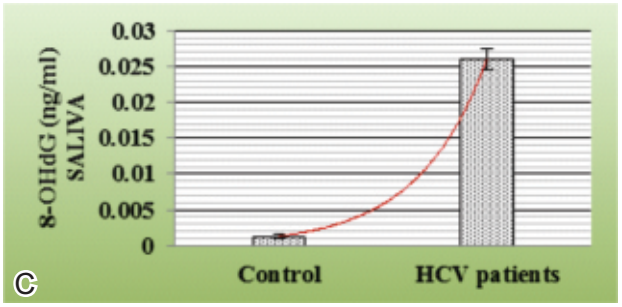


Prognostic Variables of Oxidative Stress in HCV Patient's Saliva Receiving Ifn-α
Prognostic Variables of Oxidative Stress in HCV Patient's Serum Receiving Ifn-α

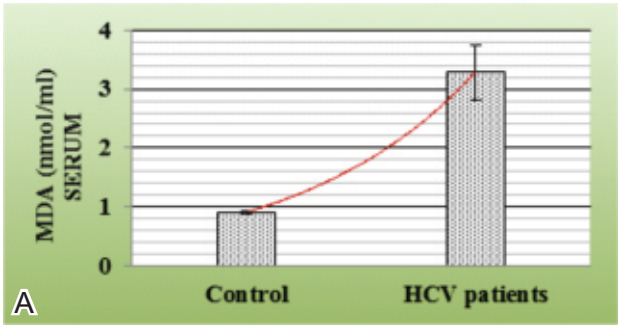
DISCUSSION

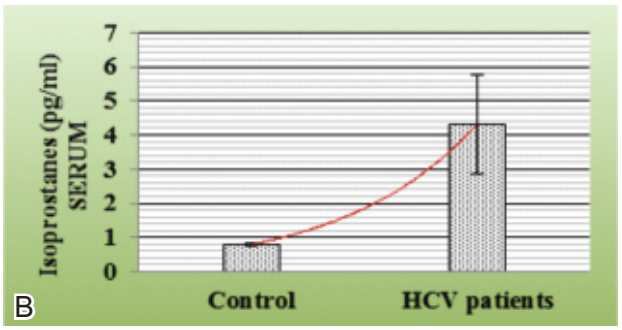
Hepatitis C virus infection is a common health problem. Unfortunately no vaccine available for it in the world. A great numberof infected patients are not able to clear the virus even after having complete treatment so they become chronic. Patients with this infection should have hepatitis A and B vaccination because of the increased risk of morbidity and mortality with

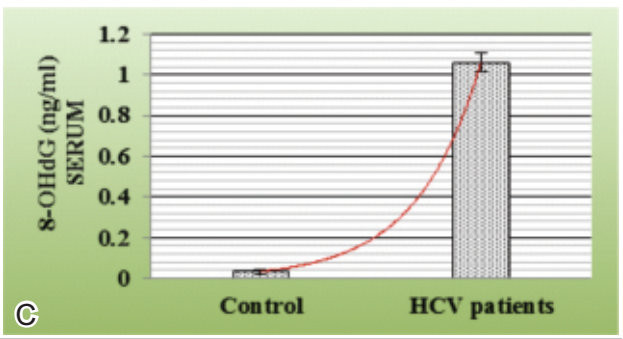




coinfection. HCV is not transmitted efficiently and the average rate of seroconversion after an exposure







positive blood through accidental needle stick is only about 1.8%. Acute hepatitis C can be treated with the combine therapy of pegylated interferon alpha and ribavirin from which only 15% patients can be resolved but about 85% patients become chronic. 80% of Chronic patients can be stable after treatment and 20% patients may become cirrhotic. 75% of cirrhotic patients slowly progresses their disease but 25% patients can develop hepatocellular carcinoma, transplant liver and have early death.[8]

Human liver has produces antioxidants to prevent oxidative damage. Normally, ROS produce in small amount in our body but when hepatic intracellular defects occur, its production increases as compared to our anti-oxidant system, which leads to DNA damage and increased lipid per-oxidation of polyunsaturated fatty acids in hepatocyte membrane.[9] Anti-oxidants in our body are catalase, superoxide dismutase, vitamin C and vitamin E. In chronic hepatitis C cases activation of cytochrome P-450 enzyme increases the production of reactive oxygen species.[4] ROS causes mitochondrial damage which is responsible for a wide series of pathologies.[8] Primary are the hydrogen peroxides and secondary are the isoprostanes, Malondialdehyde and 8 hydroxy nonenol. Highly cytotoxic metabolites are produced in large amounts and can diffuse from their site of origin to distant target points and destroy their functions.[3]

Rosser founds that proteins and nucleic acids are destroyed by lipid per-oxidation due to increased production of reactive oxygen species.[10] He confirmed that MDA causes hepatocyte damage. De-Maria et al. confirms that MDA level increased in hepatitis patients is a cause of hepatocyte damage.[11] Another study showed the increased level of MDA and Isoprostane in the peripheral blood of chronic hepatitis C patients.[12] Romero et al. confirmed that after combination therapy of interferon and ribavirin the level of MDA is relatively low as compared to untreated patients.[13]

Oxidative stress is an imbalance condition between oxidants and anti-oxidants which can lead into production of free highly reactive radicals and hence causes cell damage.[14] Oxidative stress increases the lipid peroxidation in our body which causes the disruption of membranes by increased metabolism of poly unsaturated fatty acids results in formation of malondialdehyde, isoprostanes and 8 hydroxy guanosine.Lead to progression of fibrosis in liver.[15] Antioxidants present in our body which may be produce by cell itself and by our diet have protective role against these oxidants. Commonly include glutathione, vitamin C and E and various enzymes including catalase, superoxide dismutase.[16,17]

In our study, the MDA and Isoprostane levels are significantly higher in both serum and saliva of hepatitis C disease as compared to healthy individuals. So, there is direct co- relation between the oxidative stress parameters, MDA and Isoprostane with the progression of disease. These two parameters are the secondary by products of lipid per-oxidation whose increased values shows the increased fibrosis and necrosis of hepatocytes.[18] Increased levels of MDA and Isoprostane result in DNA damage, mitochondrial dysfunction and cox-2 activation of hepatocytes. From these changes there is DNA mutation and inflammation of the cell. These increased level results in chronic hepatitis.[19,20]

CONCLUSION

Current study demonstrates the fact that patients of HCV who received the IFN therapy show increased lipid peroxidation and oxidative stress. Levels of MDA, 8-OHdG and Isoprostanes in serum and saliva of subjects were higher when they were compared with the controls which helped us to bring about a conclusion that IFN may serve as a reason for increased lipid peroxidation and oxidative stress in the patients of HCV.

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COMPARISON OF ANALGESIC EFFICACY OF PENTAZOCINE AND TRAMADOL DURING LABOR

Sumaira Fatima Sabir,[1] Asifa Shoukat[2]

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Abstract

Objective: To compare efficacy of Pentazocine and Tramadol during labor in terms of analgesia.It was a Randomized controlled trail.

Methods: The study was conducted in department of Obstetrics and Gynecology, Jinnah hospital Lahore with study period of 14-08-2013 to 13-02-2014. Total 210 cases 105 in each group pregnant women between 20-40yrs in active labor with effective painful uterine contractions were included through a non-probability consecutive sampling. Data was entered and analyzed in SPSS ver: 19.0. Quantative variables were presented as mean and SD. Qualitative varaibles as frequency and percentages. Efficacy was measured in term of pain relief and fetal distress.

Results: Pentazocine 30 mg was effective in 47 [44.8%] while Tramadol 100 mg effective in 39 [37.1%] subjects, the difference between two groups was statistically non-significant. (p=0.261).

Conclusion: Both Pentazocine and tramadol are effective in pain relief. Statistically there was no difference between them however, Pentazocine provide better labor analgesia then tramadol both are useful labor analgesia options where epidural analgesia is not available.

Key words: Labor, analgesia, Pentazocine, Tramadol.

Globally, approximately 140 million births occur every year. The majority of these are vaginal births among pregnant women with no identified risk factors for complications, either for themselves or their babies, at the onset of labour. However, in situations where complications arise during labour, the risk of serious morbidity and death increases for both the woman and baby. [1]

Pain management during labour is an essential part of good obstetric care. Though this severe pain during labour is not life threatening, it can have neuro-psychological consequences.[2] Postnatal depression may be more common when labour analgesia is not used. Pain during labor has also been correlated with the development of posttraumatic stress disorder[3].

Gynecologist and anesthetics agree that epidural analgesia is one of the most effective procedures for relief of during labor and many consider it the "gold standard" for pain relief in labor. Regrettably epidural analgesia is not available as a routine procedure in most obstetric departments in hospitals in developing countries the reasons being mainly the cost of analgesia and preferences by the mother. Majority of obstetric departments in hospitals therefore prefer systemic opioids for relief of labor pain as the cost effective easy to administer and almost always available in every setting.[3,4]

Epidural analgesia, when compared with other methods, provides superior analgesia for labor. However there can be situations where either it is not available or it is not feasible. Parenteral opioids, thus, are still popular for pain relief in labor in many countries throughout the world.[4]

A recent Cochrane review emphasized that as parenteral opioid drugs are very widely used for labor

1. Sumaira Fatima Sabir
2. Asifa Shoukat
1,2. Lahore General Hospital Lahore

Correspondence:
Dr. Sumaira Fatima Sabir, *Senior Registrar, Lahore General Hospital Lahore, E-mail: doctorsumaira01@gmail.com*

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analgesia, it is important that more research is carried out so that women can make informed choices about these forms of pain relief.[5]

Perception of pain comprises of variety of different factors that are emotional, sensory, behavioral and environmental in nature. Opioid analgesic Pethidine has been used since 1939 and it became the most common drug that is used as intra-muscular opioid for relieving labor pains. However, there are some serious apprehensions that have been raised about its efficacy and side effects especially depressing respiration in newborns.[7]

The most commonly labor analgesia in obstetric practice are Pentazocine and tramadol[5,8]. Pentazocine act as a agonist on specific kappa-receptors that produces analgesia but with no or minimal respiratory depression. This has been proved in many researches that its use in reliving labor pain not only have shown an equal analgesia effect but also a better safety profile as compared to Pethidine.[5] Tramadol is another synthetic equivalent of codeine with a mechanism of action which binds itself to μ- receptors for opiate and impedes uptake for norepinephrine and serotonin. Tramadol offers a potent analgesic effect without respiratory depression both to mother and the neonate as this is very common with other opioid drugs and with an additional benefit of not delaying gastric emptying.[6] Different studies have reported that tramadol gives better pain relief, shortens the labor and is safe for the mother and the neonate.[5,9,10]

Pregnant women in our setting is not very well versed regarding the risks and benefits of the different procedures or drugs for of relief of pain that can perpetuate her anxiety during parturition.[11] The rationale of this study was to compare the analgesic efficacy of two drugs. as to explore the controversy regarding pain relief and side effects reported by gynecologists based on their personal experience. The objectives of the study was to compare efficacy of Pentazocine and Tramadol during labor in terms of analgesia.

METHODS

A randomized controlled trial was conducted at Obstetrics and Gynecology Unit I, Jinnah Hospital, Lahore after approval from ethical committee from 14-08-2013 to 13-02-2014.Sample size of 210(105 in each group) was calculated using win-pepi ver: 11.15 with 1% significance level and a 90% power of study, with expected percentage for effectiveness of tramadol and Pentazocine in terms of satisfactory pain relief during labor i.e. 37% and 14% and at 1 hour respectively through a Non-probability / purposive sampling (Tripti et al)9. Primigravida between 20-40 years of age active labor at term having 3 to 4 regular, affective and painful uterine contraction within 10 minutes and at least 4cm cervical dilatation measured by researcher herself were selected. Chronic medical diseases like diabetes, hypertension, asthma and cardiac disease were excluded from the study. After an informed consent the patients were divided in to two groups randomly by using random numbers table. Randomization was done by doctor. Group A was given intramuscular injection of pentazocine 30 mg and Group B was given intramuscular injection of tramadol 100mg. The attending gynecologist was blinded for two interventions that recorded the clinical data and evaluated the analgesia effect on verbal rating scale. Pulse, Blood pressure, respiratory rate and labor pains were evaluated immediately before and 60 minutes after injection of both drugs. VRS was used to assess severity and efficacy of analgesia as difficulties with graphic instruments like the visual analogue scale (VAS) among patients have been reported, whereas the Verbal Rating Scale (VRS) has been found to have low error rates.[12] Severity of labour pain was categorize as 2 as Moderate and 3 for severe pain. Efficacy was evaluated at 30 and 60 minutes after the Injection of both drug. Verbal Rating Scale (VRS) was used to measure severity and analgesic efficacy. Efficacy was as 0 for no pain, 1 as Mild, 2 as Moderate and 3 for severe pain at 1 hour after administration of drugs.

Data was entered and analyzed using SPSS version 12. Age of the patients was presented by calculating mean and standard deviation. Frequency was calculated for outcome variable, labor pains (Mild/Moderate/ Severe') were presented in the form of frequency and

percentages. Chi square test was be used to compare the efficacy in term of pain relief (no pain/mild pain) in both groups. P-value <=0.05 was be considered as significant.

RESULTS

A total of 210 patients (105 in each group) were included in this study. Mean age of the patients was 26.89±3.90 in Pentazocine group and 26.01±4.02 years in tramadol group, respectively (Table-1). In group-A, labor pains before administration of drug were moderate in 61 patients (58.1%) and in group-B moderate labor pains were noted in 59 patients (56.2%). In group-A, 44 patients (41.9%) were having severe labor pains and in group-B severe labor pains were found in 46 patients (43.8%) (Table-2). In Group A (Pentazocine 30mg) 47 (44.8%) while in Group B (Tramadol 100mg) 39(37.1%) of patient had complete relief of paint and difference between two groups was statistically non-significant (P= 0.261) (Table-3). In Pentazocine group drug was efficacious in 59.5% who had moderate labor pain and 40.5% were having severe labor pains as compared to tramadol group where 59.0% had moderate labor pain and 41.0% were having severe labor pains whom drug was efficacious but the difference between two groups was statistically non-significant (P 0.184) (Table- 3). No fetal distress was noted among both groups.

DISCUSSION

Many women appreciate some form of pain relief in labour and would like a choice of options given to them. The evidence suggests that opioids probably provide some relief from pain during labour despite being widely available and used, pethidine is not the preferred opioid option, as shorter-acting opioids tend to have fewer undesirable side-effects.[13]

Table 1: *Distribution of cases by labor pains before administration of drug*

Pain intensity	Group A (Pentazocine 30mg)		Group B (Tramadol 100mg)		Chi-square P value
	Frequency	Percentage	Frequency	Percentage	
Moderate	61	58.1	59	56.2	**X^2=0.078**
Severe	44	41.9	46	43.8	**P= 0.780**
Total	**105**	**100.0**	**105**	**100.0**	

Table 2: *Distribution of cases by efficacy*

Efficacy (No pain / Mild pain)	Group A (Pentazocine 30mg)		Group B (Tramadol 100mg)		Chi-square P value
	Frequency	Percentage	Frequency	Percentage	
Yes	47	44.8	39	37.1	**X^2=1.260**
No	58	55.2	66	62.9	**P= 0.261**
Total	105	100.0	105	100.0	

Table 3: *Stratification for severity of labor pain with regard to efficacy*

Pain intensity	Efficacy				Chi-square P value
	Group A (n=47) (Pentazocine 30mg)		Group B (n=39) (Tramadol 100mg)		
	Frequency	Percentages	Frequency	Percentages	
Moderate	28	59.5	23	59.0	**X^2=1.764**
Severe	19	40.5	08	41.0	**P= 0.184**
Total	**47**	**100.0**	**39**	**100.0**	

In developing countries like Pakistan health care providers in a tertiary health care setting counsel women about the efficacy or potential side-effects of opioids analgesics, including maternal drowsiness, nausea and vomiting, and neonatal respiratory depression, and about availibity of alternative pain relief drugs. In a systematic review of qualitative studies looking at what matters most to women during intrapartum care, findings suggest that majority of women, especially those giving birth for the first time, are apprehensive about childbirth (high confidence in the evidence), and in certain contexts and/or situations may welcome interventions that provide relief from pain.[14]

These findings suggest that some women value opioids to help them cope with intense and unmanageable labor pains. Mixed responses were identified in terms of whether the pain relief was effective or ineffective and whether it had a positive or negative impact on their labour and childbirth experience. The data available for this qualitative review were very limited: only three studies, including two in HICs and one in

an upper-middle-income country.

One study contained minimal data to inform the review, and one involved qualitative interviews with women involved in an RCT evaluating different opioid regimens. All participants were women who had requested pain relief. It was not possible to identify, within the included studies, whether women had had augmentation, induction of labour or other forms of intervention that may have influenced their valuation of the outcomes associated with this form of pain relief. [15]

Chandnani et al compared Tramadol and Pentazocine for pain relief during labour and study findings showed that in 80% of cases in Tramadol group while in Pentazocine group pain relief was observed in only 60% cases with delayed onset and concluded that Tramadol is an effective and safe labour analgesic, producing moderate to satisfactory. Besides it also significantly shortens the duration of labour.[16] In my study Pentazocine was effective in 44.8% of patients and tramadol was effective in 37.1% of patients in term of pain relief. Pentazocine provided higher level of analgesia when compared with tramadol. However, the difference was not significant statistically. Our results are comparable with a study by Kuti et al[8] but contrary to Chandnani et al study.[11]

The outcome of these two researches done in a different setting i.e. post-operative pain and pain during labor is probably due to the different characteristics of the pain. Pain during labor is progressive in nature and is more likely to be accompanying with anxiety. Several researches have shown superior analgesic effects when sedatives or combination drugs are given along with opioids during labor pains. Shetty et al in her study found analgesic effect of the Pentazocine and tramadol statistically non-significant, neither of these analgesics was effective towards the end of the first stage. However, in the tramadol group, the majority of women (55.0%) rated pain as severe, whereas in the Pentazocine group, the majority of women (60.0%) rated pain as moderately severe.[4] Our study showed In Pentazocine group drug was efficacious in 59.5% who had moderate labor pain and 40.5% were having severe labor pains as compared to tramadol group where 59.0% had moderate labor pain and 41.0% were having severe labor pains whom drug was efficacious. In a local study by Wali et al comparing tramadol with pentazocine showed a mean VAS score declined signifi cantly in both the groups aft er analgesia (pvalue< 0.001), but found no significant difference between the two groups (p =0.839). Overall maternal satisfaction recorded at 2 hours of delivery, showed significantly more women satisfied in Pentazocine group (p=0.05). No significant difference was observed for maternal and neonatal outcomes. Sedation was found to be significantly more in Pentazocine group (p-value<0.001).[17] Our study has shown both Tramadol and Pentazocine to be safe for the mother and the neonate and this study found no fetal distress as a side effect of these two analgesic effects.

The limitation of my study was use of single dose further studies with multidose regimen of these analgesics are worth looking into also as both offers potent analgesia outcome in terms of side effects may be explored in future studies and studies evaluating analgesia effect of these two drugs must be compared with epidural analgesia.

CONCLUSION

The study concluded that both Pentazocine and tramadol in injectable form are efficacious in relieving moderate to severe labor pains and can be used as labor analgesic options in settings where Epidural analgesia is not available.

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ROLE OF HYSTEROSCOPIC TECHNIQUES IN THE TREATMENT OF FEMALE GENITAL PATHOLOGY

Rehana Kanwal,[1] Nilofer Mustafa,[2] Maimoona Hafeez,[3] Faisal Ashraf,[4] Shazia Tazion,[5] Qudsia Nawaz[6]

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Abstract

Background: Hysteroscopy is visualization in the endometrial cavity with a telescope. A camera is commonly attached to the proximal end of the hysteroscope that is a telescope for viewing on the screen. Uterine cavity is distended with the medium for visualization different distension medias are used depends upon whether doing diagonastic or operative hysteroscopy and it is performed without anaesthesia when vaginal distension is done with the same media by occluding the vaginal orifice with closure of both labias by assistant then there will be no need for use of sim speculum and tinaculum. Where there is a need for operative hysteroscopy general anesthesia is preferred until any concomitant health issue.

Methods: This was a retrospective study which presents the results of hysteroscopic treatment of various gynecological diseases in Hameed Latif Hospital Lahpore period from 2016 to 2020. Total 210 cases were enrolled. 190 underwent hysteroscopic surgery in general anesthesia and 20 cases underwent hystroscopic suregery without anesthesia. The results were statistically analyzed

Results: Total number of patients is 210. The incidence is highest in the age 28-50 years (80%). Endometrial polyp is the most common pathological condition in 78%, myoma submucosal in 8%, extraction of IUD 7%, septum uteri 5% cavity formation for Asherman syndrome is 1%, removal of calcification 1%

Conclusions: Conclusions: Hystroscopy is only available treatment for intra uterine pathology without opening the peritoneal cavity so as to avoid major surgical procedure and at the same time minimal invasion to the uterus with better treatment outcome particularly in subfertility. It leads to fast recovery and reduce hospital stay with cost affectiveness. It has totally replaced D&C in abnormal uterine bleeding and polyps.

Keywords: General anesthesia, Hysteroscopy, Uterine cavity

Hysteroscopy is to view uterine cavity with small telescope through vagina and it allows magnified visualization on the screen with the help of camera head that is attached on the distal end of the telescope and images is reflected on the screen first time hysteroscopy was done in 1869[1] but at that time distension media was not introduced so resulted in insufficient distension and view. In 1925, Rubin first used CO_2 to distend the uterus, when liquid distension media was introduced initially it was used by Urologist for transurethral resection of the prostate and then it was modified as hysteroscope for intra uterine pathology in next fifty years hysteroscopy nearly replaced Dilatation and Curettage for intra uterine pathalogy.[2]

Hysteroscopy is a one step procedure not only to find the problem in the uterine cavity but simultaneously offers treatment in the same setting[3,4] fibroid, polyps, septum and synichea are not only visualized but simultaneously treated and it is 80% effective in identifying these problems.[5,6]

Hysteroscopic diagnosis of intracavitary abnormalities in women with AUB carries a sensitivity of 94% and specificity of 89% and compares favourably with the

1. Rehana Kanwal
2. Nilofar Mustafa
2. Maimoona Hafeez
4. Faisal Ashraf
5. Shazia Tazion
6. Qudsia Nawaz

1,2,6. Department of Obs/Gynae Dept. CMH Lahore Medical College,
3,5,.Department of Gynae, Sharif City Medical College Lahore.
4. Department of Gynae & Obs. Jinnah Hospital Lahore

Correspondence:
Dr. Rehana Kanwal, *Associate Professor Obs/Gynae Department. CMH Lahore Medical College.*
E Mail: drrehanakanwal136@yahoo.com

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accuracy of saline infusion sonography, which has a reported 95% sensitivity and 88% specificity.[7,8] The diagnosis for endometrial cancer through hysteroscopic Biopsy has high sensitivity and specificity as compared to conventional dilatation and Curettage, and pipelle sampling[9] MRI is also used to find out intra uterine pathology but it is expensive test with no feasibility of biopsy.[10]

In patient with AUB where there is no atypia and fertility concern there is option of endometrial ablation that result in reduced flow or sometimes amenorrhea[11,13] so comparable to hysterectomy in some patient it may lead to irregular spotting and second look hysteroscopy and nearly ten percent only dissatisfaction due to no change of flow and hysterectomy.[13] In 70% decrease of flow is documented and in 20-30% amenorrhea develops[14] fertility work up is not completed without viewing the uterine cavity so with laperoscopy for pelvic pathology when done in infertile patient hysteroscopy is also done[15,16] if any intra uterine pathology is found in these patient that is simultaneously treated and pregnancy rate of 50-78% has been reported incase of polypectomy when there is no other cause of infertility.[17-21] Fibroids occur in 20% of reproductive age group, although not symptomatic in all women but is most common in benign pelvic tumor.[22] Symptomatic fibroid lead to AUB, dysmenorrhea, chronic pelvic pain, dyspareunia, subfertility and urinary symptoms submucosal fibroid is mostly associated with AUB than other types and needed surgical intervention[23] in which hysteroscopy is preferred and beneficial, than laparotomy not only because of shorter hospital stay and fast recovery but at the same time minimal invasion to the uterus leading to better fertility outcome in infertile patients, only few patients needed second look procedure for remaining fibroid or further surgery.[24]

METHODS

In this retrospective study, we included 210 patient after Gynaecological and Radiological assessment. In 190 patient it was done under general anesthesia in lithotomy position after painting and draping, bladder was emptied, sim's speculum is used to retract posterior vaginal wall and cervics was held with tinaculum. After assembling Hysteroscope was introduced into the cervical os traversing through cervical canal into the uterine cavity so as it was visualized being distended by distension media. Operative procedure is done keeping in view the inflow of the distention media. In 20 patients it was done without anesthesia because of nonoptimization of health conditions like coronary heart disease, restrictive lung disease, acute bronchitis, morbid obesity, severe hypertension in these patients holding of the cervix and retraction of vaginal wall was not done. Both labias were sealed by holding so that vagina was distended with media and cervix was visualized and direct insertion of hysteroscope was done.

RESULTS

Total number of patients included in the study were 210. Table 1 shows the demographic charatceristics of the patients under going hysterscopic surgery. The incidence is highest in the age 28-50 years (80%)

DISCUSSION

In patient with AUB where there is no atypia and fertility concern there is option of endometrial ablation

Table 1: *Demographic Characteristics of women undergoing hystersocopic surgery*

Age In Years	No. of Patients	Percentage
18-28	30	15%
29-39	65	30%
40-49	72	34%
50-59	19	9%
60-69	14	7%
70-79	10	5%

Table 2: *Hysteroscopic findings of women undergoing hysteroscopic surgery*

Characteristic findings	No. of patients	Percentage
Endometetial Polyp	164	78
Submucosal fibroid	17	8
Lost IUCD	14	7
Uterine Septum	11	5
Uterine Calcification	2	1
Uterine Synechiae	2	1

that result in reduced flow or sometimes amenorrhea[11,13] so comparable to hysterectomy in some patient it may lead to irregular spotting and second look hysteroscopy and nearly ten percent only dissatisfaction due to no change of flow and hysterectomy.[13] In 70% decrease of flow is documented and in 20-30% amenorrhea develops[14] fertility work up is not completed without viewing the uterine cavity so with laperoscopy for pelvic pathology when done in infertile patient hysteroscopy is also done[15,16] if any intra uterine pathology is found in these patient that is simultaneously treated and pregnancy rate of 50-78% has been reported incase of polypectomy when there is no other cause of infertility.[17-20] Fibroids occur in 20% of reproductive age group, although not symptomatic in all women but is most common in benign pelvic tumor.[20] Symptomatic fibroid lead to AUB, dysmenorrhea, chronic pelvic pain, dyspareunia, subfertility and urinary symptoms submucosal fibroid is mostly associated with AUB than other types and needed surgical intervention in which hysteroscopy is preferred and beneficial, than laparotomy not only because of shorter hospital stay and fast recovery but at the same time minimal invasion to the uterus leading to better fertility outcome in infertile patients, only few patients needed second look procedure for remaining fibroid or further surgery.[20]

CONCLUSION

Hysteroscopy is low risk minimally invasive day case and outdoor procedure that leads to high sensitivity and specificity incase of intra uterine pathology like polyps submecosual fibroid, intra uterine adhesions, lost IUCD, intera uterine classifications and for bicornuate uterus. It is cheap, simple, short anesthesia, short hospital stay, minimal analgesia, and better outcome and patient satisfaction rate. It has totally replaced Laparotomy for intra uterine Pathology. Although hysteron pathology is 100% diagonostic for endometrial cancer but under direct visualization with hysteroscope endometrioal sampling is done from suspicious areas that leads to increase sensitivity.

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A COMPARISON OF SELF-MEDICATION AMONG UNDERGRADUATE MEDICAL AND UNDERGRADUATE NON-MEDICAL STUDENTS IN PAKISTAN

Biah Mustafa,[1] Ahmad Nawaz,[2] Ayesha Hussain,[3] Minaam Farooq,[4] Huzaifa Ahmad Cheema,[5] Abia Shahid[6]

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Abstract

Background: Self-medication usually corresponds to the self-administration of a medication in the absence of a currently valid prescription or without consulting a healthcare professional. Self-medication is usually employed for minor ailments that people diagnose and treat themselves.

Methods: This observational cross-sectional study was conducted from 8th April 2021 till 15th April 2021, after obtaining ethical approval from the Institutional Review Board, King Edward Medical University. An online questionnaire was developed using Google Forms. The link of the questionnaire was disseminated through Facebook, Instagram, WhatsApp, various other social networking sites and through text messages. Confidentiality and anonymity were thoroughly ensured and no names or email addresses were asked. A total of 790 people filled out the questionnaire.

Results: The questionnaire was completed by 790 students, of which 475 (60.1%) were females 315 (39.9%) were males. 418 (52.9%) belonged to medical schools and 372 (47.1%) belonged to non-medical institutes spreading all across Pakistan. Self-medication in the past 6 months was reported by 524 out of the total 790 students (66.3%), which were found to be slightly more prevalent in medical students (67.0%) than students belonging to non-medical institutions (65.6%). The chi-square value for this test was $X^2(1, N=790) =171$, $p=0.679$ making the difference statistically insignificant.

Conclusion: Self-medication is a common practice among both medical and non-medical university students of Pakistan. Medical students do, however, realize that self-medication is not a safe practice. It is important to take measures to thwart this growing trend.

Key words: Self-medication, undergraduate students, medical, non-medical

Self-medication usually corresponds to the self-administration of a medication in the absence of a currently valid prescription or without consulting a healthcare professional. Self-medication is usually employed for minor ailments that people diagnose and treat themselves.[1]

According to the WHO's definition, self-medication is the use of drugs to treat self-diagnosed disorders or symptoms, or the intermittent or continued use of a prescribed drug for chronic or recurrent diseases or symptoms.[2] It involves the use of medication (modern and/or traditional) for self-treatment without consulting a physician either for diagnosis, prescription, or surveillance of treatment.[3]

Self-medication among university students has been surveyed in different parts of the world. In a survey conducted among final year medical students in Slovenia, 94.1% students stated that they self-medicated.[4] According to a survey analysing 1257 university-going French students from various academic sectors, a great majority of 95% reported self- medication.[1] Other studies reported prevalence to be 81.8% in Nigeria,[5] 38.5% in Ethiopia6 and 98.0% in Palestine.[7]

Multiple studies have been conducted in various regions of Pakistan to assess the prevalence of self-medication amongst university students. A study conducted in Karachi in 2007 established a prevalence

1. Biah Mustafa 2. Ahmad Nawaz
3. Ayesha Hussain 4. Minaam Farooq
5. Huzaifa Ahmad Cheema 6. Abia Shahid
1-6 King Edward Medicial University, Lahore.

Correspondence:
Dr. Biah Mustafa, *King Edward Medicial University, Lahore.*

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of 76%8 whereas a similar survey in 2008 reported a frequency of 80.4%.[9] According to a study conducted in Abbottabad, prevalence in a single university was found to be 95.5% but there was a statistically insignificant difference between health-related and non-health related students.[10]

Medical students have better access to healthcare information and facilities, creating an open arena for self-medication practice.[11] Inclined towards medical and pharmacological information, they are more likely to perform self-diagnosis and hence, self-medication. As they are future drug prescribers and health educationalists, their attitudes towards self-medication practices may possibly cause health hazards and morbidity, thus degrading overall health quality.[12]

The purpose of this research was to assess self-medication practices amongst medical and non-medical undergraduate students of Pakistan, identify common types of illnesses and frequently used drugs, to outline determinants of self-medication, and to devise strategies to prevent this growing trend.

METHODS

This observational cross-sectional study was conducted from 8th April 2021 till 15th April 2021, after obtaining ethical approval from the Institutional Review Board, King Edward Medical University. An online questionnaire was developed using Google Forms. The link of the questionnaire was disseminated through Facebook, Instagram, WhatsApp, various other social networking sites and through text messages. Confidentiality and anonymity were thoroughly ensured and no names or email addresses were asked. A total of 790 people filled out the questionnaire. The inclusion criteria included medical and non-medical Undergraduate students, who understand English language and have internet access. Incomplete forms were excluded. The questionnaire consisted of a preliminary letter and two sections. The preliminary letter defined Self-Medication and the purpose of the survey. The first section featured questions regarding socio-demographic information of the participants such as sex, curriculum, year of study, residential setting and whether they had self-medicated in the past 6 months (yes/no). The second section assessed the patterns and habits of the participants regarding self-medication. All data analyses were performed using Statistical Package for Social Sciences (SPSS) software, version 26. Descriptive statistics were calculated for all the variables in the study. Chi-square test was applied to compare responses based on gender, curriculum and year of study, and find possible statistical correlations. A value of P <0.05 was considered statistically significant.

Table 1(a): Demographics in relation with curriculum

Factor	Total sample size (790)	Medical (418), N(%)	Non-medical (372), N(%)	P value
Sex				
Male	315 (39.9%)	252 (51.3%)	223 (46.9%)	0.92
Female	475(60.1%)	116 (52.7%)	149 (47.3%)	0.92
Curriculum	790 (100%)	418 (52.9%)	372 (47.1%)	
Year of study				
1st year	171 (22.4%)	51 (28.8%)	126 (71.2%)	<.001
2nd year	151 (19.1%)	93 (61.6%)	58 (38.4%)	<.001
3rd year	222 (28.1%)	163 (73.4%)	59 (26.6%)	<.001
4th year	173 (21.9%)	74 (42.8%)	99 (57.2%)	<.001
5th year	67 (8.5%)	37 (55.2%)	30 (44.8%)	<.001
Residential setting				
Urban	728 (92.2%)	384 (52.7%)	344 (47.3%)	0.751
Rural	62 (7.8%)	34 (54.8%)	28 (45.2%)	0.751

Table 1(b): Demographics in relation with practice of self-medication

Factor	Total Sample size (790), N (%)	Self-medication		P value
		Yes	No	
Sex				
Male	315 (39.9%)	195 (61.9%)	120 (38.1%)	0.032
Female	475(60.1%)	239 (69.3%)	146 (30.7%)	0.032
Year of study				
1st year	171 (22.4%)	105 (59.3%)	72 (40.7%)	0.005
2nd year	151 (19.1%)	97 (64.2%)	54 (35.8%)	0.005
3rd year	222 (28.1%)	147 (66.2%)	75 (33.8%)	0.005
4th year	173 (21.9%)	118 (68.2%)	55 (31.8%)	0.005
5th year	67 (8.5%)	57 (83.1%)	10 (14.9%)	0.005
Residence				
Urban	728 (92.2%)	489 (67.2%)	239 (38.8%)	0.086
Rural	62 (7.8%)	35 (56.5%)	27 (43.5%)	0.086

RESULTS

The questionnaire was completed by 790 students, of which 475 (60.1%) were females 315 (39.9%) were males. 418 (52.9%) belonged to medical schools and 372 (47.1%) belonged to non-medical institutes spreading all across Pakistan. The detailed demographics of the students under study are given in Table 1(a). A greater number of females (69.3%) than males (61.9%) reported to have self-medicated in the past 6 months (X^2 (1, N=790) =4.592, p=0.032). It was also recorded that more students reported self-medication as the year of study increased. The details of these demographics have been provided in table 1(b).

Self-medication in the past 6 months was reported by 524 out of the total 790 students (66.3%), which was found to be slightly more prevalent in medical students (67.0%) than students belonging to non-medical institutions (65.6%). The chi-square value for this test was X2(1, N=790) =171, p=0.679 making the difference statistically insignificant.

Headache, cold/flu and fever were found to be the most common symptoms for which self-medication was practiced, with percentages 77.9%, 56.7% and 55.0% respectively. Among different symptoms and their prevalence between medical and non-medical students cold/flu, sleeping problems and stress were calculated to be significant: X^2 (1, N=790) =13.338, p<0.001, X^2 (1, N=790) =9.025, p=0.003 and X^2 (1,

Table 2(a): *Patterns of self-medication*

Factor	Total count (524), N (%)	Medical (280), N (%)	Non-Medical (244), N (%)	P value
Self-medication				
Yes	524 (66.3%)	280 (67.0%)	244 (65.6%)	0.679
No	266 (37.7%)	138 (33.0%)	128 (34.4%)	0.679
For which disease/symptom did you self-medicate for?				
Headache	408 (77.9%)	211 (75.5%)	197 (80.7%)	0.139
Cold/flu	297 (56.7%)	138 (49.3%)	159 (65.2%)	<0.001
Cough	259 (49.4%)	131 (46.8%)	128 (52.5%)	0.195
Fever	288 (55.0%)	150 (53.6%)	138 (56.6%)	0.493
Nausea/ vomiting	125 (23.9%)	62 (22.1%)	63 (25.8%)	0.325
Diarrhea/ constipation	180 (34.4%)	101 (36.1%)	79 (32.4%)	0.374
Toothache	70 (13.4%)	32 (11.4%)	38 (15.6%)	0.164
Sleeping problems	77 (14.7%)	29 (10.4%)	48 (19.7%)	0.003
Allergy	132 (25.2%)	63 (22.5%)	69 (28.3%)	0.129
Heartburn	62 (11.8%)	34 (12.1%)	28 (11.5%)	0.813
Menstrual problems	95 (18.1%)	44 (15.7%)	51 (20.9%)	0.124
Eye infection	40 (7.6%)	18 (6.4%)	22 (9.0%)	0.266
Muscle pain	159 (30.3%)	72 (26.1%)	86 (35.2%)	0.023
Stress	85 (16.2%)	35 (12.5%)	50 (20.5%)	0.013

Table 2(b): *Patterns of self-medication*

Factor	Total count (524), N (%)	Medical (280), N (%)	Non-medical (244), N (%)	p value
For what reasons did you self-medicate?				
It saves time	152 (29.0%)	68 (24.3%)	84 (34.4%)	0.011
I used an old prescription for the same illness	220 (42.0%)	96 (34.3%)	124 (50.8%)	<.001
Doctors have a high medical consultation fee	47 (9.0%)	16 (5.7%)	31 (12.7%)	0.005
My symptoms were minor/manageable at home	401 (76.5%)	232 (82.9%)	169 (69.3%)	<.001
I do not trust doctors/I do not like answering their questions	20 (3.8%)	7 (2.5%)	13 (5.3%)	0.092
I have ample knowledge about medicines and when to use them	141 (26.9%)	78 (27.9%)	63 (25.8%)	0.600
Which medicines did you take?				
Painkillers	434 (82.8%)	232 (82.9%)	202 (82.8%)	0.983
Health supplements	150 (28.6%)	78 (27.9%)	72 (29.5%)	0.677
Anti-Allergy	343 (65.5%)	173 (61.8%)	170 (69.7%)	0.058
Laxatives	56 (10.7%)	34 (12.1%)	22 (9.0%)	0.248
Cough suppressants	170 (32.4%)	89 (31.8%)	81 (33.2%)	0.731
Antibiotics	235 (44.8%)	121 (43.2%)	114 (46.7%)	0.421
Herbal/homeopathic remedies	91 (17.4%)	36 (12.9%)	55 (22.5%)	0.004
Oral contraceptives	11 (2.1%)	4 (1.4%)	7 (2.9%)	0.251
Antidepressants	32 (6.1%)	14 (5.0%)	18 (7.4%)	0.257
Sleeping pills	48 (9.2%)	19 (6.8%)	29 (11.9%)	0.044

Table 2(c): *Patterns of self-medication*

Factor	Total count (524), N (%)	Medical (280), N (%)	Non-medical (244), N (%)	p value
What is your source of knowledge for taking a medicine/drug?				
The internet	134 (25.6%)	59 (21.1%)	75 (30.7%)	0.011
Medicinal knowledge	268 (51.1%)	197 (70.4%)	71 (29.1%)	<.001
Family/Friends	329 (62.8%)	143 (51.1%)	186 (76.2%)	<.001
Past experience	349 (66.6%)	170 (60.7%)	179 (73.4%)	0.002
Advertisements	20 (3.8%)	7 (2.5%)	13 (5.3%)	0.092
Pharmacists	82 (15.6%)	37 (13.2%)	45 (18.4%)	0.10
Where did you obtain the drugs and remedies for selfmedication?				
Pharmacy	413 (78.8%)	216 (77.1%)	197 (80.7%)	0.315
Homeopath	24 (4.6%)	3 (1.1%)	21 (8.6%)	<.001
Relatives and friends	37 (7.1%)	15 (5.4%)	22 (9.0%)	0.103
It was available at home	337 (64.3%)	172 (61.4%)	165 (67.6%)	0.140
At what point would you consider visiting a doctor?				
Worsening of symptoms	385 (73.5%)	206 (73.6%)	179 (73.4%)	0.957
Appearance of new symptom/side effect	185 (35.3%)	104 (37.1%)	81 (33.1%)	0.165
Not getting better after 1 week	302 (57.6%)	152 (54.3%)	150 (61.5%)	0.097
I would try some other medication but notvisit a doctor	16 (3.1%)	10 (3.6%)	6 (2.5%)	0.460
Do you think taking medicines on your own to treat yourself is safe? Would you advise selfmedication to others?				
Yes	66 (12.5%)	32 (11.4%)	34 (13.9%)	<.001
No	212 (40.4%)	141 (50.36%)	71 (29.1%)	<.001
Maybe	225 (42.9%)	98 (35.0%)	127 (52.0%)	<.001
I don't know	21 (4.0%)	9 (3.2%)	12 (4.9%)	<.001
Which of these drugs do you think are safe to take without a doctor's prescription?				
Painkiller	422 (80.5%)	234 (83.6%)	188 (77.0%)	0.060
Sleeping pills	25 (4.8%)	13 (4.6%)	12 (4.9%)	0.883
Health supplements	173 (33.0%)	88 (31.4%)	85 (34.8%)	0.408
Anti-Allergy	218 (41.6%)	90 (32.1%)	128 (52.5%)	<.001
Laxatives	61 (11.6%)	37 (13.2%)	24 (9.8%)	0.229
Cough suppressants	171 (32.6%)	80 (28.6%)	91 (37.3%)	0.034
Antibiotics	77 (14.7%)	35 (12.5%)	42 (17.2%)	0.129
Herbal/homeopathic remedies	77 (14.7%)	35 (12.5%)	42 (17.2%)	0.129
Oral contraceptives	118 (22.5%)	57 (20.4%)	61 (25.0%)	0.204
Antidepressants	11 (2.1%)	5 (1.8%)	6 (2.5%)	0.592

N=790) =6128, p=0.013 respectively, with non-medical students self-medicating more. The details of all patterns are given in table 2(a).

The most common reason for students to self-medicate was that they found the symptoms to be easily manageable (76.5%), but a greater number of medical students found the symptoms manageable (82.9%) than non-medical students (69.3%). The Chi square test value for this came out to be X^2 (1, N=790) = 13.415, p<0.001, making the difference very significant. Pain-killers (82.8%), anti-allergy (65.5%) and antibiotics (44.8%) were the most common drugs used for self-medication, but it was found that more non-medical than medical students were using sleeping pills and antidepressants, described in detail in table 2(b).

Table 3: *Encountering adverse effects from medication*

Factor	Total count (524) N (%)	Medical 280, N (%)	Non-medical (244), N(%)	p value
Have you ever encountered any adverse side effects?				
Yes	43 (8.2%)	22 (7.8%)	21(8.6)	0.582
No	436 (83.2%)	238 (85.0%)	198 (81.2%)	0.582
Maybe	45 (8.5%)	20 (7.2%)	25 (10.2%)	0.582

When asked about the source of knowledge for

Table 4: Prevention of self-medication

Factor	Strongly agree	Agree	Neutral	Disagree	Strongly disagree	p value
Prevent the supply of medicines without prescription	195 (37.2%)	118 (22.5%)	126 (24.0%)	60 (11.5%)	25 (4.8%)	
Medical	115 (41.1%)	68 (24.3%)	57 (20.4%)	26 (9.3%)	14 (5.0%)	0.057
Non-medical	80 (32.8%)	50 (20.5%)	69 (28.3%)	34 (13.9%)	11 (4.5%)	0.057
Awareness and education regarding implications of self-medication	309 (59.0%)	117 (22.3%)	74 (14.1%)	14 (2.7%)	10 (1.9%)	
Medical	186 (66.4%)	49 (17.5%)	34 (12.1%)	5 (1.8%)	6 (2.1%)	0.004
Non-Medical	123 (50.4%)	68 (27.9%)	40 (16.4%)	8 (3.7%)	4 (1.6%)	0.004
Working towards making health care facilities more affordable	359 (68.5%)	87 (16.6%)	54 (10.3%)	11 (2.1%)	13 (3.5%)	
Medical	187 (66.8%)	48 (17.1%)	32 (11.4%)	6 (2.1%)	7 (2.5%)	0.893
Non-medical	172 (70.5%)	39 (16.0%)	22 (9.0%)	5 (2.0%)	6 (2.5%)	0.893
Making health care facilities easily accessible	389 (74.2%)	76 (14.5%)	38 (7.3%)	10 (1.9%)	11 (2.1%)	
Medical	211 (75.4%)	36 (12.9%)	21 (7.5%)	6 (2.1%)	6 (2.1%)	0.834
Non-medical	178 (73.0%)	40 (16.4%)	17 (7.0%)	4 (1.6%)	5 (2.0%)	0.834

self-medication, medical students were relying more upon their medical knowledge (70.4%) than non-medical students (29.1%) X^2 (1, N=790) =88.825, p< 0.001. Non-medical students, on the other hand, were relying more upon past experiences and friends and family as a source of knowledge. Most of the subjects were obtaining the drugs from pharmacies (78.8%) or reported that the drugs were already available at home (64.3%) with a statistically insignificant difference between medical and non-medical students.

When asked if the subjects thought self-medication was a safe practice or not, a greater percentage of medical students (50.36%) believed it was unsafe despite having practiced it in the past 6 months, whereas only 29.1% of non-medical students believed it was an unsafe practice. This difference was found to be significant (X^2 (1, N=790)=25.123, p<0.001). Painkillers were believed to be the safest drugs by 80.5% of the subjects. These results are displayed in detail in table 2(c).

43 out of the 524 subjects (8.2%) reported to have faced adverse effects from the medication that they were taking while 45 (8.5%) of them were unsure and the rest 436 (83.2%) believed they did not face any adverse effects. These results are displayed in table 3. When asked what would be the best step to prevent the ongoing trend of self-medication amongst undergraduate students, 75.4% of medical students and 73.0% of non-medical students strongly agreed that healthcare facilities should be made easily accessible as described in detail in table 4.

DISCUSSION

The main aim of this study was to assess the pattern of self-medication among undergraduate medical and non-medical students in Pakistan. The current study revealed that self-medication is quite common in Pakistani university students and prevalence was found to be 66.3% which is very much similar to studies conducted in Egypt (62.9%)[13] and Northwest Ethiopia (64.5%).[14] A possible reason for this high average consumption is that university students usually seek quick relief of illnesses, and thus consume multiple remedies at once.[15] The prevalence reported by our study is significantly lower than that reported in Jordan (96.8%)[16] and Iraq (92.4%)[17] whereas it is much higher than that observed in a previous study in Ethiopia (38.5%)[6]. These differences might be explained partially by the variable sample size and the time differences between the conductance of the studies.

Female students (69.3%) were more likely to practice self medication, as compared to male students (61.9%). This difference was significant and may be partly due to the female monthly menstrual cycle during which there are hormonal changes and relatively low immunity, resulting in frequent illnesses. At such times

in their cycle, females may feel reluctant to visit the hospital and hence their higher frequency of self medication.[18]

It was also noticed that an increasing number of students practiced self-medication in more senior years. Similar findings were reported in a previous study in Nigeria[5] and Ethiopia.[19] As the students' year of study increases, their courses become more practical-oriented. Hence, their knowledge and understanding about drugs and diseases would also increase, which resulted in high uptake and purchase of medication without prescription.[20] More senior students were aware about textbooks and Pharmacopoeias' as sources of drug information in contrast to their junior counterparts who relied more on the internet, media and package inserts.[21]

Self medication practice was found to be more prevalent among medical students (67%) in contrast to non medical students (65.6%). The p value for this was 0.679 making the difference insignificant. The slight difference can be attributed to the higher level of medical and pharmaceutical knowledge about medications and their uses among medical students. Thus, it is likely that this knowledge is sufficient to practice self-treatment. The high level of self-medication observed among non-medical students indicates that students are becoming more familiar with medicines and their uses and that may be attributed partially to the large willingness to know and learn about medications from other sources like newspapers, Internet websites and family/friends.[16]

When asked about the rationale behind their self-medication practices, more medical students reasoned that their "symptoms were minor/ manageable at home" as compared to the non-medical students. The difference was significant with $p<0.001$. A probable reason for this finding is that medical students do not find these symptoms as alarming as a student who has no prior medicinal knowledge. 42% of the respondents said that they treat themselves by using "an old prescription for the same illness". More non-medical than medical students selected this option, making the difference significant with $p<0.001$. This reiterates the idea that non-medical students rely on a doctor's prescription, albeit an old one, rather than their own intuition. More non-medical students said that "doctors have a high medical consultation fees" and that "I do not trust doctors/I do not like answering their questions" which is why they resort to self-medication. Medical students are future doctors explains why they trust and agree that doctors do not overcharge. One of the aims of our study was to see if medical students employ their medicinal and pharmacological knowledge to practice self-medication and 26.9% of the respondents agreed that they "have ample knowledge about medicines and when to use them". However, contrary to our expectations, the difference between medical and non-medical students was not significant ($p=0.600$).

A striking majority of the respondents (82.8%) self-medicated with painkillers in the past 6 months. This finding has also been reported in previous studies.[22,23] Painkillers are OTC drugs that are available at every pharmacy and sold without a doctor's prescription. They are considered to be safe and effective as long as the directions on the leaflet are followed. More non-medical students reported the use of herbal/ homeopathic remedies ($p=0.004$) and sleeping pills ($p=0.44$) This can be explained by the fact that medical students, in accordance with the nature of their field and curriculum, are believers and followers of allopathic medicine, rather than herbal/homeopathic remedies. Medical students, having studied pharmacology, would know that sleeping pills like benzodiazepines are not safe and usually have a range of adverse effects.

78.8% of the participants said that the drugs they self-medicated with, were purchased from a "pharmacy", whereas 64.3% said that these drugs were "available at home". This was also reported in similar studies previously.[8] There were no significant differences observed between medical and non-medical students, in their ways of obtaining drugs for self-medication except that more non-medical students sought a homeopath ($p<0.001$).

When asked about whether they believe self-medication is a safe practice and if they would advise

it to others, a significantly ($p<0.001$) greater number of medical students chose "no". This suggests that despite practicing self-medication, a good percentage of medical students would not advise it to other people, knowing the possible adverse effects that can occur. Only 12.5% of the total participants said "yes", more of which were non-medical students. This difference was significant with $p<0.001$.

Out of all the participants, 80.5% thought that "painkillers" are safe to take without a doctor's prescription, which explains why 82.8% of the respondents self-medicated with painkillers in the past 6 months. It should be noted that more non-medical students considered anti-allergy drugs to be safe, the difference being significant with a $p<0.001$. It was reassuring to find out that only 2.1% of the respondents believed that "antidepressants" are safe to be taken without prescription.

A great majority of the respondents (83.2%) reported that they had not experienced any adverse side effects after self-medicating. This might have encouraged the participants to keep taking medicines and drugs on their own. While it was beyond the scope of our current study to investigate the possible side effects, a vast amount of literature is available on this topic. The risks of self-medication range from delays in seeking appropriate medical advice/medical treatment and potential adverse skin reactions, to dangerous drug reactions like anaphylaxis, masking of severe disease by symptomatic treatment, drug resistance, and the risk of dependence and abuse.[24]

This study also aimed to outline strategies which can be employed to prevent the growing trend of self-medication in Pakistan. 74.2% of the respondents strongly agreed that making health-care facilities easily accessible would be the most crucial step in preventing self-treatment among students. 68.5% believed working towards making health-care facilities more affordable would also improve the current situation. Prevention of supply of medicines without prescription should also be enforced as pharmacies were the major source of procuring medicines in our study. Medicines that are not over-the-counter drugs should not be given without prescription and a strict system of checks and balances should be implemented to prevent this problem from escalating.[8] Educational interventions regarding this issue should also be taken into consideration, because self-medication among future healthcare professionals can represent a serious threat to professionalism in medicine. Moreover, for those affected by mental health conditions, it may be difficult to recognize the consequences of self-medication. It is very important for loved ones and healthcare professionals to be aware of the signs of mental illness and self-medication in order to provide appropriate guidance toward proper treatment.[24]

This study has several limitations. The survey was conducted online and was self-reported which may have contributed to inconsistent understanding of questions between students. It may also have led to under- or over-reporting of self-medication practices. A recall bias may also have existed as the participants were asked about their experiences in the past 6 months. Students of other health-related programs (i.e. nursing, dentistry, pharmacy etc) also study about medicines and their side effects in depth, in their undergraduate curricula and hence should be considered in further similar investigations.

CONCLUSION

Self-medication is a common practice among both medical and non-medical university students of Pakistan. Medical students do, however, realise that self-medication is not a safe practice. It is important to take measures to thwart this growing trend.

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IMPACT OF DENGUE VIRUS ON HEMATOLOGICAL AND BIOCHEMICAL PARAMETERS IN DENGUE PATIENTS REPORTING TO A TERTIARY CARE SETTING

Kokab Jabeen,[1] Fareeha Imran,[2] Saima Inam,[3] Aasma Noveen Ajmal,[4] Saira Zafar[5]

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Abstract

Background: This study reveals clinical manifestation and alterations in hematological and biochemical parameters in connection to spectrum of severity of dengue fever (DF), dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).

Methods: The study was conducted on seropositive cases of dengue at Jinnah Hospital Lahore (tertiary care hospital) from January to December 2018. Patients were divided into three groups (DF, DHF and DSS) per criteria of world health organization (WHO).

Results: The frequency of various symptoms and alterations in hematological and biochemical parameters were compared between patients with classic DF and patients with complicated form of dengue disease as DHF and DSS. Total 345 patients those visited with suspected dengue illness, 108 (31.3%) patients were serologically confirmed for dengue infection. Out of 108 seropositive cases, patients were classified as classical DF- 81(75%), DHF- 22(20.4%) and DSS -5 (4.6%). Mean age was 32.3±12.4 years, with male 80 (74%) and female 28 (25.9%).

Conclusion: Common symptoms for dengue were fever and headache (100%), arthralgia (82%), myalgia (80.5%), retro-orbital pain, (68.5%), vomiting (48%) and bleeding tendencies (38%).

Keywords: Dengue fever (DF), Dengue hemorrhagic fever (DHF), Dengue shock Syndrome (DSS) hematological parameters, biological parameters, clinical findings

Dengue is global threat as it is expanding in more than 100 countries located in tropical and sub-tropical regions of the world where climatic condition and rapid growth of population favors their expansion (Shepard et al. 2011; Jakribettu et al. 2015). Dengue is caused by the four circulating serotypes of dengue virus namely DEN1, DEN2, DEN3, DEN4, that are transmitted through the bite of female mosquitoes of genus Aedes, mainly *Aedes aegypti* and *Aedes albopictus* species. Dengue virus is 40-50 nm in diameter spherical shape particle that comprises of 11kb single stranded RNA genome, with its single open reading frame. (Srinivas and Srinivas, 2015; Muller et al., 2017; Tslim et al., 2018). According to the severity of disease World health organization (WHO) has classified dengue infection into three classes i.e. dengue fever (DF), dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS) (Guzman et al., 2010; WHO, 2012).

Pakistan has been suffering from dengue out breaks for decades. The first dengue epidemic in Pakistan was reported in 1994 by which dengue serotype DENV1 and DENV2 were isolated. The dengue remerged in Karachi in 2005, decade after the first epidemic and serotype DENV 3 was found to be involved. In 2006 another outbreak was reported that affected the population in the North to South of Pakistan and 3500 confirmed cases with 52 deaths were reported across the country (Khan et al., 2008). Significant morbidity and mortality were illustrated in dengue outbreak in 2007 (Siddiqui et al., 2009) while in 2008 dengue outbreak number of affected people raised to

1. Kokab Jabeen
2. Fareeha Imran
3. Saima Inam
4. Aasma Noveen Ajmal
5. Saira Zafar

1,2,4. Department of Pathology, Lahore General Hospital, Lahore.
3. Sharif Medical & College, Lahore.
5. Continental Medical College, Lahore

Correspondence:
Dr. Kokab Jabeen, Department of Pathology, Lahore General Hospital, Lahore.

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3280 with 30 deaths. During the period of 2010 and 2011, Pakistan faced adverse floods that had not only destroyed property and lives of the people but also increased breeding sites for dengue virus. As a result, worst outbreaks have been reported during these years (Rasheed et al., 2013). Maximum dengue cases (17493) with 290 deaths were reported from Lahore, Punjab. However, there was severe deficiency of thorough studies related to dengue outbreaks in Lahore. Dengue infection can produce several complications including hemorrhagic shock, liver failure, renal dysfunction and encephalopathy. Keeping this in view, a comprehensive study was conducted to monitor dengue infection effect on different clinical hematological and biochemical parameters in dengue patients of Lahore region and to evaluate the extent of damage. Significant alterations in hematological and biochemical parameters can be used as predictor to severity of disease.

METHODS

Blood samples from total 345 suspected Patients of dengue infection, visiting Jinnah hospital Lahore and Mayo hospital Lahore were collected for this prospective study, during a period of one year from January 2018 to December 2018. Blood samples of 20 individuals with other febrile illness (OFI) were taken as control.

According to WHO criteria Patients with more than two days of acute febrile illness with any two of the symptoms of headache, Retro orbital pain, myalgia, arthralgia, rash and bleeding, shock, low platelet count and serologically positive to immunoglobulin (IgM) or both IgM and IgG or non-structural protein[1] (NS1) test to dengue were included in the study (WHO, 1997).

Patients with identified bacterial infection, any other specified chronic infection and only IgG antibodies diagnosed were not included in the study.

Suspected dengue patients, both male and female, age ranged between 10-70 years, were thoroughly checked by the physician and their details regarding name, age, sex, days of fever, previous history of dengue, and location of the patients were entered in proforma. 20 persons with other febrile (non- dengue) illness (OFI) were included in study as control (Villar-Centeno et al., 2008). Blood samples (10 ml) of suspected dengue patients were taken and divided into three vacutainers for haematological, biochemical and diagnostic studies. Blood samples for diagnostic and biochemical studies were centrifuged and serum was stored at -20°C until testing. Hematological parameters were performed on the same day.

Presence of Non-structural protein 1(NS1) of dengue and IgG/IgM antibodies due to dengue virus infection was detected in patient sera in vitro by ICT method using commercially available dengue diagnostic kit, of Standard Diagnostic Inc; Korea, naming (SD) Bioline and by ELISA method using commercially available kits of NS1 antigen, IgM and IgG antibodies, manufactured by (Diagnostic Automation/ Cortez Diagnostics. USA. All samples were analyzed according to manufacturer protocol.

Blood samples that were confirmed serologically positive by both ICT and ELISA method were divided into three groups DF, DHF and DSS revealing severity of disease per WHO criteria and were included in further studies.

Haematological parameters: Haemoglobin (HB), haematocrit (HCT) or packed cell volume (PCV), total leucocyte count (TLC) and platelet count (PT) in blood were analysed by five compartment differential count system "Sysmex XT 2000' of USA.

Biochemical parameters: Biochemical markers for liver function test (LFT), renal function tests (RFT), cardiac enzymes, lipid profile and electrolytes were determined from the serum of dengue patients to assess the extent of damage caused by dengue virus. Biochemical markers determined for liver function tests (LFT) were, total protein (TP), albumin (ALB), bilirubin (Bili), alanine transaminase (ALT), aspartate transaminase (AST) and alkaline phosphatase (ALP). Parameters included in renal function tests (RFT) were urea, creatinine (Cr) and uric acid (UA) while parameters estimated for lipid profile were cholesterol (CH), triglyceride (TG), high density lipoprotein- cholesterol (HDL-c), low density lipoprotein cholesterol (LDL-c) and very low-density lipoprotein cholesterol (VLDL-

c). To determine heart involvement cardiac enzymes, creatine kinase (CK), lactate dehydrogenase (LDH), and creatine kinase-MB (CK-MB) were estimated. Serum electrolytes that have been estimated in dengue patients were calcium, phosphorus, sodium and potassium. Serum calcium and serum phosphorus were estimated by using AU kits while serum sodium and potassium electrolyte were analyzed by ion selective electrode method using the instrument the "Easylyte" of Medica Corporation of USA. Biochemical parameters were estimated on automatic chemistry analyzer "BECKMAN COULTER AU 480" by standard AU reagents according to the manufacturer instructions. Levels of ALT, AST, ALP, CPK, CK-MB and LDH were measured with liquid UV Kinetic methods. Levels of Bili, TP, ALB, urea, UA, CH, TG, HDL, LDL were estimated with colorimetric end point method.

Calibration of each chemistry parameter was performed according to the instruction of instrument. To check the accuracy of analysis quality control sera was analyzed for all chemistry parameters and results were within range.

The SPSS software version 21 was used for statistical analysis. The statistical tests used were t-test, ANOVA, chi-square& Fisher's test wherever applicable. Continuous variables were expressed as mean ± SD and categorical variables were expressed as number (%). Association between patient factors (age, sex, co-morbidities, Hb, HCT, TLC, PLT, LFT, RFT, Lipid profile, cardiac profile and electrolyte disturbances) were studied using chi-square test or Fisher exact test for categorical variables and ANOVA test for continuous variables. $P<0.05$ was considered to be statistically significant.

RESULTS

Blood samples 345 in number of suspected dengue patients were subjected to serological testing and 108 (31.3%) samples were confirmed positive by both serological methods (ICT& ELSA).

The mean age of the patients in this study was 32 years with a range of 11-70 years. The maximum number of patients (n=55;50.9%) belonged to age group 11-30 years. There were 28 (25.9%) female and 80(74%) were male. However, there was no significant difference in age and sex in patients with DF compared to patients with DHF and DSS. Of the 108 dengue serologically confirmed cases 81 (75%) patients were classified as dengue fever (DF), 22 (20.4%) patients as dengue hemorrhagic fever (DHF) and 5 (4.6%) patients as dengue shock syndrome (DSS).

Dengue frequency was seen on increase through the months of July to September and then declined through months of October to December. Most of the cases 74 (68.5%) were reported from the month of July to September. Fig shows the prevalence of dengue in different months of year.

DISCUSSION

In this study various clinical features, haematological parameters and biomarkers were compared in DF, DHF, DSS and control group. According to this study prevalence of dengue infection was more in male population as compared to female population. Similar findings were reported by other working groups (Anker and Arima, 2011; Namvongsa et al., 2013; Gandhi and Shetty, 2013). However, in studies from North America and Vietnam equal populations of male and female or more female than male were reported to be affected by dengue infection (Trravassos

Haematological parameters

Table 1: *Comparison of haematological parameters among dengue fever, dengue haemorrhagic fever, dengue shock syndrome and control patients*

Parameters	DF (n=81)	DHF (n-22)	DSS (=5)	Control (n-20)	p- value
Hemoglobin (g/dl)	12.7± 1.9	13.03± 2.1	14.3±0.54	13.4± 1.55	0.119
Hematocrit (%)	42.2±5.77	43.9±6.53	46.4±5.62	35.29±5.88	0.000
Total leucocyte count	3248±762	3097±895	2660±594	7024±1409	0.000
Platelet Count	73741±19203	33227±11803	19560±3642	327544±67556	0.000

Table 2: *Comparison of Liver function biomarkers among dengue fever, dengue hemorrhagic fever, dengue shock syndrome and control*

Biomarkers	Reference range	DF (n=81)	DHF (n=22)	DSS (n=5)	Control (n=20)	P
AST(U/L)	11-50	94.3±95.0	145±128	301±109	31.7±10.2	0.00
ALT(U/L)	11-50	73.6 ±78.8	104 ±78.3	155.4±94.8	26.5±11.6	0.00
ALP(U/L)	Up-to 300	141±65.8	181.4±75.3	192.2±61.8	159.6±70.2	0.72
Bilirubin(mg/dl)	0.4-1.2	0.96±0.82	1.37±.83	1.80±0.1.3	0.64±0.20	0.00
Albumin (g/dl)	4.5-5.2	3.6±0.59	3.1±0.49	2.6±0.5	4.4±0.79	0.00
Protein (g/dl)	6.6-8.5	6.8±0.96	6.1±0.74	5.7±0.63	7.7±0.64	0.00
Urea (mg/dl)	11-43	24.4±6.4	47±41.7	71.0±45	23.2±5.9	0.00
Creatinine (mg/dl)	.0.7-1.1	0.64±0.22	1.03±1.18	1.9±1.21	0.68±0.15	0.00
Uric Acid (mg/dl)	3.5 -7.2	4.5±0.92	4.1±1.4	4.0±0.66	4.1±0.99	2.08
Cholesterol (mg/dl)	180-200	140±34.7	121.9± 28	112± 5.7	199 ±31.5	0.00
Triglycerides (mg/dl)	< 150	213±54.8	235±75.2	259± 59.3	193 ±60.5	0.03
HDL-c (mg/dl)	40-60	25±6.5	23.9±4.1	19.8± 0.83	36 ±6.4	0.00
LDL-c (mg/dl)	100-129	92.8±27	84.3± 22.6	80.6± 2.87	12 9±28.6	0.00
VLDL-c (mg/dl)		41.6±12.2	46.6±15.1	51.6±11.8	38.6±12.0	0.25
CPK IU/L	24-171	225±199	274±89.5	378.6±200	137±38.4	.148
CK-MB IU/L	Up-to 25	36±4.7	46±26.8	78±45.1	14±5.5	.029
LDH IU/L	208-378	341±134	467±149	504±83.1	265±106.7	.007
Sodium (mmol/l)	135-147	132±6.0	128.1±3.8	124.8±4.0	135.1±6.1	.00
Potassium (mmol/l)	3.5-5.2	4.6±1.28	3.0±0.35	2.66±0.26	4.66±0.79	.00
Calcium (mg/dl)	8.8-10.5	8.5±0.74	7.38±.70	6.8±0.39	9.0±0.92	.00
Phosphorus (mg/dl)	2.4 4.5	3.81±2.3	3.34±1.2	2.8±0.60	3.84±0.53	0.57

et al., 2000; Gunther et al., 2009). The male population in Pakistan being bread winner spends more time outdoor and exposed to mosquitoes than female. Moreover, females in Pakistan cover themselves with clothes properly as compared to North America and Vietnam.

Prevalence of dengue infection was higher in teenagers and young people (11-50 years) age as compared to elderly people (50-70years) age. High frequency of disease in these groups was due to large population size in this age category and more exposer to mosquitoes due their outdoor activities. Other studies on dengue patients also supported that most of the subjects were 16-30 years old age group (Namvongsa et al., 2013).

Dengue infection had the tendency to spread during monsoon season post monsoon season due to the availability of abundant breeding sites for mosquitoes. Maximum cases are reported during months of July to September. The most common clinical features included fever, headache, myalgia, and arthralgia and these findings were in consistence with previous studies (Gomber et al., 2001; Bhaskar et al., 2010; Yadav, 2018). Clinical feature such as persistent vomiting, bleeding, severe abdominal pain and petechiae were associated with severe form of dengue as DHF and DSS and similar findings were reported in another study conducted in India (Jain et al., 2013).

According to hematological findings in this study hemoconcentration (hematocrit level), leukopenia and thrombocytopenia were associated to severity of disease. Difference in hemoglobin level among dengue groups was not statistically significant. Mean hemoglobin levels in male and female were within reference range. Only few cases with bleeding were presented with low hemoglobin. Hematocrit levels in in non-dengue patients were significantly low when compared to dengue patients. Highest mean hematocrit levels were estimated in DSS patients. The rise in hematocrit level in dengue patients was associated to plasma leakage due to increase in vascular permeability. A 20% rise in hem concentration was documented previously as cut off for diagnosis of DHF. But in this study, elevation in hematocrit levels was less than the

expected rise. Similar findings have been documented and lesser than the expected rise in hematocrit was also observed in previous studies (Kalayanarooj et al., 1997, Narayanan et al., 2002 and Jain et al., 2013; Lokanatha et al., 2017). There is need to develop new recommendation for haematocrit rise and its use in dengue diagnosis (Jain et al., 2013). Most frequently observed leukopenia and thrombocytopenia in dengue patients was due to bone marrow suppression and binding of dengue antigens to platelets. There was significant variation in total leucocyte count and Platelet count regarding severity of dengue infection. platelet count less than 50000 were frequently observed in DHF and DSS patients.

Hematological abnormalities, in the form of thrombocytopenia, was found in most of the patients (90%) in present study that was in consistence to the results of other studies (Kirtlaxmi, 2013; Karoli et al., 2012; Yadav, 2018). However, Kirtlaxmi reported thrombocytopenia in 79 % dengue patients, Karoli diagnosed in 89% patients and Yadav reported in 92% patients.

Biochemical liver dysfunction was, universal in all dengue groups as 94% patients were with elevated transaminase level in present study. Studies from other parts of the world were also in consistence to our study, and reported incidences of elevated transaminases; 97.5% in India, 86% in Singapore to 97% in Vietnam (Trung et al., 2010; Gupta et al., 2014). Brazil had reported elevated transaminases level in 64% that is relatively low (Souza et al., 2004 and Lee et al., 2012). The serum AST/ ALT levels in dengue infection tend to be greater and this differ from the pattern in viral hepatitis. Dengue virus attacked other body organs and released AST enzyme from heart, skeletal muscle, red blood cells, kidneys, brain, and liver, so raised AST level was not entirely due to liver damage (Lee et al., 2012). Comparing three groups of dengue infection (DF, DHF, DSS), frequency of liver dysfunction (raised AST and ALT) levels was significantly high in DHF and DSS as compared to DF Patients. In this study increased levels of ALP and serum bilirubin were not frequently reported in dengue patients, that is in accordance with the results of (Chhina et al). Serum bilirubin levels were found to significantly raised in DSS patients that was in consistence to the findings of the Chhina et al. Serum albumin levels were significantly low in DHF and DSS group as compared to DF group. Plasma leakage due to increase vascular permeability in DHF and DSS causes causes hypoalbuminemia. Similar findings were reported by Villar-Centeno et al., 2008. Protein levels in DSS and DHF groups were significantly low as compared to DF and control group. That could be due to acute liver damage caused by dengue virus as protein is synthesized in liver.

Renal parameters urea, creatinine and uric acid were evaluated in dengue patients to document the effect of dengue infection on kidney. Renal parameters were not impaired in DF patients when compared to DHF and DSS patients. Renal impairment was associated to severity of disease as raised levels of urea and creatinine were observed in 60% DSS and in 18% DHF cases. Uric acid in all patients was within reference range. Results of present study were in consistent with the results reported by Lee et al 2006 who reported 4.9% cases of Acute Renal Failure (ARF) suffering from DHF/DSS and Abboud in 2012, that reported 5% of acute renal failure cases in DHF patients.

In present study frequency of occurrence of hyponatremia, hypokalaemia and hypocalcaemia in DHF and DSS group was significantly high as compared to DF and control group. Other studies also suggested hyponatremia (132mmol/l) in dengue patients (Mekmullic et al., 2014; Lumpaopong et al. 2010 and Syed et al., 2014). The result of sodium level in DF group (132.7mmol/l) and sodium levels below130 mmol/l in DHF and DSS group in present study were in consistence with the previous studies (Mekmullic et al. 2005; Lumpaopong et al. 2010 and Syed et al. 2014). In present study the decrease in potassium level was observed in DHF and DSS patients only and were associated with severity of disease, while in DF patient's potassium levels were within normal range. However, previous researchers have reported mild hypokalaemia

(serum potassium level < 3.5mmol/L) in DF patients (Lumpapong et al. 2010 and Bhagyamma et al. 2015) The estimated mean calcium level in all dengue groups were below the reference range of calcium (8.5-10.5 mg/dl) while phosphorus level in all groups were within reference range in present study. Other studies also revealed that low blood calcium levels were associated with dengue infection and hypocalcaemia was significantly correlated with dengue severity (Constantine et al., 2014; Shivanthan and Rajapakse, 2014). Calcium is important for platelet aggregation and derangements in calcium level is supposed to be associated with myocardial dysfunction observed in dengue patient (Shivanthan and Rajapakse, 2014). However, further studies had been recommended to evaluate the role of serum calcium as prognostic indicator and use of calcium therapy to prevent the dengue complications.

Lipid profile studies suggested that significantly decreased levels of total CH, HDL-c and LDL-c and significantly increased levels of TG were associated to severity of disease. Finding of this study were in line with the result of previous study of dengue virus infected patients (Ray et al., 1999; Van Gorp et al., 2002). Alterations in lipid profile levels could be used as prognostic markers to predict clinical outcome. However, low levels of cholesterol and triglycerides were found to associated to severity of disease in study conducted by Villar-Centeno et al., 2008. The estimated mean levels of TG, VLDL and Cholesterol levels (211.7 mg/dl, 41.9 mg/dl and 115.4 mg/dl respectively) estimated by Survana and Rane, in 2009 were comparable with the present study.

In this study elevated levels of cardiac enzyme, CK-MB and LDH in patients with DHF and DSS were correlated to the severity of disease. Other studies conducted on dengue patients also established rise in LDH, CPK, CK-MB and AST levels (Villaro-Centeno et al., 2011; Aarti et al., 2009). These biomarkers could be used as indicator of severity in dengue infection.

CONCLUSION

On the basis of above finding it can be concluded that the haematological parameters, thrombocytopenia, leukopenia and raised haemconcentration were relevant to severity of disease. Clinical recovery monitoring is dependent on hematological parameters. The hematological profile can be used as screening tool to asses early therapeutic response. This study suggested that some biochemical alterations as raised transaminases, urea, creatinine and triglyceride levels and decreased serum levels of albumin, sodium, potassium and calcium, cholesterol, HDL, LDL can be used as predictor of dengue complication.

Patients with deranged parameters should be treated with extra care to avoid complication. Patients with normal hematological and biochemical parameters can be managed normally.

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CONVENIENCE TO ACCESS LECTURE MATERIALS PERCEPTION OF STUDENTS ON THE USE OF QR CODE VERSUS TRADITIONAL MODES

Attka Maryam,[1] Nosheen Khurram,[2] Mamoona Gulshan,[3] Mehwish Tahir,[4] Uzma Aziz,[5] Madiha Afzal[6]

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Abstract

Objectives: With expansion of the Internet, there has been significant enhancement in the use of innovative methods in classrooms. One such technological innovation is QR codes. QR codes have become a part of our everyday life because of their versatility. Many industrial sectors such as healthcare, manufacturing and supply-chain are using them for the purpose of communication and information exchange. Academia has also explored their use for different purposes such as sharing of research content and study material with students. However, assessment of its use in medical education is underexplored especially in medical colleges in Pakistan.

Objective of this study is to obtain students' perception on the use of QR code for sharing lectures in comparison with traditional modes of sharing including USB drives and emails.

Methods: All first year MBBS students were included in the study. All students were asked to download QR code scanner on their mobile phones. Classroom lectures were delivered three times a week for 3 months. During each lecture, study material was shared with students in the form of a QR code. After three months, students were given an online questionnaire and students' perception was assessed using a 4-point Likert scale satisfaction survey.

Results: According to results of this study, 88% to 92.8 % of students including both girls and boys found it easier to access study material with a QR code. Overall, they preferred use of a QR code for accessing lectures and study material over previously used methods.

Conclusion: The results provide insight to academia and teachers in medical education institutions that use of QR code improve access to study material for students and enhance student's satisfaction compared to old traditional methods.

Keywords: QR code, USB, email, URL

Medical education is rapidly evolving with integration of new technological innovations. There are greater opportunities to incorporate new technological tools into undergraduate medical education for more effective and efficient sharing of information.[1] Good learning should have comprehensive supporting factors such as teaching materials, either in the form of compulsory teaching materials or additional methods, media and other supporting tools.[2]

Quick Response Code (QR Code) is a two-dimensional symbol. It was developed by Denso Wave - a company owned by Toyota, in 1994. The aim of this QR Code is to transfer information quickly and to also get responses quickly. The QR Code was formerly used for tracing vehicle parts for manufacturing.[3] QR code provides high data storage capacity, fast scanning for the users and omnidirectional readability. Today,

1. Attka Maryam
2. Nosheen Khurram
3. Mamoona Gulshan
4. Mehwish Tahir
5. Uzma Aziz
6. Madiha Afzal

1,2,5,6: Rashid Latif Medical College, Lahore
3-4: Shalamar Hospital, Shalamar Institute of Health and Sciences, Lahore

Correspondence:
Dr. Nosheen Khurram, *Department of Histopathology, RLMC, Lahore*
E-Mail: nosheenkhurram@gmail.com
Submission Date: 22-10-2021
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QR code is applicable in different fields related to marketing, security, and even academics. Gradually more people are learning about this technology and using it for different purposes. The popularity of QR code has grown rapidly with exponential use of smartphone devices.[4]

A student simply uses the smartphone camera to scan the QR code and is directly connected to the stored data or the uniform resource locator (URL) embedded within the code. With the advancement of technology, Apple iPhones and most Android phones now have a QR reader preinstalled in the device, and many other free QR scanners can be also downloaded on any smartphone. QR codes is a good option to be adopted in medical education to direct learners to online resources selected by the educator.[5]

The barcodes were previously used for directions to locations and businesses but its use has been extended to get access to course information and study materials.[6] In the higher education sector like medical colleges students are mostly responsible for self-learning and research work, however it is also essential that medical institutions provide a fast, flexible, convenient and user-friendly mechanism for students to access content and learning materials online.[7]

METHODS

QR stands for Quick Response. It is simply a quick, easy to scan image similar to a barcode, that has a specific digital destination, which students or audience are aiming for. QR codes can guide you to a mobile number, text, link, email, SMS, picture, audio, bookmark and more. USB stick is a removable data storage device that includes flash memory. This is a quantitative study. Rashid Latif Medical College, Lahore. Three months after the approval of synopsis. Medical students in their first year were sampled. Non- probability consecutive sampling. All students in Medicine 1st year were sampled for this study.

All first-year students were included in the study. Students were asked to download QR code scanner in their mobile phones. Class lectures were delivered for three months and for each lecture QR code was provided to students. Students were asked to scan the QR code via their mobile phone, after which they had full access to study material of lecture in no time. Students also had access to lecture content at any time from their computers and mobile devices. Lectures were delivered three times a week for 3 months. After three months, students were given an online questionnaire to assess their perception using a 4-point Likert scale satisfaction survey.

To determine statistical significance, comparison of mean using the one sample student-t test was done. This was performed using a test value of 2.5. Mean values above 2.5 were considered as agreeing to the question statement while mean values below 2.5 were considered as disagreeing to the question statement. All p values with 95% confidence interval with $p < 0.05$ were considered statistically significant. Statistical analysis was performed using Latest SPSS version.

Questionnaire

Convenience to access Lecture materials- Percep-tion of students on the use of QR code versus tradi-tional modes.

Assessment of students' perception on accessing lecture by QR code:

At the end of 3 months, medical students were asked to complete a self-administered online questionnaire created using google forms. Students were asked to rate their experience of accessing lectures by QR code as compared to the traditional USB method. For students to rate their experience, a 5-point Likert scale was used where '1' represented 'strongly disagree' and '5' represented 'strongly agree'. The link to questionnaire was shared on the class WhatsApp group as a QR code and all students were asked to participate. Participation was voluntary and they were allowed to complete the survey at leisure without interruption.

Questionnaire:

Answer the questions using the following scale

1= Strongly Disagree

2=Disagree

3= neither agree nor Disagree

4=Agree

5=Strongly Agree

1. As compared to my previous ways of accessing lecture material
   a. I found QR codes easier to access for scanning of lecture material
   b. It was easy to learn 'scanning methods' using QR codes on my mobile device
   c. It was quicker to access lectures using a QR code for scanning
   d. QR codes were simple and convenient to use
2. The QR codes made access to website/ video links in lectures easier as compared to traditional methods.
3. It is a good idea to use QR code to support learning activities as compared to traditional methods.
4. I have positive feelings towards using QR codes in the classroom.
5. I intend to use QR codes in the future.
6. I will suggest other lecturers to use QR codes during lecture delivery.
7. I will prefer using QR code for accessing lectures over the traditional modes.

RESULTS

In this study 142 online questionnaire were filled, whereas 17 (11.97%) questionnaires were duplicate. 17 (11.97%) did not mention their identity. Among 108 students 26 (24.1%) were male and 82 (75.9%) were female.

DISCUSSION

QR code technology has shown great value in education system. It facilitates the provision of great variety of visual learning material. Integration of verbal and visual learning material in education speed up the process of remembrance and reduce the split attention effect.[8]

Many studies were done in the past on learning through QR code methods and questionnaire responses from these studies clearly showed an improvement in participant engagement. In one study gross anatomy learning was done through this method and overall students responded positively to the use of QR codes. Just like in present study, over 80% of students agreed the codes augmented their learning of anatomy and that they found QR codes to be more useful than traditional learning aids. Only noticeable objection reported by students to using QR codes was reluctance to bring

Frequency Distribution According to response

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
As compared to my previous ways of accessing lecture martial:					
a. I found QR codes easier to access for scanning of lecture material	4(3.2)	2(1.6)	3(2.4)	71(56.8)	45(36.0)
b. It was easy to learn scanning methods using QR codes on my mobile device	2(1.6)	4(3.2)	1(0.8)	64(51.2)	54(43.2)
c. It was quicker to access lecture using a QR code for scanning	3(2.4)	3(2.4)	8(6.4)	59(47.2)	52(41.6)
d. QR codes were simple and convenient to use	3(2.4)	4(3.2)	5(4.0)	71(56.8)	42(33.6)
The QR codes made access to website/ video links in lecture easier as compared to traditional method	2(1.6)	6(4.8)	6(4.8)	60(48.0)	51(40.8)
It is a good idea to use QR code to support learning activities as compared to traditional methods	2(1.6)	5(4.0)	2(1.6)	60(48.0)	56(44.8)
I have positive feelings towards using QR codes in the classroom	3(2.4)	4(3.2)	9(7.2)	58(46.4)	51(40.8)
I intend to use QR codes in the future	3(2.4)	6(4.8)	8(6.4)	68(54.4)	40(32.0)
I will suggest other lecturers to use QR codes during lecture deliver	4(3.2)	6(4.8)	11(8.8)	64(51.2)	40(32.0)
I will prefer using QR code for accessing lectures over the traditional mode	2(1.6)	6(4.8)	7(5.6)	65(52.0)	45(36.0)

Comparison of response regarding gender

	Male	Female	p-value
As compared to my previous ways of accessing lecture martial:			
a. I found QR codes easier to access for scanning of lecture material	4.35±0.85	4.22±0.83	0.502
b. It was easy to learn scanning methods using QR codes on my mobile device	4.54±0.51	4.32±0.83	0.202
c. It was quicker to access lecture using a QR code for scanning	4.35±0.75	4.30±0.87	0.828
d. QR codes were simple and convenient to use	4.31±0.79	4.18±0.80	0.490
The QR codes made access to website/ video links in lecture easier as compared to traditional method	4.19±0.85	4.24±0.90	0.796
It is a good idea to use QR code to support learningactivities as compared to traditional methods	4.27±0.83	4.37±0.84	0.609
I have positive feelings towards using QR codes in the classroom	4.15±0.92	4.27±0.86	0.563
I intend to use QR codes in the future	4.27±0.72	4.11±0.92	0.420
I will suggest other lecturers to use QR codes during lecture deliver	4.12±0.86	4.09±0.95	0.886
I will prefer using QR code for accessing lectures over the traditional mode	4.15±0.78	4.24±0.90	0.647

Independent sample t test
There was no statistically significant difference between responses of students regarding gender.

their smartphone devices into the gross anatomy lab. The authors of the study also came to know that QR codes can act as a cost-effective self-assessment solution.[9]

In another study QR codes were found to be useful for learning about anatomy and pathology museum specimens in a medical institution. Just like our study, majority of students agreed or strongly agreed that specimen information was easy to access via QR codes. Major benefits of QR codes mentioned by authors are its low-cost and adaptableness in any learning environment. It also reduces damage to specimens from real handling.[10]

Many studies proved that this method of learning can also be used for paramedical staff. Lin et al. used QR codes for third year nursing students during a pharmacology course in Taiwan and concluded most participants had positive attitudes towards QR codes, with their convenience for learning activities being cited as a key benefit. Lin at al. noted that when used for scenario based learning, a subsection of students performed better in asking questions and discussions than they did prior to the introduction of QR codes.[11] Rosario et al. also did study on labour room nurses and demonstrated that QR codes provide high levels of functionality, usableness and effective way of spreading information to health care staff.[12]

Many articles also proved that QR method also help in learning skills on equipment-use, especially linked to a video clip that the user can watch.[13] Tracey et al. in his study revealed that students response was overwhelmingly positive because they didn't have to wait for the facilitator to demonstrate any skill again and again, as students and health care staff feel easier to access the study material at their own convenience.[14] In a similar manner, Siderits et al. used QR codes to substantially increase the amount of educational content that can be conveyed during a presentation at tumor board presentations.[15]

In today's world of technology innovation, QR code use is widespread for information sharing. Supplementary information provided through QR codes not only enhance learner's ability to prepare lecture and consolidate study material but also elicit questions for the teachers.[16] With advancement in clinical medical teaching, QR codes can be embedded into clinical notes to link videos of patient's ultrasound, echocardiogram and stethoscope examination. QR codes are ideal for clinical simulations and can engage young learning doctors to apply knowledge and act in real time clinical scenarios.[17]

The important benefits of using QR codes for healthcare education lie in their capability to share timely, multimodal information in a cost-effective manner to both male and female students. Several studies demonstrated an improvement in engagement

and learning capacity of students and faculty.[9,10,11,18,19,20,21] Research done by Karia et al. reviewed 24 articles of QR code and its utility and importance in health care education. Most of the articles were published in last five years showing an enhanced interest in this method of teaching and learning which likely is due to ease of use, availability and proximity compared to other available methods of accessing information. Additional benefits lie in adaptability, simplicity in creation and potential environmental benefits of QR codes. There was a strong desire to continue using them in the future for various classroom exercises.[22]

Like this study, many teachers in educational institutions are using QR code to share lecture material which increase student's interest, strengthen understanding and enhance satisfaction in their field of study.

CONCLUSION

In conclusion, QR codes are a reliable tool to increase accessibility to online resources of lecture material, including videos, related web sites and practical examination question and answers. Additionally, electronic means of transmission of information to students and post graduate trainees promote interactivity in class discussions and skill improvement in field of medicine.

LIMITATIONS OF STUDY

1. Smartphone is required for QR code accessibility
2. Internet facility is not available everywhere.
3. Major limitation of this study is that the learning effects were not measured. Future experiments should consider measuring the impact of QR codes on learning.

Authors' Contribution

AM: Substantial contribution to conception, design, and acquisition of data.

NK: Analysis and interpretation of data and drafting this article.

MG: Contribution to conception and design.

MT: Contribution to conception and design.

UA: Drafting the article and revising it for important intellectual content.

MA: Drafting the article and revising it for important intellectual content.

Conflict of Interest: *None*

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THE PATTERN OF ACUTE POISONING IN CHILDREN IN CHAUDHRY MUHAMMAD AKRAM TEACHING AND RESEARCH HOSPITAL LAHORE

Nosheen Iftikhar,[1] Imran Abbas,[2] Shabir Ahmed,[3] Waheed Ahmad,[4] Nayyab Butt,[5] Allah Nawaz[6]

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Abstract

Background: Acute poisoning is one of the recognized causes of morbidity and mortality in children under the age of 5 years. The prevalence and type of substance ingested vary from place to place and over time.

Objectives: To assess the pattern and frequency of acute poisoning in children in Chaudhry Muhammad Akram Teaching and Research Hospital Lahore.

Methods: This retrospective study was conducted at the Pediatrics Emergency of Chaudhry Muhammad Akram Hospital from July 2017 to June 2019 (2 year). All cases of acute poisoning in children that presented within that period were reviewed and important information extracted by retrieving data from hospital records and patients files.

Results: One hundred children were referred to pediatrics emergency departments of Chaudhry Muhammad Akram Hospital due to acute poisoning. 55 (55%) were between 2-5 year of age group, 27 (27%) were between 6-10 year of age group and 18 (18%) were between 11-14 year old. 60 (60%) were male and 40 (40%) were female. There was Ingestion of poison in 97 (97%) and 3 (3%) had poisoning through skin contamination. The most common poisoning agent was Corrosive 71 (71 %), followed by Hydrocarbon 11 (11%), Drugs 9 (9%), Agrochemical 7 (7%), Plants and Insect poisoning 1 (1%) respectively. According to symptoms 47 (47%) presented with Nausea & Vomiting, 21 (21%) with Abdominal pain, 20(20%) with Loose stools, other presented with unconsciousness, Drowsiness & Dizziness and Skin irritation 3 (3%) respectively.

Conclusion: Acute poisoning is a significant cause of morbidity among children in developing countries. Acute poisoning is common in Pakistan, with appreciable mortality, Bleach being the most common agent now a days.

Key Words: Acute, Poisoning, Emergency, Children, Corrosives

Poisons are substances that can cause death, injury or harm to organs, usually by chemical reactions or other activity on the molecular scales, when an organ is exposed to a sufficient quantity. The word poison comes from the Latin word –potio, to drink. Most poisons are swallowed (ingested), but poisons can also enter the body in other ways: by breathing, through the skin, by IV injection, from venom from snake bite and insect bite.

Acute Poisoning in children contains a noteworthy segment of damage related to morbidity and mortality.[1] The incidence of acute poisoning in both developed and developing countries is increasing throughout the world during recent years. This makes issue of children poisoning prone to death.[2]

Acute poisoning in children is a significant medical issue and often leads to admission in emergency

1. Nosheen Iftikhar
2. Imran Abbas
3. Shabir Ahmed
4. Waheed Ahmad
5. Nayyab Butt
6. Allah Nawaz

1,2,6. *Sharif Medical and Dental College Lahore*
3-5. *Azra Naheed Medical College Lahore*

Correspondence:
Dr Shabir Ahmed, *Associate Professor, Sharif Medical and Dental College Lahore. E-mail: ashabir76@yahoo.com*

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units. Homes are the places intended to be protected and secure. In many studies, home mishaps are the most common reasons for poisoning incidents. This gives the feeling that homes are not that shelter as one may suspect[3]. There are studies on changes in incidence and pattern of children poisoning, the unusual presentation with child-resistant containers and changes in endorsing propensities.[4]

The most widely recognized ingested substances were agro chemicals. Others include Alkaline cleaners (12.6%), Opiates (11.9%), Tricyclic Antidepressants (8.4%) and Benzodiazepines (7.7%). About 2.8% of cases were multi-tranquilizer poisoning. Sedatives were the most widely recognized cause of poisoning in less than half year old infants. Diminished level of consciousness (67.6%) and retching (50%) were the most well-known signs and symptoms.[5]

Acute poisoning is a health related Emergency in pediatric unit. Poisoning is typically common throughout the late spring season and lamp fuel (Kerosene) was seen as most common cause. It was common because of simple accessibility. In most cases of lamp oil (kerosene) poisoning children took this substance which was kept in the disposed of container of sodas and mineral water bottles and so on.[6]

Acute organophosphorus pesticide poisoning is an expanding issue, especially in rural zones.[7] Iron is a main source of death because of poisoning in young children. Since antenatal iron supplements are common, the relationship between iron poisoning in young children and the birth of sibling is investigated. Pregnancy is a significant risk factor for iron poisoning in young children, and the period following after delivery is related with the most serious hazards.[8]

Generally guardians are unaware of toxic substances inside plants. The six main plants that most commonly are the wellspring of harmful substances are the pepper plant, peace lily, philodendron, holly, poinsettia, and pokeweed. Signs and symptoms of ingestion include burning and bothering of oral mucosa, queasiness, retching, gastric disturbance, nervousness, breathing challenges, and change in level of consciousness.[9] The constituents of the substance ingested and its dose per kilo body weight ought to be recognized as precisely as could be allowed. In younger children the amount of substance taken is very hard to find out. Some thought of the greatest measure of substance that could have been ingested can be calculated from contrasting the quantity of tablets, or volume of fluid staying, with details on packaging.[10]

Children with acid ingestion in developing nations are regularly treated at home, or referred frequently late to emergency and often leads to stricture formation. At the point when dilatations are performed out, the stricture is often entrenched, making dilatation increasingly troublesome. The mean interval among ingestion and endoscopy was 8.8 months. Intermittent strictures and a long term dilatation treatment should be expected.[11] The aim of our study was to clarify the present pattern of acute poisoning in children at Chaudhry Muhammad Akram teaching and research hospital Lahore.

METHODS

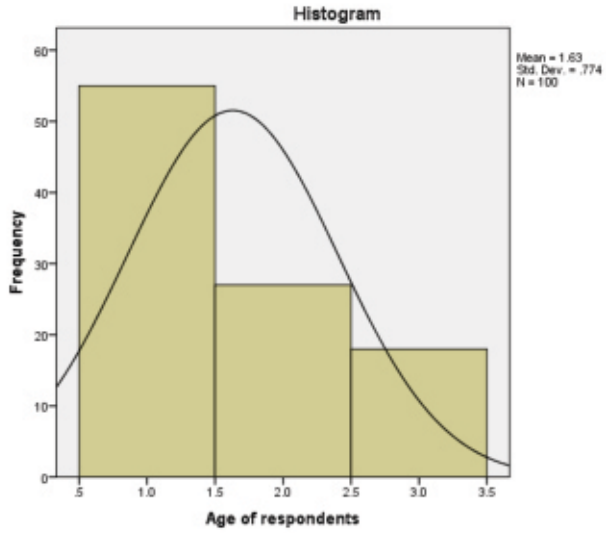
A retrospective study was conducted, which involved daily visits to Chaudhry Muhammad Akram Teaching and Research Hospital Lahore. The record of all children (defined as less than 14 years) admitted from July 2017 to June 2019 to the hospital or attended the emergency department, and that were diagnosed with acute poisoning by the attending doctors, were assessed.

Data was collected from Emergency and ward registers. The following information was obtained: age, sex, address, reason of hospital admission, type of poison, route of poisoning, time of poisoning, duration of ingestion prior to medical attention, container details, history of the event, outcomes and morbidity.

Table 1: *Frequency Distribution of Respondents According to their Age, CMATRH*

Age of respondents	Frequency	Percentage
2-5 years	55	55%
6-10 years	27	27%
11-14 years	18	18%
Total	100	100%

RESULTS

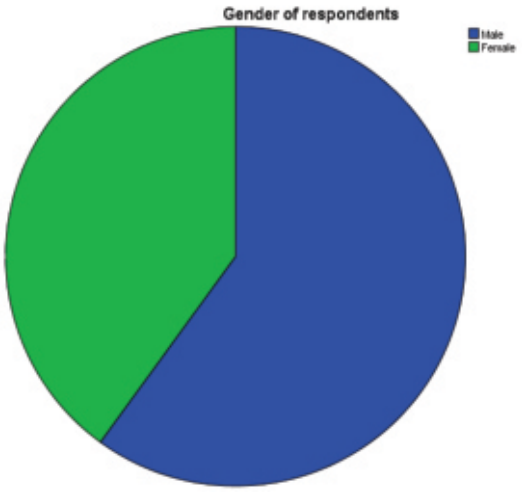


This table shows that among 100 Patients of acute poisoning in CMATRH 55 (55%) are between 2-5 year of age group, 27 (27%) are between 6-10 year of age group and 18 (18%) are between 11-14 year old.

Table 2: *Frequency Distribution of Respondents According to their Gender, CMATRH*

Gender of respondents	Frequency	Percentage
Male	60	60%
Female	40	40%
Total	100	100%

Figure 1: Frequency Distribution of Respondents



According to their Age, CMATRH

Table identifies that among 100 respondents of acute poisoning 60 (60%) were male and 40 (40%) were female.

Figure. 2

Table 3: *Frequency Distribution of Route of Poisoning, CMATRH*

Route of poisoning	Frequency	Percentage
Ingestion	97	97%
Skin Contamination	3	3%
Total	100	100%

Table 4: *Frequency distribution of Type of Poisoning, CMATRH*

Type of poison	Frequency	Percentage
Corrosive	71	71%
Hydrocarbons	11	11%
Drugs	9	9%
Plants	1	1%
Agro chemicals	7	7%
Insect sting	1	1%
Total	100	100%

This table shows the most common route of poisoning was ingestion of poison in 97 (97%) and other through skin contamination which was 3 (3%).

This table clarifies that among 100 patients of acute poisoning; the most common agent was Corrosive 71 (71 %), followed by Hydrocarbon 11 (11%), Drugs 9(9%), Agrochemical 7 (7%), Plants and Insect poisoning 1 (1%) respectively.

Table 5: *Frequency distribution of Location of the Poisoning Event, CMATRH*

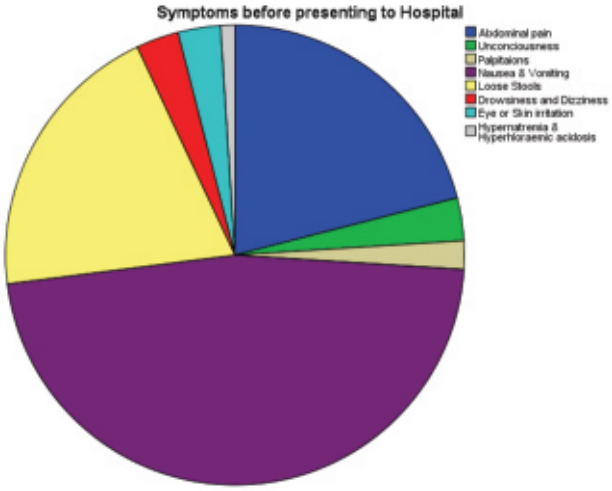
Location of the poisoning event	Frequency	Percentage
Bed Room	9	9%
Washroom	49	49%
Kitchen	22	22%
Out-side Room	20	20%
Total	100	100%

This table shows location of poisoning event, washroom was the most common location of poisoning 49 (49%), Followed by kitchen 22 (22%), outside the room 20 (20%) and bed room 9 (9%).

This table demonstrate symptoms before presenting to Hospital, among 100 patients 47 (47%) with Nausea & Vomiting, 21 (21%) Abdominal pain, 20 (20%) Loose stools, other presented with uncon-

Table 6: Frequency distribution of Symptoms before presenting to Hospital, CMATRH

Symptoms before presenting to Hospital	Frequency	Percentage
Abdominal pain	21	21%
Unconsciousness	3	3%
Palpitations	2	2%
Nausea & Vomiting	47	47%
Loose Stools	20	20%
Drowsiness and Dizziness	3	3%
Eye or Skin irritation	3	3%
Hypernatremia &Hyperhloraemic acidosis	1	1%
Total	100	100%



sciousness, Drowsiness & Dizziness and Skin irritation 3(3%) respectively, 2 (2%) palpitations and 1(1%) Hypernatremia & Hyperchoraemic acidosis.

Figure. 5

Table 7: Frequency distribution of Outcome of Poisoning, CMATRH

Outcomes of poisoning	Frequency	Percentage
Discharged	100	100%

This table shows that patients presented in Emergency of Chudary Mohammad Akram teaching and research hospital Lahore with acute poisoning discharged after primary treatment.

DISCUSSION

In our study, One hundred children were referred to pediatrics' emergency departments of Chaudhry Muhammad Akram Teaching and Research Hospital Lahore .This retrospective study was conducted at the Pediatrics Emergency of Chaudary Muhammad Akram Teaching and Research Hospital Lahore from July 2017 to June 2019 (Two years).

Acute poisoning in children as a rule happen with household items (beauty care products, cleaning substances ,analgesics, plants, pesticides, nutrients, expressions and specialty supplies in home and furthermore with hydrocarbons or with different medications). Early assessment and management of poisoning ought to be done to give emergency medication competency. Emergency observing of patient with associated harming requires checking the level with consciousness including Airway, Breathing, and circulation. Vital signs incorporate pulse, heart rate, respiratory rate, blood pressure and glucose level.

By taking careful history with a complete physical examination and case oriented focused labs the doctor can accurately analyze and treat most ingestion in a successful way.

Numerous past studies have demonstrated that kids under five years old are especially in danger from unintentional poisoning.[12,13] Our study favors this finding. In any case, in contrast to the finding in Japan[14], poisoning underneath the age of one year was uncommon in our study. In a study in Denmark,[12] 180 of 524 kids (34%) admitted to hospital because of a household chemical poison. Cleaning substances were the most widely recognized, with dishwasher detergents outnumbering all other chemicals.

In our study The most common agent was Corrosive 71(71%), followed by Hydrocarbon 11(11%), Drugs 9(9%), Agrochemical 7(7%), Plants and Insect poisoning 1(1%) respectively.

Similarity ingestion of household items establishes the significant reason for unplanned poisoning in Basra, Iraq.[15] Household chemicals are along these lines a significant wellspring of poisoning for kids and these will in general be kept in effectively opened or open containers. Bug sprays have extensive potential for harm, yet they were experienced in just seven cases, all were without lethal result.

Common therapeutic agents, for example, anal-

gesics and anti-inflammatory drugs were seen as the most powerful wellspring of poisoning, in our study 9 cases detected. Children who had ingested a toxin were shifted rapidly to an emergency clinics. Fortunately, no deaths occurred in our study. No long-term morbidity was seen in the children within this study.

Previous work has recommended that the pattern of acute poisoning in children changing as per the advancement status of the nation16. In developing nations insect stings and ingestion of paraffin and medicine is common. For example, those in Western Europe and North America with household items and pharmaceuticals being the overwhelming agents of childhood poisoning. Substances that are generally associated with death from poisoning are antidepressants, benzodiazepines and analgesics.[17]

In the present study there were no cases of poisoning with opioid analgesics, which are widely available in Lahore.

CONCLUSION

Acute poisoning is still a significant cause of morbidity and mortality among children in developing countries. Acute poisoning in children is common in Pakistan, with appreciable mortality, Bleach being the most common agent now a days. Awareness and education about the potential toxicity of commonly used drugs and household substances may help in reducing the incidence of acute poisoning in children.

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FREQUENCY OF THROMBOCYTOPENIA IN FEMALES WITH PREGNANCY INDUCED HYPERTENSION

Iram Inam,[1] Faisal Ashraf,[2] Mizrah Mahreen,[3] Ghias-ul-Hasan,[4] Shazia Sehgal,[5] Nagina Sohail[6]

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Abstract

Preeclampsia thrombocytopenia (PIH) is defined as hypertension (HTN) that occurs in pregnancy for the first time after 20 weeks of gestation, disappearing following delivery of the baby. Thrombocytopenia is defined as a platelet count of less than 150×103 µl. It is commonly diagnosed and has attracted more interest from researchers during recent years, especially in Hypertensive disorders of pregnancy.

Objective: The objective of this study is to find frequency of thrombocytopenia in females with pregnancy induced hypertension.

Methods: Cross sectional study. Department of Obs. and Gynecology Continental Medical College/Hayat Memorial Hospital and Jinnah Hospital, Lahore. The study was completed in 6 months after approval of synopsis (January 6, 2021 till July 6, 2021). After taking approval from hospital ethical committee, 282 females fulfilling selection criteria were selected from Department of Obs. and Gynecology. Informed consent and demographic information (name, age, gestational age, parity) were obtained. Venous blood samples was obtained in EDTA vacutainers and appropriately labeled. Platelet count was done using three dimensional, Hematology Auto Analyzer Humacount Plus at hospital laboratory. Thrombocytopenia was labeled as per operational definition in PIH diagnosed females. All this information was recorded in proforma by researcher herself (attached).

Results: The mean age of cases was 27.61 ± 4.59 years with minimum and maximum age as 18 and 35 years. The mean gestational age was 33.83 ± 5 weeks with minimum and maximum gestational age as 23 and 40 weeks. A total of 180(63.8%) females had parity < 3 and 102(36.2%) females had parity 3-6. The frequency of thrombocytopenia was found in 157(55.7%) of the cases.

Conclusion: It was concluded that frequency of thrombocytopenia is found very high. Hence, it is further concluded that hypertensive disorders of pregnancy are recognized as a major cause of gestational thrombocytopenia. Careful follow up during and after pregnancy is recommended.

Key Words: Eclampsia, preeclampsia thrombocytopenia, pregnancy induced hypertension

Pregnancy induced hypertension (PIH) includes gestational hypertension, preeclampsia, and eclampsia.[1] PIH is one of the most common and potential life threatening complications of pregnancy[2] with maternal and perinatal morbidity and mortality with incidence of 5-7% of all pregnancy.[3] Platelets are produced in the bone marrow and remain in blood for about 2 weeks before they are destroyed in the reticuloendothelial system. In PIH, lower the platelet count, greater are maternal and fetal morbidity and mortality.[1,4] Thrombocytopenia is defined as a platelet count of less than 150 × 103 µl. It is commonly diagnosed and has attracted more interest from the researchers in pregnant women during the last 20 years, especially

1. Iram Inam
2. Faisal Ashraf
3. Mizrah Mahreen
4. Ghias-ul-Hasan
5. Shazia Sehgal
6. Nagina Sohail

1,6. Continental Medical College, Lahore.
2,3,5. Jinnah Hospital Lahore.
4. Lahore General Hospital, Lahore.

Correspondence:
Dr. Iram Inam, *Associate Professor, Continental Medical College, Lahore*

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in hypertensive pregnant women.[4] Thrombocytopenia is second only to anemia as the most common hematologic abnormality encountered during pregnancy.[5] Thrombocytopenia complicates about 7-8% of all pregnancies.[6] The frequency of thrombocytopenia increases in females with pregnancy induced hypertension as a local study reported that the frequency of thrombocytopenia in all patient groups was 21.8%.[7] One more study reported that thrombocytopenia was seen in 76% among 100 females with PIH.[8]

The rationale of this study is to determine frequency of thrombocytopenia in females with pregnancy induced hypertension in local population. Though local and international studies are available but there is huge variation in these statistics i.e. 21.8%7- 76%[8], moreover the studies on local populations are not widely available. The study is necessary to find frequency in local population as thrombocytopenia in PIH is linked to the significant morbidity and mortality. The can add bulk to the local literature and may prove useful while planning strategies for female having pregnancy induced hypertension.

The objective of this study is to find frequency of thrombocytopenia in females with pregnancy induced.

METHODS

Study Design: Cross sectional study

Sampling Technique: Non-Probability, consecutive sampling

Setting: Department of Obs. and Gynecology Continental Medical College/Hayat Memorial Hospital and Jinnah Hospital Lahore.

Duration: The study was completed in 6 months after approval of synopsis (January 6, 2021 till July 6, 2021)

Sample Size: A total of 282 females were taken in this study. The sample size is estimated using expected frequency of thrombocytopenia as 76%[8] in females diagnosed of PIH. We used 5% level of significance and 95% confidence level.

Selection Criteria:

Inclusion criteria:

- Females of age 18-35 years of any parity with diagnosis of PIH as per operational definition
- Gestational age 21-40 weeks

Exclusion criteria:

- Abnormal liver function reports (AST>40IU, ALT>40IU),
- Females with chronic systemic problems i.e. diabetes (BSR>186mg/dl),
- Abnormal renal function reports (creatinine >1.2mg/dl),
- Cardiovascular disease (abnormal ECG and medical record), autoimmune diseases (medical record)

After taking approval from hospital ethical committee, 282 females fulfilling selection criteria were selected from Department of Obs. and Gynecology Jinnah Hospital and Continental Medical College Lahore. Informed consent and demographic information (name, age, gestational age, parity) were obtained. Venous blood samples was obtained in EDTA vacutainers and appropriately labeled. Platelet count was done using three dimensional, Hematology Auto Analyzer Humacount Plus at hospital laboratory. Thrombocytopenia was labeled as per operational definition in PIH diagnosed females. All this information was recorded in proforma by researcher herself.

Pregnancy induced hypertension was classified and sub graded into four categories.

i. Gestational HTN: Systolic BP ≥140 or diastolic BP ≥90 mm Hg for first time during pregnancy with no proteinuria on dipstick method
ii. Mild preeclampsia: With BP of 140/90 160/110 mm of Hg with persistent proteinuria by dip stick method (1+ or more) with or without pathological edema.
iii. Eclampsia: HTN and proteinuria with seizures that cannot be attributed to other causes in a woman with preeclampsia or coma
iv. Severe preeclampsia: BP of >160/110 mm of Hg with proteinuria (3+ or more), with or without pathological edema

Thrombocytopenia was labeled if the platelet

count is less than 150×103/µl that was assessed in females with gestational age > 20 weeks on USG after diagnosis of PIH (it was diagnosed within a week after PIH diagnosis)

Data was entered and analyzed in SPSS version 20. Quantitative data like age, gestational age was presented as mean and standard deviation. Qualitative data like thrombocytopenia was presented as frequency and percentage. Parity was also presented as frequency and percentages. Data was stratified for age, gestational age, parity, BMI and types of PIH to address effect modifiers. Post stratification Chi-square test was applied by considering p-value ≤ 0.05 as significant.

RESULTS

The mean age of cases was 27.61 ± 4.59 years with minimum and maximum age as 18 and 35 years. Table -1. The mean gestational age was 33.83 ± 5 weeks with minimum and maximum gestational age as 23 and 40 weeks. Table -2. A total of 180(63.8%) females had parity < 3 and 102(36.2%) females had parity 3-6. Fig-1. The frequency of thrombocytopenia was found in 157(55.7%) of the cases. Fig-2. When data was stratified for age, gestational age, parity, BMI and types of PIH, the frequency of thrombocytopenia was statistically same in all stratum, p-value > 0.05 i.e. Table -3 to 7. Frequency of thrombocytopenia was statistically same in both age groups 58.6% in 18-29 years old and in 41.4% cases with 30-35 years old, p-value = 0.105. Table -3. Frequency of thrombocytopenia was statistically same in both groups of gestational age i.e. 54.1% in females having 21-36 weeks and in 45.9% females having 37-40 weeks of gestation, p-value = 0.324. Table -4. Frequency of thrombocytopenia was statistically same in females having parity < (64.3%) and in females having parity as 3-6 (35.7%), p-value = 0.844. Table -5. Frequency of thrombocytopenia was statistically same in obese versus non-obese, 61.8% versus 38.2%, p-value = 0.074. Table -6. Frequency of thrombocytopenia was statistically same in eclampsia (43.9%), pre- eclampsia (33.1%) and sever preeclampsia (22.9%), p-value = 0.123. Table -7

Table 1: *Descriptive statistics of age (years)*

Age (years)	
Mean	27.61
S.D	4.59
Range	17.00
Minimum	18.00
Maximum	35.00

Table 2: *Descriptive statistics of gestational age (weeks)*

Gestational age (weeks)	
Mean	33.82
S.D	5.00
Range	17.00
Minimum	23.00
Maximum	40.00

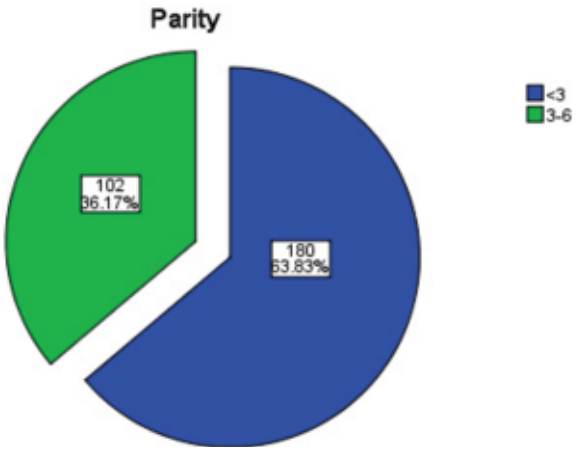

Fig 1: *Distribution of Parity*

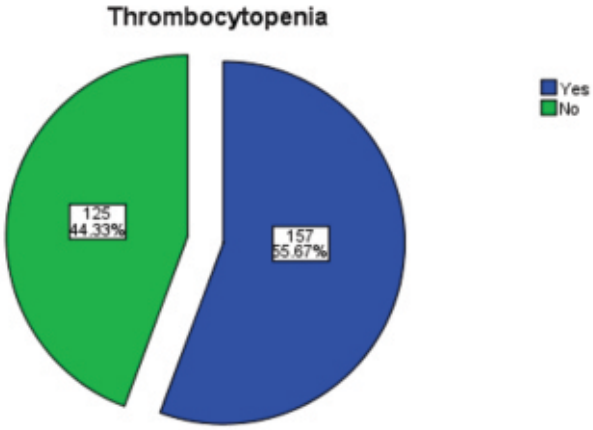

Fig 2: *Distribution of Thrombocytopenia*

Table 3: *Comparison of Thrombocytopenia in different Age Groups (Years)*

		Thrombocytopenia		Total
		Yes	No	
Age groups (years)	18-29	92(58.6%)	85(68.0%)	177(62.8%)
	30-35	65(41.4%)	40(32.0%)	105(37.2%)
Total		157(100.0%)	125(100.0%)	282(100.0%)

Chi-square =2.632 p-value = 0.105 (Insignificant)

Table 4: *Comparison of Thrombocytopenia in different in different Gestational age (weeks)*

		Thrombocytopenia		Total
		Yes	No	
Gestational age (weeks)	21-36	85(54.1%)	75(60.0%)	160(56.7%)
	37-40	72(45.9%)	50(40.0%)	122(43.3%)
Total		157(100.0%)	125(100.0%)	282(100.0%)

Chi-square = 0.974 p-value = 0.324 (Insignificant)

Table 5: *Comparison of Thrombocytopenia in different in different Parity*

		Thrombocytopenia		Total
		Yes	No	
Parity	<3	101(64.3%)	79(63.2%)	180(63.8%)
	3-6	56(35.7%)	46(36.8%)	102(36.2%)
Total		157(100.0%)	125(100.0%)	282(100.0%)

Chi-square = 0.039 p-value = 0.844 (Insignificant)

Table 6: *Comparison of Thrombocytopenia in different in different BMI*

		Thrombocytopenia		Total
		Yes	No	
BMI	Obese	97(61.8%)	64(51.2%)	161(57.1%)
	Non-obese	60(38.2%)	61(48.8%)	121(42.9%)
Total		157(100.0%)	125(100.0%)	282(100.0%)

Chi-square = 3.182 p-value = 0.074 (Insignificant)

Table 7: *Comparison of Thrombocytopenia in different types of PIH*

		Thrombocytopenia		Total
		Yes	No	
Types of PIH	Eclampsia	69(43.9%)	40(32.0%)	109(38.7%)
	Pre-eclampsia	52(33.1%)	50(40.0%)	102(36.2%)
	Sever preeclampsia	36(22.9%)	35(28.0%)	71(25.2%)
Total		157(100.0%)	125(100.0%)	282(100.0%)

Chi-square = 4.192 p-value = 0.123 (Insignificant)

DISCUSSION

Platelets are produced in the bone marrow and remain in blood for about 2 weeks before they are destroyed in the reticulo-endothelial system. The normal platelets count ranges between 150 and 450 × 103 µl which is also the same as that is mostly recorded during the normal pregnancy.[9] Gestational thrombocytopenia (GT)—thrombocytopenia during pregnancy (PIT)—occurs in late gestation, and its frequency increases during the last few weeks of gestation, and it occurs also during the last few weeks of the second trimester. PIT is commonly mild (>100 × 103 µl), and resolves usually completely after delivery; however, severe thrombocytopenia (<70 × 103 µl) rarely occurs.[11]

Several studies have reported fetal and/or neonatal thrombocytopenia in 4–13 % GT's mothers. During pregnancy, fluid retention occurs because of sodium and water retention under estrogen and progesterone hormone effects, leading to hemodilution. This leads to lower hematocrit (dilution or pseudo-thrombocytopenia). Burrows and Kelton reported that the frequency of PIT was 5 %, while Kaplan et al. observed PIT in about 7 % of pregnancies.[10,12]

In current study the mean age of cases was 27.61 ± 4.59 years with minimum and maximum age as 18 and 35 years. The mean gestational age was 33.83±5 weeks with minimum and maximum gestational age as 23 and 40 weeks. A total of 180(63.8%) females had parity < 3 and 102(36.2%) females had parity[3-6]. The frequency of thrombocytopenia was found in 157 (55.7%) of the cases, the frequency in current study was lower than reported study i.e. the frequency of thrombocytopenia in all patient groups was 21.8%.[7] One more study reported that thrombocytopenia was seen in 76% among 100 females with PIH.[8] This frequency is higher than found in current study.

Recently another study was done to estimate the incidence of thrombocytopenia in pregnant women diagnosed with hypertensive disorders of pregnancy and to correlate its severity with the degree of thrombocytopenia. Hypertensive disorders of pregnancy cases were classified into: Gestational hypertension, mild preeclampsia, severe preeclampsia, haemolysis, elevated liver enzyme levels, and low platelet levels

(HELLP) syndrome and eclampsia. The result has showed that Preeclampsia- mild (29.25%) and severe (22.5%), accounted for most of the cases followed by eclampsia (3%) and gestational HTN (1.5%). Among these hypertensive patients, mild thrombocytopenia was noted in 60 cases (40%), moderate thrombocytopenia 48 (32%), severe thrombocytopenia 12 (8%), and normal platelet counts 30 (20%) were noted.[13] Similarly another Prospective observational study was performed to correlate severity of PIH with degree of thrombocytopenia and the degree of thrombocytopenia with fetal and maternal outcome. The main findings of the study demonstrated that 66% of all the cases had severe preeclampsia and 56% had thrombocytopenia. There was very high significant relationship between the degree of thrombocytopenia with the severity of the PIH (at $p<0.001$). 12% of the fetuses had IUD, 10% had IUGR, 4% died after birth and 2% had severe birth asphyxia. 5 % of the mothers had DIC, 3 % showing HELLP syndrome, and 1% died.[14] In 2015, another retrospective study was done to estimate the incidence of thrombocytopenia in pregnant women diagnosed with PIH and to correlate the severity of PIH with the degree of thrombocytopenia. The result has showed that Preeclampsia - mild (56%) and severe (36%), accounted for most of the cases followed by eclampsia (6%) and gestational HTN (2%). In the 100 cases, mild thrombocytopenia (41%), moderate thrombocytopenia (29%), severe thrombocytopenia (6%), and normal platelet counts (24%) were encountered. Varying platelet levels were seen in the five groups with 23.4% of severe eclampsia and 50% of eclampsia cases having normal platelet counts and 7.1% of mild preeclampsia cases showing severe thrombocytopenia. Poor maternal outcome was seen 11% cases due to HELLP syndrome, postpartum hemorrhage, and maternal death. [8]

Habas et al conducted another study to assess the incidence of thrombocytopenia in hypertensive pregnant women during the third trimester of pregnancy. Therefore, only 438 pregnant women remained eligible for the study. The mean age was (32.56 ± 1.5), with their ages ranging between 18 and 49 years. Most of the included women were primigravida 179(39 %), gravid 2, para one were 72 (16.4 %), and the rest were gravid 3 or more (42.6 %). The blood pressure was 140-160/90-110 mmHg in 365 women (83.4 %), and 73 women (16.7 %) had blood pressure readings more than 160/110 mmHg. Mean platelets count was (206.49 9 103 /ll ± 3.35), and ranged between (41.0 - 449.0 9 103 /ll). Thrombocytopenia (less than 150 9 103 /ll) was recorded in 103 women (23.5%). All pregnancy cases were delivered safely with no fetal complications. So, Gestational thrombocytopenia (GT) is recognized as a major cause of thrombocytopenia particularly in hypertensive pregnant women during the third trimester. Careful follow up during and after pregnancy for those women is recommended.[15]

CONCLUSION

Through the findings of current study it is concluded that frequency of thrombocytopenia is found very high. Hence, it is further concluded that hypertensive disorders of pregnancy are recognized as a major cause of gestational thrombocytopenia. Careful follow up during and after pregnancy is recommended.

Limitations of the Study

The study reveals that Hypertension does have a remarkable effect on the platelets in pregnancy but it needs to be confirmed in a larger population and especially a rural one where the general health, dietary patterns, medical facilities are not as readily and properly available as in urban areas.

Conflicts of Interest *None*

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Contribution by Authors

Dr. Iram

Concept, Patient selection and paper writing

Dr. Faisal

Data collection and Interpretation

Dr. Mizrah Mahreen

Patient follow up and Data filling

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USE OF SMART PHONES AND WEB BASED DEVICES DURING THE CONDUCT OF ANESTHESIA AND ITS CONSEQUENCES.

Muhammad Muazzam Butt,[1] Sara Yousaf,[2] Hamza Waheed,[3] Umer Farooq,[4] Saamia Yousuf,[5] Anum Zeb[6]

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Abstract

Objective: To determine the frequency of smart phones use by anesthetist during conduct of anesthesia inside operating room and to determine the frequency of distractions due to smartphone use in operating room

Methods: 50 anesthetist were enrolled. Questions regarding smartphone use in operating room during conduct of anesthesia, its nature and consequence asked and their responses based on personal subjective assessment noted on pre-decided Performa. All the collected data was entered and analyzed on SPSS version 20.

Result: 90% of respondents used smartphones during anesthesia inside operating room and distraction events were noted in 76% cases.

Conclusion: Smart phones are frequently used by anesthetist during conduct of anesthesia, invariably causing a distraction.

Keywords: Anesthesia, Operating Room, Distraction, Smartphones.

Smartphone use has recently undergone large-scale increases worldwide and have become an indispensable part of daily life. These small, handy technological devices have provided unique opportunities for use in medicine, as in many other aspects of life.[1] In the developing world, smartphones may be used for anesthesiology practice including: team member communication, knowledge acquisition through internet or downloaded applications, information transfer, e-learning, telemedicine or remote monitoring.[2] Studies have been published on the use of smartphones as oximetry devices[3] or stethoscopes,[4] for determining neuromuscular function[5], maintaining 15° of left lateral tilt during caesarean section[6], fiber optic bronchoscopy education[7], pain scoring[8], and diagnosing arrhythmia/dysrhythmia.[9] Frequency of smartphone and internet use for educational purpose among anesthesia residents was found 93.7% in a study.[10] Another study reported that 55.6% of anesthesiologists use smartphones during conduct of anaesthesia.[11] Personal distraction by cell phone use that negatively affected performance was admitted by 7.3%, whereas witnessing another perfusionist distracted with phone/text while on cardiopulmonary bypass was acknowledged by 33.7% of respondents.[11] Another study showed that 12.7% had distraction (as 87.3% stated that they were never distracted because of smartphone use); however, 41% had witnessed their colleagues in such a situation at least once.[10] This study is conceived with an idea to assess the frequency of smartphone use during the conduct of anesthesia, nature of its use and its impact on patient care in our setup. So that strategies be formed for fair usage to benefit

1. Muhammad Muazzam Butt
2. Sara Yousaf
3. Hamza Waheed
4. Umer Farooq
5. Saamia Yousuf
6. Anum Zaib

1,6. Department of Anesthesia AMC/PINS/Lahore General Hospital/PGMI Lahore
2,3. Hameed Lateef Hospital Lahore,
4. Department of Anesthesia Gujranwala Medical College, Gujranwala
5. Department of AnesthesiaFJMC/Sir Gangaram Hospital, Lahore

Correspondence:
Dr. Muhammad Muazzam Butt, *Assistant Professor Anesthesia AMC/PINS/Lahore General hospital/PGMI Lahore,*
Email: dr.muazzambutt@gmail.com

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the patients in operating rooms.

METHODS

This cross sectional study was conducted at Department of Anesthesia, Hameed Latif Hospital, Lahore. Objectives were to determine the frequency of use of smartphone by anesthetist during conduct of anesthesia inside operating room (primary objective) and to determine the frequency of distractions due to smartphone use in operating room (Secondary objective). Use of smart phones was labeled 'Yes' if candidate admitted that he/she use smartphone device during conduct of anesthesia to the patients undergoing surgery. Distraction was defined as something which would not normally be considered within the anesthetist's primary role of maintaining anesthesia and appropriate physiological variables. It was labeled Yes if candidate had score ≥4 out of 9 as per questions asked in a predesigned Performa. All anesthesia personnel of either gender practicing in Hameed Latif Hospital Lahore were included in this study. Anesthesia doctors not willing to take part in study; anesthesia doctors who didn't have a smartphone or web- based device; and Trainees of other specialties on rotation in anesthesia were excluded. Sample size of 50 was calculated with 95% confidence level, 7% margin of eror and taking expected percentage of smartphone use i.e. 93.7% among anesthesia doctors during conduct of anesthesia[10] (OpenEpi calculator). 50 anesthesia doctors fulfilling above criteria were included in the study from Hameed Latif Hospital. An informed consent was taken. Demographic information (age, gender, field experience) was noted. Then they were interviewed by researcher. Questions regarding smartphone use in operating room during conduct of anesthesia, its nature and consequence asked and their responses based on personal subjective assessment were noted on predesigned Performa. Conduct of anesthesia was considered starting from theater preparation before procedure to shifting of patient to recovery room. Data was entered & analyzed by using SPSS version 20. Mean and standard deviation was calculated for quantitative variables like age, field experience. Qualitative variables like gender and use of smartphone, positive and negative consequence would be presented as frequency and percentage. Data was stratified for age, field experience. Post-stratification, chi-square test was used to compare stratified groups with p-value ≤0.05 as significant.

RESULTS

In this study total 50 anesthesiologist participated. The mean age of the respondents was 30 ± 5.99 years with minimum and maximum ages of 25 & 62 years respectively. 29(58%) respondents were males and 21(42%) respondents were females. Male to female ratio of the respondents was 1.38:1. The mean field experience of respondents was 4.85 ± 7.01 years with minimum and maximum field experiences of 0 & 38 years respectively. Consultant anesthesiologist were 11(22%) and the trainee anesthesiologist were 39(78%). Respondents who use smartphones during conduct of anesthesia were 45(90%) and who does not use smartphones during conduct of anesthesia were 5 (10.0%). The respondents who never use smartphone during conduct of anesthesia were 6(12%), who use smartphone once were 9(18%), who use 2-5 times were 10(20%), the respondents who use > 5 times the smartphones were 13(26%) and who always use smartphones during conduct of anesthesia were 12(24%). (Table 1) The mean total score of the respondents was 5.04 ± 2.48 with minimum and maximum values of 0 & 9 score respectively. Distraction due to smart phone during conduct of anesthesia was found in 38(76%) cases. (Figure 1) Data were stratified for age (≤ 30 years and > 30 years); gender (male and female); and years of experience (<5 years and ≥5 years) but results were statistically insignificant. (Table 2)

DISCUSSION

Table 1: *Frequency Distribution of use of Smartphones during Conduct of Anesthesia*

Frequency of use	Frequency	Percentage
Never	6	12.0
Once	9	18.0
2-5 times	10	20.0
> 5 times	13	26.0
Always	12	24.0
Total	**50**	**100.0**

This present cross sectional study was carried out at Department of Anesthesia Hameed Latif Hospital, Lahore to determine the frequency of use of smartphone by anesthetist during conduct of anesthesia inside operating room and to determine the frequency of distractions due to smartphone use in operating room. Health care-related apps provide valuable facts and have added a new dimension to knowledge sharing. Smartphones can perform many of the common functions of a computer with the added advantage of "always being available" and maximum versatility, much like a Swiss Army knife. The boosting prevalence of the health care-related smartphone technology generates a constantly increasing worldwide interest. Anesthesiology, as a profession, has been one of the first departments to adopt new technologies.[12]

Table 2: *Stratification of Distraction with Age, Gender and Years of Experience.*

Strata		Distraction		Total	p-value
		Yes	No		
Age (years)	⩽ 30	30	10	40	*1.000*
	> 30	8	2	10	
Total		38	12	50	
Gender	Male	20	9	29	*0.201*
	Female	18	3	21	
Total		38	12	50	
Field Experience	< 5 years	28	8	36	*0.718*
	⩾ 5 years	10	4	14	
Total		38	12	50	

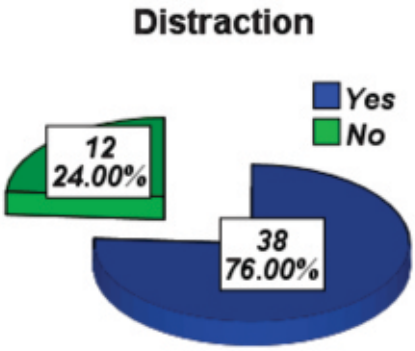

Figure 1: *Frequency Distribution of Distraction during Conduct of Anesthesia*

In this study the respondents who have smartphones were 49(98%) and the respondents who use smartphones during conduct of anesthesia were 45(90%). In our study the distraction due to smart phone during conduct of anes-thesia was found in 38(76%) cases. Some of the studies are discussed below showing results in favour of our study as. A study by MS Green et al documented that Among the survey participants, 99.3% (n = 410) were using smartphones and 0.7% (n = 03) of the participants were not using the smartphones.[12] A study showed personal distraction by cell phone use that negatively affected performance was admitted by 7.3%, whereas witnessing another perfusionist distracted with phone/text while on cardiopulmonary bypass was acknowledged by 33.7% of respondents.[11] Another study showed that 12.7% had distraction (as 87.3% stated that they were never distracted because of smartphone use); however, 41% had witnessed their colleagues in such a situation at least once.[10] A study by Kasana Raksamani et al[13] demonstrated that Fifty-three of 72 anesthesia residents responded to the questionnaire (73.6%). All owned a smartphone and all admitted to using a smartphone while administering an anesthetic. Most used their smartphone to access the Internet (96.2%, n=51), including social networks (81.1%, n = 43). The majority felt positive towards smartphone use (94.3%, n=50), particularly their educational value. A minority reported that smartphones distracted from patient care or impaired their interactions with colleagues. One study showed that the frequency of smartphone and internet use was 93.7% among anesthesia residents for educational purpose.[10] But another study showed that use of a cell phone was reported by 55.6% of anesthesiologists during conduct of anaesthesia.[11] Smith et al. reported that 55.6% of 439 perfusionists admitted that they used cell phone while Cardiopulmonary bypass and 7.3% admitted that it had a negative impact on their performance. Cain established that accessory social media via smartphone while performing work related tasks was more problematic than accessing social media via computer as smartphone was portable and hence constant source of disruptions.[14] McBride's analysis indicated that cellular phone users were so engrossed in this activity that they were often unaware of their own misuses and might not realise that they were distracted.[15] One study by Kasana Raksamani et al[13] concluded that the rate of smartphone use among

anesthesia residents in the operating room is high. Residents' awareness of the potential for distraction by smartphones during the conduct of anesthesia is low, and should be highlighted as part of their clinical clerkship. One more study by HüseyinUlaş Pınar et al[16] resulted that 96.7 % of respondents indicated that smartphones were either never or seldom used during critical stages of anesthesia. Most respondents (87.3 %) stated that they were never distracted because of smartphone use; however, 41 % had witnessed their colleagues in such a situation at least once. H. Jothiraj et al[17] presented that the sixty distracting events were observed among 3557 events while the anaesthetist was preparing or administering drugs (~2 per case). Distracting events involving the anaesthetist are common, but approximately two-thirds of these events have no externally visible effect.

We could not see any patient related adverse events due to distraction caused by smartphone usage in our study. Future studies may be designed in this regard. Another shortcoming of this study was that it was completed at a single centre. A national level multicenter trial may be designed for better sample size and significant results. With high usage of smart phones in our daily and practice life, we feel that it is the requirement of the time to rationalize the use of smartphones in operating room.

CONCLUSION

We concluded that smart phone usage is very high among anesthetist frequently causing distraction events. However we could not neglect the positive use of smart phones. We recommend to rationalize the use of mobile phones in operating room to a minimum level without causing a distraction. A guideline must be made at national or international level to rationalize this issue.

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COMPARISON OF SURGICAL OUTCOME OF INTERTROCHANTERIC FRACTURE OF FEMUR WITH PROXIMAL FEMORAL NAIL (PFN) VERSUS DYNAMIC HIP SCREW (DHS)

Muhammad Zafar Iqbal Shahid,[1] Tanveer Haider,[2] Usman Ali,[3] Maqsood Akhtar,[4] Faizan Majeed[5]

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Abstract

Background: Intertrochanteric fractures account for more than half of the hip fractures out of which 50% of these fractures are unstable. Proximal femoral fractures incidence has increased in the presence of osteoporosis and rise in life expectancy in elderly people while road traffic accidents are the leading cause in young people.

Objective: To compare and evaluate the surgical outcomes of proximal femoral nail and Dynamic Hip Screw in unstable intertrochanteric fractures of femur.

Methods: This prospective comparative study was conducted from January, 2018 to January, 2020. A total no. of 60 patients with unstable type II intertrochanteric fractures was included in the study. These were divided in two equal groups. Each group had 30 patients. The approval for the study was obtained from the Hospital ethical and review board. Before the procedure, each patient was counseled regarding the procedure and a written consent was obtained from each patient. Each patient was followed at weekly interval up to 6 weeks and then at 3rd, 6th and 12th month. Each patient was assessed both clinically and radiologically. Functional assessment was done with Harris Hip Score. In group A we performed PFN and in group B we performed DHS.

Results: Age range in our study was 25-70 years (average 62 years). In group A there were 20 males and 10 females, while in group B there were 25 males and 5 females. Most of the fractures were as a result of Road traffic accident (46 patients) while in 14 patients it was as a result of slip and fall. Size of incision duration of surgery, blood loss and return to pre injury status was much less in patients where PFN was done as compared to DHS. Moreover Harris hip score was better in patients where PFN was done and these patients started early weight bearing as compared to patients where DHS was done.

Conclusion: It was concluded from the study that PFN is better implant for unstable intertrochanteric fractures than DHS. It results in less blood loss and reduced duration of surgery. There was reduced hospital duration and early weight bearing in case of PFN. Moreover the complications rate was also less.

Keywords: Proximal Femoral Nail (PFN), Dynamic Hip Screw (DHS), Intertrochanteric Fractures, Unstable intertrochanteric fractures, Harris Hip Score

Intertrochanteric fractures are extra-capsular fractures that cause the break of femur in between greater and lesser trochanter and are composed of dense trabecular bone. Greater trochanter is insertion site for abductors while lessor trochanter is insertion site for iliopsoas. Calcar is the area of dense bone that extends from posteromedial aspect of femur shaft to the posterior aspect of femur neck. These structures are important as they determine whether the fracture is stable or unstable. Metaphyseal region has got abundant blood supply which contributes to the fracture union. Intertrochanteric fractures account for 50% of all fractures of proximal femur.[18] Since average age is increasing worldwide, mean age for hip fractures is also increasing

1. Muhammad Zafar Iqbal Shahid
2. Tanveer Haider
3. Usman Ali
4. Maqsood Akhtar
5. Faizan Majeed

1-5. *Services Institute of Medical Sciences / Services Hospital.*

Correspondence:
Muhammad Zafar Iqbal Shahid, *Services Institute of Medical Sciences / Services Hospital, Lahore. E-mail: drzafar2014@gmail.com*

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rapidly. This change is causing increased problems regarding the treatment and rehabilitation of these patients.[19,20] Intertrochanteric fractures are 2nd leading cause of hospital admissions in old population. These fractures are commonly seen in elderly population because of osteoporosis and poor bone stock. Mechanism of injury is low energy trauma to these patients. In young population intertrochanteric fractures are result of high energy trauma such as motor vehicle accident or as a result of fall from height. These are associated with high morbidity and mortality. Despite of aggressive operative treatment, one year mortality is as high as 10-20%.[21] Female to male ratio is 2:1. Stable fractures has got intact posteromedial cortex and these fractures resist the medial compressive forces when reduced. Unstable fractures have comminution of posteromedial cortex. These fractures are at subtrochanteric level and also in reverse oblique potion. These fractures will collapse into varus and retroversion when weight is exerted. These fractures need some sort of intramedullary fixation.[1,2,3] Understanding the pathophysiology and proper treatment will reduce the risk for morbidity and mortality after this injury.

There are several classifications which divide the intertrochanteric fractures into stable and unstable fractures. Compared with the stable fractures, unstable fractures have higher rate of complications and hip function may be more compromised in unstable fractures, if not fixed adequately.

The intertrochanteric fractures usually have good prognosis as there is no compromise of blood supply in these patients that is why AVN or non-union of these fractures is uncommon. A lot of treatment options are available to treat these fractures. The goals of surgery are to provide the stable construct to restore the mobility and to decrease the risk of long term recumbency and restore the patient to pre-operative status. While treating these fractures with dynamic hip screw require the correct reduction and placement of screw into the center of head is of vital importance. Tip apex distance act as a guide to accurate lag screw placement. It should be less than 25mm in both AP and lateral views combined. Ideally the screw should be in the center of head within 5-10mm of sub-chondral bone and increasing rate of cutout or poor reduction occur if the lag screw is incorrectly placed. Moreover it should not be used in the intertrochanteric fractures in reverse oblique position. As the DHS does not control the collapse and fracture compression rather it allows the shear forces to act at fracture site, medial displacement of distal fragment, excessive sliding and eventual screw cutout. Proximal Femoral Nail is another option used to fix unstable intertrochanteric fracture.[17] It is advantageous in the sense being less invasive technique, short operative time, early rehabilitation and short hospital stay.[5,6,7,8] PFN is biomechanically more stable construct. It reduces the distance between hip joint and implant.[9,10,11] It also prevents the lateral translation of proximal fragments. Its intramedullary location at the junction between nail and Lag screw resist the bending forces and allows the early weight bearing in unstable intertrochanteric fracture.[13,14,16] But, PFN is comparatively more expensive than DHS.[22]

Post-operative rehabilitation program for these devices is uniform. It includes the isometric quadriceps strengthening exercises, knee bending, sitting at the bedside and abductor strengthening exercises. Weight bearing and toe touching should be allowed as soon as the patients pain tolerance and general condition is stable with the help of walker. Other option to treat these fractures include compression hip screw (CHS), MEDOFF sliding plate, LISS, PFNA, Gamma Nail to provide the optimal surgical intervention for treatment of intertrochanteric fractures.[12,15]

METHODS

This prospective randomized control comparative study was conducted at Services Hospital, Lahore from January, 2018 to January, 2020. A total number of 60 patients with unstable intertrochanteric fracture were included in the study. We used the Boyd and Griffin classification of classify these fractures. All these patients having age between 25-70 years were divided into two equal groups A and B, each group having 30 patients. There were twenty males and ten females in Group A. Group B included twenty five

males and 5 females. All fractures were fixed with PFN in group A while in group B we used DHS for fixation of fractures. This study was approved from institutional review board Services Hospital Lahore. Written consent was taken from each patient before inclusion in the study. All patients were admitted through emergency department of this hospital. After initial resuscitation following ATLS protocol. Each patient underwent the X-ray of Pelvis with both Hip joints AP and Lateral views. These patients also had X-rays of hip and knee joints with shaft of femur AP and lateral views. Length of Lag screw, Neck shaft angle and Diameter of PFN was measured with the help of these radiographs on the normal side

Patients with poly-trauma, Fractures with open wounds, pathological fractures and patients with fractures of more than two weeks duration were excluded from the study. All patients were operated on the same day on the standard fracture table under image intensifier. The standard operative technique for each procedure was used for the patients under spinal anesthesia.

Post op rehabilitation was started on the day of surgery. Isometric quadriceps strengthening exercises, knee bending exercise and sitting on the side of the bed was allowed on the day of surgery. Patients were allowed toes touching 2-3 days after surgery as soon as general condition and pain tolerance allowed it. These patients were discharged 4-5 days after surgery with instructions to walk with walker with toe touching. Each patient was followed weekly for 6 weeks, then at 3rd, 6th and 12th months. At each follow up we evaluated the patients clinically and radiologically. Functional outcomes and mal-union were evaluated by Harris Hip score. (We consider the mal-union if varus was greater than 10 degree). Demographic data and functional assessment were done at 6th, 12th week, 6th month and at 1 year. Length of incision, blood loss and duration of surgery were measured intraoperatively.

Statistical analysis was performed by using SPSS ver.20 and p value was calculated by using student t-test. A p value of <0.05 was considered as significant.

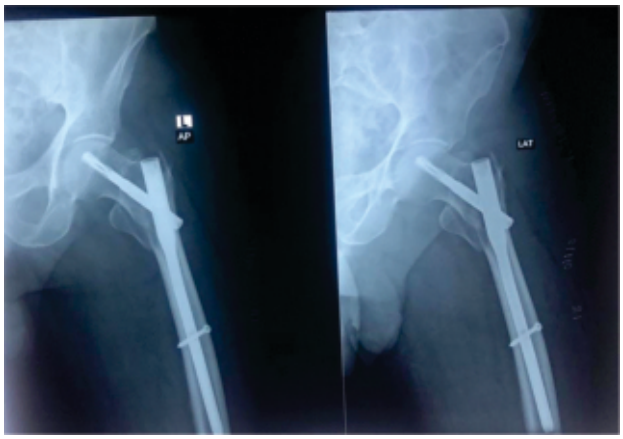

Figure 1: *Post-Operative X-ray of PFN in Unstable Intertrochanteric Fractures*

RESULTS

Total number of patients in our study was sixty. Age range was 25-70 years (mean 62 years). Out of 30 patients in group-A there were 20 males and 10 females. In group B there were 25 males and 5 females. Most of the fractures in group A were as a result of RTA (22 patients) while rest of the patients had history of fall (8 patients). In group B 24 patients had history of RTA that resulted in intertrochanteric fractures while 6 patients had history of slip and fall. Each patient underwent surgical procedure on the same day after admission. Average duration of surgery for PFN was 90 minutes while for DHS it was 110 minutes (p value = 0.04). Incision size in patients with PFN was 7 cm while in DHS the incision size was 12.5cm. Average blood loss was 250mL for patients who underwent for DHS, while for PFN it was 200mL (p-value= 0.02). 2 patients with DHS required blood transfusion post-operatively. Hospital stay for patients where PFN was done was 3-5 days (average 4 days). For patient where we performed DHS it was 5-7 days (average 6 days) (p-value=0.04). Full weight bearing was started after 6 weeks where PFN was done and at 7th week where DHS was done. Pre-injury walking level was achieved after 9 weeks in patients with PFN while it was achieved after 12 weeks in patients who underwent DHS. The average limb shortening in PFN group was 5mm and in DHS group it was 10mm (p-value= 0.02). Radiologically each patient was assessed at 2nd

week, 3rd and 6th month and then at 12 months.

At 3rd month all patients show attempted callus formation except 3 patients in DHS group resulted in attempted callus formation with a gap. At 3rd month in PFN group all patients had good union. 3 patients with PFN had backing out of proximal screw but still in these 3 cases fracture got united.

In DHS group at 6 month, 4 patients had collapse at the fracture site while one patient had varus mal union of 115 degrees because of increased collapse, while in patients with PFN there was no collapse at the fracture site.

At 12 month postoperatively all fractures united in both groups except in one patient which had varus mal-union of 115 degrees which did not progress further.

No infection was noted in group A while there was one case of infection in DHS group which was superficial one and resolved after IV antibiotics and wound dressings after 5-7 days. Harris hip score calculated at 3 months in PFN was 50 while for DHS it was 36. At 6 months it was 80 for PFN and 60 for DHS. The average functional hip score was 92 in PFN group while it was 80 in DHS group.

DISCUSSION

Unstable intertrochanteric fractures are always challenging for the orthopedic surgeons.[11] No single fixation device is ideal for these fractures because of complexity of these fractures.[9,10,12,13] Optimal fixation device for unstable intertrochanteric fractures is still controversial.[15] These fractures are always treated surgically unless the patient is unfit for surgical procedure because of associated co-morbidities. In the present study we used PFN and DHS to fix the unstable intertrochanteric fractures. DHS has been used as the definitive fixation devices for several decades to treat the intertrochanteric fractures. But he problems associated with DHS are long operative time, more blood loss,[23] longer hospital stay, longer union time and problems associated with screw cut-out especially in case of unstable intertrochanteric fractures. Moreover these fractures also result in mal-union when fixed with DHS.[16,17] PFN is an intramedullary device for fixation of unstable intertrochanteric fractures which had been treated with DHS up till now.[14]

A large number of studies have been conducted to compare the results of intertrochanteric fractures fixed with PFN and DHS.[22] These studies shows that fixation of intertrochanteric fracture is better with PFN than with DHS.

In a study conducted by Yeganeh A1, he compared the intramedullary nailing method (PFN) with DHS in the treatment of unstable intertrochanteric fractures. Because of reduced hospital stay, reduced blood loss and duration of surgery in intramedullary nailing method, the author recommends that intramedullary nailing (PFN) is the first option to treat these fractures.

In his study regarding the fixation of unstable intertrochanteric fractures Faisal M et al[2], deduced that PFN provides the more stable construct by reducing the distance between the hip joint and the implant.

Table 1: *Gender Distribution Among Subjects*

Sex	Group A (PFN) n= 30	Group B (GHS) n= 30	Total
Male	20 (66.7%)	25 (83.3%)	45 (75.0%)
Female	10 (33.3%)	5 (16.7%)	15 (35.0%)
Total	30 (100.0%	30 (100.0%)	60 (100.0%

Table 2: *Postoperative Mobility Status for PFN and DHS*

Mobility Status n = 60	Group A (PFN) n= 30 Mean ± SD	Group B (GHS) n= 30 Mean ± SD	T test p-value
Walking with walker (days)	6.4 ± 2.45	5.36 ± 1.03	<0.05
Partial weight bearing / toe touching (weeks)	4.5 ± 1.65	5.5 ± 2.14	<0.05
Full weight bearing (weeks)	6.8 ± 2.31	7.9 ± 1.14	<0.05
Return to pre-injury status (weeks)	9.2 ± 2.94	12.3 ± 1.12	<0.05

Table 3: *Harris Hip Score among two groups*

Duration	Group A (PFN) n= 30 Mean ± SD	Group B(GHS) n= 30 Mean ± SD	T test p-value
3 months	50.6 ± 2.45	36 ± 8.45	<0.05
6 months	80.6 ± 8.45	60.8 ± 3.45	<0.05
12 months	92.6 ± 8.10	80.2 ± 4.82	<0.05

PFN has got short operative time and lesser dissection is needed to fix these fractures. They concluded from their study that PFN is better fixation device than DHS in fixation of unstable intertrochanteric fractures.

The study conducted by S Mittal et al, in international journal of orthopedic sciences in 2017, he compared the functional and radiological outcomes of unstable intertrochanteric fractures treated with PFN and DHS. He concluded that the blood loss, operative time and complications are significantly higher in DHS group. PFN is better fixation device for unstable fractures.[3]

Likewise Basasvaraj S et al[4] also compared the results of DHS with PFN in unstable intertrochanteric fractures in adults. They concluded that PFN provides more stability biomechanically by reducing the distance between hip and implant. PFN is a better fixation device for most of the unstable fractures.

In his study Cyril Jonnes deduced that PFN is better than DHS in type-II intertrochanteric fractures in terms of decreased blood loss, duration of surgery, hospital stay and early weight bearing.[5]

In the study conducted by PB Das on unstable intertrochanteric fractures, he concluded that PFN is better choice for unstable intertrochanteric fractures in elderly patients. PFN act as a better load sharing device and has a good biomechanical advantage in terms of indirect reduction.[6]

The study conducted by Pathania VP also reveals that PFN being intramedullary is biomechanically advantageous over DHS as it allows better fixation of unstable intertrochanteric fractures. It permits early mobility and better rehabilitation in elderly population.[7]

Dr Amandeep Singh Bakshi et al. concluded from his study that PFN gives better results in intertrochanteric fractures in terms of blood loss, duration of surgery and results in early mobilization.[8]

All these studies concluded that PFN is gold standard for unstable intertrochanteric fractures of femur. PFN is better than DHS in terms of small incision, less blood loss, reduced operation time, and reduced hospital stay, early mobility and fewer complications.

CONCLUSION

Our study and all other studies have compared the PFN with DHS in unstable intertrochanteric fractures of femur. We have concluded that PFN is advantageous over DHS in unstable intertrochanteric fractures. It has got small incision, less operative time, less blood loss and early rehabilitation. Moreover the union time required for PFN is less than DHS. It was also revealed from our study that although the principles of intramedullary nailing are note more complicated than other fixation methods. In order to improve results, it requires the need for continuous training for proximal femoral nail.

Limitations of Study

In our study the sample size was small. A large multicentric study with large sample size should be conducted. Furthermore the study should be better designed randomized control trial of longer duration to establish the full benefits of this mode of treatment.

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Conflict of Interest *None*

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SURGICAL MANAGEMENT OF FISTULA –IN-ANO WITH SETON

Liaqat Ali Deokah,[1] Balakh Sher Zaman,[2] Humayun Siddique,[3] Samina Rashid,[4] Rizwanullah,[5] Javaid Sajjad Hashmi[6]

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Abstract

Objective: To determine the Recurrence and Healing rates Fistula-In-Ano managed by Seton.

Methods: A total of 120 Fistula-in-anno patients were included in this study. Ethical approval and consents were obtained. All patients with FIA were managed by surgical procedure i.e. Seton placement, Effectiveness of Seton by finding Healing and Recurrence rate. Effect of co-morbid disease like DM, Hypertension and CV disease was also determined.

Results: 120 Patients with FIA were included in this study. There were 90(75%) male and 30(25%) female patients. Healing rate = 50(41.66%) in 30(25%) patients. Recurrence rate was = 10(8.33%) in 90(75%) patients and > 10(%) in 30(%) patients

Conclusion: The management of Fistula-In-Ano has always tested the Patience of Colo Rectal Surgeons. The Goal of Fistula surgery is to cure the Fistula while preserving the Anal continence.

Keywords: Healing, Fistula-In-Ano, Seton

A Fistula-In-Ano is a track lined by grannualtion tissue which opens internally into the Anal canal or Rectum and superficially (Externally) onto the skin around the Anus.[1]

It usually results from an Ano Rectum Abscess which either bursts spontaneously or was operated without lying open the entire track. In adequate drainage of the Ano Rectum Abscess is the most common cause of Fistula-In-Ano.[2]

FIA can be low level or high level with relation to the Analsphincter. Park has classified FIA into Inter sphincteric, Transphicteric, supra sphincteric and Extra SphincticFistulal.[3]

The diagnosis of FIA is mostly clinical Examination Bat MR, is also very much helpful I its diagnosis. There are several modalities of treatment.

Placement of Seton and colostomy are present whatever modality of treatment is adopted. The utmost care by Surgeon should be for preservation of Anal sphincter mechanism, Low Recurrence rate, Adequate post operation care for wound healing. The Co-morbid diseases (diagnosed by Fistula track Histopathology report) like Cronh's disease.[4]

Tuber culosis, Carcinoma showed also be addressed. The care of DM, Hypertention and Liver disorders is also done. In the present study the FIA was treated by placement of seton. The Seton may be loose seton or cutting Seton.[5]

The our present study aimed to determine. The healing and recurrence rates of FIA with Seton placement.

METHODS

A Retero-Spective study was conducted in Department of Surgery, North Surgical Ward Mayo Hospital Lahore from January 2019 to December 2020. 120 patients with FIA were included in this study. All these 120 patients with FIA were admitted in Surgical wards (male surgical ward, Female surgical ward) through surgical Out Door Department. There were 90(75%)

1. Liaqat Ali Deokah
2. Balakh Sher Zaman
3. Humayun Siddique
4. Samina Rashid
5. Rizwanullah
6. Javaid Sajjad Hashmi

1,3,5,6. Avicenna Medical College, Lahore.
2. Mayo Hospital Lahore.
4. SR Burn Center JBRSC

Correspondence:
Dr. Liaqat Ali Deokah. Avicenna Medical College, Lahore.

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1st Revision Date: 18-12-2021
Acceptance Date: 24-12-2021

male and 30(25%) female patients. The patients with Comorbid disease (Diabetes Mellitus, Hypertension and Cardiovascular disease) diagnosed as FIA also included in the study.

The patients were between 30-65 years of age group. Ethical approval and Consent were taken from all the selected patients. Counseling about the Seton placement, its Indications Benefits, complications post-operative follow up, Healing rate and recurrence rate were explained to each patient included in the study.

RESULTS

120 patients with FIA included in this study. There were 90(75%) male and 30(25%) female patients. Out of 120 patients 80(66.66%) patients were between 35-65 years of age group and 40(33.33%) patients were 22-30 years of age group.

Healing rate= 50(41.66%) in 30(25%). Patients and > 50 in 90 (75%) patients. Recurrence rate was = 10(8.33%) in 90(75%) and >10(8.33%) in 30(25%) patients. Recurrence rate was significantly associated with DM Hypertension and CVS disease. Healing rate and Recurrence rate were insignificantly associated with age and gender.

DISCUSSION

FIA is a condition which presents as persistent discharge of a mixture of Pus and Serum, which irritates the Peri-Anal Skin and causes discomfort.[6,16]

FIA with External opening in the anterior half of Anus have direct track and those with External opening in posterior half of Anus have curved track.[7,15]

The Seton is often used for High/Recurrent fistula. A Seton is a piece of Surgical thread, Suture material which is passed through the Fistula. It is tied to drain (loose Seton) or cut slowly through the spincter muscle with muscle healing behind the advancing seton (Tight Seton).[8,14]

The FIA is common large Gut disease. Treatment of FIA is a great challenge for treating surgeon because of its complications (slow healing rate, Recurrence and Anal Incontinence).[9,10,17]

In our study Low Recurrence rate and high healing rate were observed.

Comorbid disease like DM on hypertension also affects the recurrence and healing processes.[11-13,18]

Healing process is very much slow in Diabetic patients.

In this Study, the patients were satisfied with high healing rate and low recurrence rate and significance tolerance to Seton.

CONCLUSION

FIA especially high and recurrence Fistula can be managed effectively with Seton placement with high healing rate and Low recurrence

The use of Seton is a standard way of management of Fistula-In-Ano.

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EARLY POST OPERATIVE COMPLICATIONS OF ILEOSTOMY FOR ILEAL PERFORATION

Liaqat Ali Deokah,[1] Abeera Liaqat,[2] Hummayun Saddique,[3] Samina Rashid,[4] Rizwanullah,[5] Javaid Sajjad Hashmi[6]

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Abstract

Objective: To detect early post-operative complications in patients undergoing laparotomy and ileostomy for ileal performance

Methods: 80 Patients with peritonitis having ileal perforation were included in this study Ileostomy has done. Early post operative complications of Ileostomy were Record.

Results: 80 patients were included in the study. Wound infection occurred in I6(%) patients followed by skin Excoriation in 12(%) patients

Conclusion: Stoma complications occur frequency despite advances in the surgical management of the stoma related complications. Stoma complications have great impact not only on personal life but also on social life of the patients

Key words: Ileostomy, Peritonitis, Skin Excoriation

An Ileostomy is life saving surgical procedure.[1] The Ileostomy – Diversion Stoma may be temporary for ileac performance or permanent in malignancies.[2] However ileostomy is associated with several complications, these Stoma complications have drastic effect on patients personal and social life.[3] Complica-tions may be early or late and may be Intermittent or permanent.[4] Stoma care center's nurses are necessary to minimize the incidence of complications.[5] The goal of this study was to determine the frequently and early complications of Ileostomy.

METHODS

This was Retro-Spective study. The study was conducted in North Surgical Ward MAYO Hospital Lahore from June 2019 to May 2021. All patients included in this study were 22 to 55 years of age with peritonitis because of ileac perforation.

The patients having malignancy, immune-compromised status and having multiple orgons failure were excluded from study.[6] Informed and written conscent was obtained. The duration of disease in most of the patients ranged two to three days. Early post-operative complications record were wound infection, wound dehiscence, skin excoriation, Stoma retraction and electrolytes imbalance.[7]

The data about these early complications, and more over the data for age, the gender were obtained. The help of satiation was also taken.[8]

RESULTS

80 patients with peritonitis due to ileal perforation were included in this study. The age of these patients was between 22 to 55 years, with mean age (49.5%). Of these 80 patients, 48 (60%) were male and 32 (40%) female. Of these 80 patients in our study 33 (41.25%) have tuberculous peritonitis, 21 (26.25%) had typhoid

1. Liaqat Ali Deokah
2. Abeera Liaqat
3. Hummayun Saddique
4. Samina Rashid
5. Rizwanullah
6. Javaid Sajjad Hashmi

1,3,5,6. Avicenna Medical College, Lahore.
4. Burn Center JBRSC, Lahore

Correspondence:
Dr. Liaqat Ali Deokah, *Avicenna Medical College, Lahore.*

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Acceptance Date: 29-12-2021

perforation, 22 (27.5%) had traumaperforation and 4 (5%) had Gangrenous

Appendix perforation 33 (41.25%) patients were discharged with no complications. 47 (58.75%) developed complications

The most common complication was wound infection in 16(20%) patients followed by skin excoriation in 12 (15%) patients wound dishiscense in 9 (11.25%) patients, Stroma Retraction in 6(7.5%) and electrolyte in balance in 4 (5%) patients.

DISCUSSION

The ileostomy consists of bringing the lumon of ileum through the Abdominal wall via a surgical opening. An ileostomy is life saving procedure to direct the facial stream from the colon to protect down stream anastomosis.[9] The ileostomy maybe temporary or permanent. The ileostomies are indicated in different Gastero-Intestinal disorders. The indications include thphoidileal perforation, tuber culosis intestine and Bowel obstruction for situations like cancers of colon, ulcerative colitis and Intestinal. Crohn's disease: The complications of ileostomy may occur any time.[10]

These complications can be prevented / minimized with proper surgical technique. In our study, wound infection was the most common ileostomy related complications. Skin Excoriation was another major complication in ileostomy. Excression fluid loss through stoma is another complication encountered in many patients. It is ethical for a surgeon to possess a through under-standing of stoma related complications and treatment.[11]

CONCLUSION

Ileostomy is frequently performed as life saving diverting surgical procedure. The complications are common but mangeable. Therefore it is essential to identify these complications and manage them early to remove the mortality of patient.

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EARLY POST-OPERATIVE COMPLICATIONS AFTER THYROIDECTOMY FOR BENIGN GOITERS

Liaqat Ali Deokah,[1] Usman Habib Virk,[2] Muhammad Azhar Hassan,[3] Javaid Sajjad Hashmi,[4] Samina Rashid,[5] Neelma Asghar[6]

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Abstract

Objective: To find frequency of early complications after thyroid surgery for benign thyroid conditions.

Methods: Early complications after thyroid surgery for benign thyroid conditions were studied. One hundred patients with FNAC confirmed benign goiter admitted for elective thyroidectomies were included in the study. Data was collected in the pre-designed proforma. Descriptive statistics was used to calculate frequency of each complication in the early post-thyroidectomy period.

Results: The frequency of complications after thyroidectomy was 27%. Out of them 8% developed subcutaneous haematoma,5patients(5%)wound infection ,4% tension haematoma, 4 patients (4%) hypocalcaemia, 3 patients(3%) respiratory obstruction and 3 patients (3%) developed recurrent larynge nerve paralysis.

Conclusion: Surgery for benign thyroid enlargement but may be associated with significant numbers of post operative complications including wound haematoma, wound infection and hypocalcemia.

Keywords: Thyroidectomy, heamatoma, hypocalcaemia.

Goiter can be simple, toxic, inflammatory or neoplastic.Various Modes of treatment including medicines ,Surgery and radioiodine are available and indications of each treatment are individualized on the type of goiter.[1] Antithyroid medicines are limited to toxic goiter and in their preoperative preparation. Similarly radioiodine is indicated in Graves' disease but its facilities are not available freely and prolonged follow upto detect hypothyroidism is mandatory.[2]

Surgery is the mainstay of treatment for benign thyroid enlargement. Different types of resections are being individualized on the basis of disease. Surgery is most widely used with the advantage of being freely available and rapid cure rates, but at the same time it has disadvantages of postoperative mortality, morbidity and recurrence of goiter.[3]

While complication rate of thyroid surgery has certainly decreased, but they still exist with variable frequency. The Frequency of commonly observed complications, associated with thyroidectomy for benign goiter invarious studies includes tension haematoma 5-7%, subcutaneous haematoma 2-10% , respiratory obstruction 5-10% , recurrent laryngeal nerve paralysis 1-3%, parathyroid insufficiency 3-15%, wound infection 1-5% , stitch granuloma 2-5% and thyrotoxic crisis as rare occurrence is the patient is prepare preoperatively.[4]

Goiter is common ailment seen in various regions of Pakistan. This rescriptive study is designed to detect frequency of early post-operative complications in procedures performed for benign thyroid enlargement.[5]

METHODS

This was Rescriptive-study. The data was collected randomly from adult patients of all ages admitted at North Surgical ward ,Mayo hospital Lahore with thyroid swelling for elective thyroidectomy. These swellings were confirmed benign on FNAC carried

1. Liaqat Ali Deokah
2. Usman HabibVirk
3. Muhammad Azhar Hassan
4. Javaid Sajjad Hashmi
5. Samina Rashid
6. Neelma Asghar

1-4,6. Avicenna Medical College, Lahore.
5. Burn Center JBRSC

Correspondence:
Dr. Liaqat Ali Deokah, Avicenna Medical College, Lahore.

Submission Date: 11-11-2021
1st Revision Date: 15-12-2021
Acceptance Date: 29-12-2021

out on out door basis before admission. A detailed clinical examination, Indirect layrngoscopy and lab investigations including thyroid profile, serum corrected calcium levels and complete blood picture were carried out in all patients. Patients with recurrent laryngeal nerve paralysis, lab evidence of hypoparathyroidism or recurrent goiterwere excluded from the study. Histopathologist did all cytological and histopathological studies. In all 100patients thyroid surgery was performed, 40 were operated for total thyroidectomy, 40 for sub-totaland 20 for lobectomy with isthmustectomy and operative techniques were noted. Patients were followed for initial ten post -operative days for early complications like thyrotoxic crisis, recurrent laryngeal nerve paralysis, tension hematoma, Respiratory obstruction, hypocalcemia and wound infection. All findings were recorded in the performed performa designed for this study. Descriptive statistics was used to calculate frequency of each complication in the early post-thyroidectomyperiod.

Setting: Hospitalized patients in North Surgical ward of Mayo Hospital Lahore.

Duration: May 2019 to May 2021.

Sample size: A total of 100 admitted patients with goiter included in the study.

RESULTS

In this study thyroidectomy was performed in 100 patients with benign thyroid swellings at Mayo hospital Lahore. The mean age was 36 years. Female to male ratio was 8:2. Out of 100 patients total thyroidectomy was done in 40 (40%) patients, subtotal thyroidectomy in 40 (40%) patients and in 20(20%) patients lobectomy with isthmusectomy was performed. These procedures were carried out without any peroperative complications. Among those 100 patients 20(20%) were discharged within 3 days while in 33 (33%) the hospital stay post-operatively was up to 4 days and the stay was extended upto 5 days in 36(36%) patients. These patients were directed to report at OPD for further follow up. There were 11 (11%) patients who had stayed in hospital for more than 10 days. Out of 100 operated patients 27% developed complications. 8(8%) patients developed subcutaneous haematoma, 5(5%) wound infection, 4 (4%)tension haematoma, (4%) hypocalcaemia, 3(3%) respiratory obstruction and unilateral laryngeal nerve paralysis occurred in 3(3%) patients.

DISCUSSION

Complications of thyroid surgery continued to be a significant source of morbidity in benign thyroid disorders. Surgery is the mainstay of treatment most widely used with the advantage of being freely available and rapid curerates, but at the same time it has the disadvantage of post-operative morbidity and recurrence of goiter.[6] It is documented in literature that the most common cause formultinodular goiter is dietary deficiency of iodine. The most common symptom is swelling in front of the neck. This cosmetic defect present in 100% of the patients. Dyspnoea was found in 76%dysphagia in 3% and 26% patients had pain in the neck.[7]

Different surgical options available for treatment of benign thyroid enlargement are total thyroidectomy, subtotal, near-totalthyroidectomy and lobectomy with isthmusectomy. Patients undergoing total thyroidec-

Producers	Number of Producers	Subcutaneous Haematoma	Wound Infection	Tension Haematoma	Hypocalcaemia	Respiratory Obstruction	Recurrent Laryngeal nerve paralysis
Total thyroidectomy	40	4	2	2	4	3	3
Sub Total	40	4	2	2	-	-	-
Thyriodectomy Lobectomy with Isthmusectomy	20	-	1	-	-	-	-
	100	8	5	4	4	3	3

tomy require life long replacement of thyroxin, while recurrence of goiter is frequently observed after subtotal resection. The surgery for recurrence is difficult and carries more morbidity and for this reason many thyroid surgeons favour total thyroidectomy for goiter. Total thyroidectomy, however, is more frequently associated with damage to recurrent laryngeal nerve andparathyroid gland than with other procedures.[8]

Frequency of complications was 27% in our study while it was 40% in a local study. The most common complication in our study was subcutaneous haematoma which occurred in 8 % of patients, out of them 4 pateints were operated for total thyroidectomy and 4 for subtotal thyroidectomy.[9,10]

It was found that massive goiter, short neck and difficult intubations increase the chances of developing respiratory obstruction. Recurrent laryngeal nerve paralysis was more frequent with total thyroidectomy.[11,12]

While the complications rate of Thyroid surgery has certainly decreased, surgeons must nevertheless maintain a healthy respect for the possibility of such complications. They should be able to anticipate the risk of complications associated with surgical procedures to be carried out and hence can avoid worse consequences.[13,14]

CONCLUSION

Although surgery is the most widely-used management for benign thyroid enlargement but it is associated with significant numbers of post-operative complications including wound haematoma, wound infection and hypocalcemia.

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FREQUENCY OF DIFFERENT CAUSES OF MECHANICAL BOWEL OBSTRUCTION

Liaqat Ali Deokah,[1] Balakh Sher Zaman,[2] Usman Habib Virk,[3] Fakhar-uz-Zaman,[4] Neelma Asghar,[5] Javaid Sajjad Hashmi[6]

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Abstract

Objective: To find out the frequency of different causes of mechanical intestinal Obstruction

Methods: 100 patients were included in this study all cases of Mechanical Intestinal Obstruction confirmed per-operatively.

Results: A 100 patient of Mechanical Intestinal Obstruction were treated during the study period. There were 83 male patients and 17 were female patients with male to female ratio 5:1 the patient ranged from 20-70 years of Age. 79 (%) patient were of Small intestine obstruction and 21(%) had large Bowel Obstruction. The most frequent cause of Mechanical Intestinal Obstruction was Adhesion's and Bands 38(%).

Conclusion: Absence of passage of Flatus and/or Faeces and Abdominal distention are the most common Symptoms and physical finding of patients with acute Mechanical Intestinal obstruction respectively. Adhesions flernias and large Bowel cancers are the most common causes of obstruction as well as Bowel ischemia, Necrosis and perforation.

Keywords: Acute Mechanical Bowel Obstruction, Adhesions/Bands, frequently

Acute Mechanical Bowel Obstruction is a common surgical emergency and a frequently encountered problem in abdominal surgery.[1,2] It constitutes a major cause of morbidity and financial expenditure in hospitals around the world.[3] Intestinal obstruction belongs to severe conditions requiring a quick diagnosis as well as immediate, rational and effective therapy.[4] Accurate early recognition of Intestinal strangulation in patients with Mechanical Bowel obstruction is important to decide on emergency surgery or to allow safe non-operative management of carefully selected patients. Although close and careful clinical evaluation in conjunction with laboratory and radiological studies, is essential for decision of proper management of patients with acute mechanical intestinal obstruction.[1] The etiological factors included Adhesions and bands 38. External hernias 24(24%) malignancy 14, tuberculosis 8, Volvulus 6, Intussusceptions 3, internal hernia 3, mesenteric fibrosis 2, Band of Lad and Bol us obstruction in one case each.

Mechanical bowel obstruction is an old and common surgical emergency.[1,2] Immediate and corrective diagnosis of this condition and etiology is essential and appropriate treatmentis of utmost importance.[4] The clinical picture, however, of these patients along with etiology of obstruction and strangulation prevalence are variable, while appropriate management remains controversial.[5,6] We, therefore conducted this study to identify and analyzed if ferent causes of Mechanical Intestinal Obstruction in our department, etiology of presentation as well as management of these patients.

METHODS

Retro-spectivestudy. The study was carried out

1. Liaqat Ali Deokah
2. Balakh Sher Zaman
3. Usman Habib Virk
4. Fakhar-uz-Zaman
5. Neelma Asghar
6. Javaid Sajjad Hashmi

1,3,5. Avicenna Medical College, Lahore.
2. Mayo Hospital Lahore.
4. AIMC/JH, Lahore

Correspondence:
Dr. Liaqat Ali Deokah, Avicenna Medical College, Lahore.

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Acceptance Date: 28-12-2021

in the Surgical Department of Mayo Hospital /North SurgicalWard;100Patientsfulfillingtheinclusioncrit eriawereincludedinthestudy.

Setting: Hospitalized patients in surgical department Mayo Hospital Lahore.

Duration: April 2019 to Dec 2020.

Sample Size: First hundred cases in Emergency department Mayo Hospital Lahore.

Inclusion Criteria: All cases of Mechanical Intestinal Obstruction confirmed per operatively.

Exclusion Criteria:

- Children below12 years of age.
- Ulcerativecolitis.
- Crohn's disease.

RESULTS

A total of 100 patients were treated for mechanical bowel obstruction during the study period. There were 83 males and 17 female. Male to female ratio was 5:1.

The patients ranged in age from 20-70 years. The large numbers of patients were in the 35-45 years of age.

Seventy-nine (79%) patients had obstruction of the small intestine and twenty-one (21%) had obstruction of the large intestine. Majority of the patients of the patients presented with Abdominal pain, vomiting, abdominal distention.

Adhesions and External hernia accounted for almost more than half the causes of mechanical intestinal obstruction. Among the 38 patients there were 9 females and 29 males.

Out of 24 cases of External hernia, there were only three cases of obstructed Para umbilical hernia. The history was more than twenty-four hours with intestinal obstruction.

Intra abdominal malignant caused obstruction in 14 patients (14%). In all of these 14 cases obstruction was due to primary. All of the patients in this group were above 60 years of age including 12 males and 2 females.

There were 8 cases (8%)of intestinal obstruction in the series caused by stricture in the ileum, 5female and 3 males. Tuberculosis was the cause in all of them. Pulmonary tuberculosis was associated in three females.

Among tuberculosis cases, one patient presented with perforation, which is quite rare. In six patients there were multiple strictures and two patients had ileocaecal tuberculosis and presented with mass in the right iliacfossa. Straight forward because majority of them had associated peritoneal orserosal nodules. Stricturoplasty was done in 4 cases, while Diagnosis was Usually resection of stricture and end-to-end anastomosis was done in 2 cases and right hemicolectomy was also done in 2 cases. Postoperative anti-tuberculous chemotherapy was started in all cases.

There were 6 cases of Volvulus in this series. All patients were between 50-65 years of age. Volvulus of sigmoid colon was the cause of intestinal obstruction in all the cases.

There were 3 (3%) cases of intussusception in this series and all were adult 16-44 years.

A few cases were of internal hernia, mesenteric fibrosis, band Lad and bolus obstruction.

DISCUSSION

Intestinal obstruction is one of the most common surgical emergencies. This study analyzes the age and sex incidence, frequency of various causes and evaluates the associated problems of management. Only patients with acute Mechanical Obstruction have been considered in this study. Maximum percentage

Causes of Intestinal Obstruction in100 patients:

Nature of Obstruction	No. of patients	%
Adhesions and bands	38	38
Obstructed/Strangulated Hernia	24	24
Malignancy	14	14
Tuberculosis	8	8
Volvulus	6	6
Intussusception	3	3
Internal Hernia	3	3
Mesenteric Fibrosis	2	2
Band of Lad	1	1
Bolus Obstruction	1	1
Total	**100**	**100**

of patients (23%) was in the group between 36-45 years of age in this series. While most of the studies reported high age groups, yet, due to the fact that the average life span in our country is shorter than that in western societies. Male to female ratio in our series is 4:1 The series also demonstrates that significant proportion of intestinal obstruction still occurs due to tuberculosis. Maximum incidence was in adults and five were females and three males. In all reported series the incidence of tuberculosis is higher in females,[14] although tuberculosis has been eradicated to agree at deal in the West. It is not surprising that tuberculosis is the fourth leading cause of obstruction in the series, since this is a diseases till prevailing in the Asian countries. Tuberculosis affects almost every organ in the body. Tuberculosis of the gastrointestinal tract is the next common lesion to pulmonary Koch's.

The series was also notable for the very low incidence of obstruction due to Volvulus and intussusceptions comprising of 6(6%) and 3(3%) respectively. No definite cause has been found in the cases of in tussusceptions except in one case, where multiple polyps were present in small and large gut Idiopathic intussusceptions in adults are extreme lyrare. Urgent surgery was performed in all patients within 12-24 hours of admission. In mostsurgical series, acute Intestinal obstruction is the presenting symptoms of colon carcinomain 20% of cases. In our series acute intestinal carcinoma of colon was cause of intestinal obstruction in 14(14%) of cases. All of the of patients were above 55 years of age. Emergency resection followed by primary ileocolic anastomosis is generally accepted as the treatment of choice for obstructing tumours of the right colon, even in the presence of small bowel distension andperitonitis.[15]

In our series right hemicolectomy was done in six cases with nomortality. Primary resection and end-to-end anastomosis was done for left colon obstruction in two patients.

The operative mortality for intestinal obstruction varies considerably, depending upon the age of the patient and associated illness, state of the intestine either simple organ grenous. McEntee[16] reported mortality of 11% inhisseries.

Pain[17] Reported 15% mortality in in strangulated non-viable bowel obstruction. The operative mortality for simple mechanical obstruction requiring operations approximately 1%, while operative mortality for strangulated intestinal obstruction varies, depending on the age of the patient and associated illness and may be 30% or higher.[18,19]

The highest mortality in our series was found in patients in the 6th and 7th decades of life. So the patient age has got important bearing related to mortality.[20,21]

It has been experienced that when surgical relief of intestinal obstruction is to be provided as early and as efficiently as possible.

CONCLUSION

Etiology factors of mechanical obstruction have been limited to adhesions, as the most common cause, followed by strangulated/obstructed external hernia, malignancy and tuberculosis. Abdominal pain, vomiting and constipation were the presenting symptoms almost in all cases.

A more aggressive policy aimed at earlier detection and elective treatment of both inguinal hernia and large bowel cancer in elderly patients is likely to reduce the incidence of intestinal obstruction. With increasing numbers of major elective abdominal operators.

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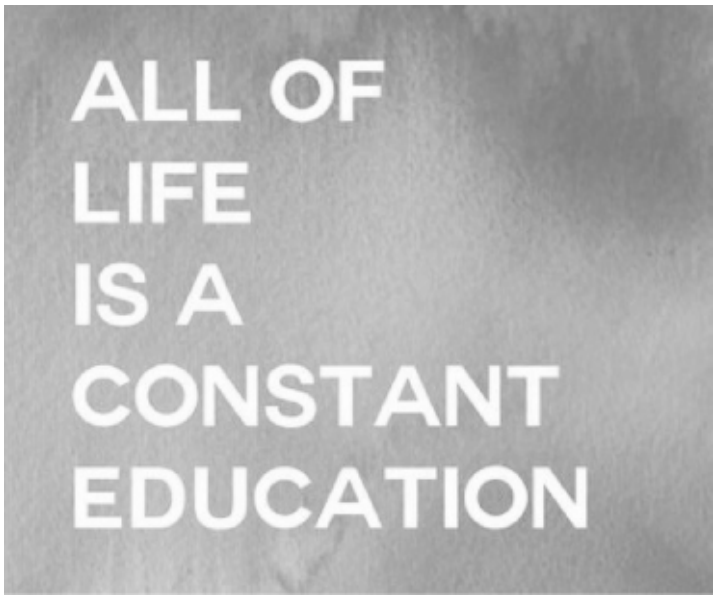

SURGICAL MANAGEMENT OF EXTRAHEPATIC BILIARY OBSTRUCTION

Liaqat Ali Deokah,[1] Balakh Sher Zaman,[2] Abeera Liaqat,[3] Fakhar-uz-Zaman,[4] Rizwan-Ullah,[5] Javaid Sajjad Hashmi[6]

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Abstract

Objective: The objectives of this study are to evaluate the surgical management, both definitive and palliative, in selected patients with biliary obstruction.

Methods: 40 cases of biliary obstruction were included. A convenient sampling technique was followed. Descriptive statistics like frequency, percentage, average etc were computed for data presentation.

Results: We selected 40 patients with features of extra Hepatic Biliary Obstruction out of these 40, 17 (%) patients sufferance benign disease, while those having malignant disease were the most common cause of Extra/ Hepatic obstruction was stone in CBD 16% patients.

Conclusion: Malignant causes of jaundice are more common than benign causes. Secondary stones are the commonest cause of non malignant biliary obstruction. Jaundice is more severe and associated with pruritis and more intolerable and persistent in malignancy. Surgical procedures are done as curative/palliative measures in Obstructive jaundice.

Keywords: Biliary Obstruction, Stone in CBD, Malignant disease

Disorders of the biliary tract affect a significant portion of the worldwide population. The overwhelming majority of are attributable to cholelithiasis and cholestasis.[1]

Extrahepatic biliary obstruction is common surgical problem usually caused by choledocholithiasis, sclerosing cholangitis, biliary strictures, periampulary growth and carcinoma head of the pancreas.[2] The diffe-rential diagnoses of jaundice remain a challenge for the primary care physician and specialists alike, Labo-ratory tests combined with newer noninvasive imaging studies usually differentiate the intrahepatic from the extra hepatic cholestasis.[3] As with awareness and better health care provision in our setup more cases of biliary obstruction are being diagnosed. A significant number of cases of obstructive jaundice malignancies, and most are unresectable forcure, The optimal form of palliation depends on multiple factors and is still debated by experts.[4]

Early detection of benign cases and their management is likely to substantially reduce the incidence of extrahepatic biliary obstruction. Early detection leads to early management, which reduces the complications and hence helps in reducing the morbidity and mortality associated with the condition.[5]

Over the last few years, the number of cases of biliary obstruction due to malignancy are increasing in comparison to those due to stones. To avoid complications of obstructive jaundice like irreversible hepatic damage and other miseries, early removal of the obstruction is important. Surgical procedures are a definitive treatment of biliary obstruction but non-surgical techniques have become the first line therapy for patients with unresectable biliary obstruction.[6]

1. Liaqat Ali Deokah
2. Balakh Sher Zaman
3. Abeera Liaqat
4. Fakhar-uz-Zaman
5. Rizwan-Ullah
6. Javaid Sajjad Hashmi

1,3,5,6. Avicenna Medical College, Lahore.
2. Mayo Hospital Lahore.
4. AIMC, Jinnah Hospital, Lahore.

Correspondence:
Dr. Liaqat Ali Deokah, Avicenna Medical College, Lahore.

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The results of management not only depend on the provision of latest investigations but also on the pre-operative preparation, skill and experience of the surgeon, the type of the surgical procedure and the postoperative care of the patient. Despite great improvements in the management techniques, the morbidity and the mortality in patients with obstructive jaundice is still very high.[7]

METHODS

40 cases of biliary obstruction were included using convenient sampling. The patients included were hospitalized cases admitted either through the out patient department or referred to from other Hospitals Provisional diagnosis was made on the basis of clinical features and standard biochemical tests. Biochemical tests were followed by abdominal ultrasonography (USG) in all patients. Further imaging tests like endoscopic retrograde cholangiopancreatography (ERCP), percutaneous transhepatic cholangiography (PTC), computerized Tomography or magnetic resonance cholangio pancreatography (MRCP) were used where appropriate to determine the exact nature of obstruction.

Metabolic and biochemical arrangements were attempted at correction in the preoperative period. After appropriate investigations and correction of coagulopathy, surgical intervention was undertaken. All the patients received preoperative antibiotics and IV fluids to maintain urinary flow. These were continued in the postoperative period .

The operative and histological findings were recorded.

Descriptive statistics were computed for data presentation.

RESULTS

We selected 40 patients with features of extrahepatic biliary obstruction, (that is obstructive jaundice). Out of these 17 (39.5%) patients suffered from benign diseases while those having malignant disease were 23(60.5%).The age varied from 21 years to 85 years. THE mean age is 50.49 years. Amongst the patients, 24 (58 %) were females and 16 (42%) were males. The reasons for obstruction were stones in the common bile ducts in 16 (37%) patients, chronic pancreatitis in 1(2.5%), CBD ca in 3(8%), gall bladder ca in 6 (16%), ca pancreas in 11 (37%), metastatic ca in 1(2.5%) and periampulary ca in 2(5%) patients. Surgical managements of patients are given in table. out of whom 9(45%) suffered wound sepsis. Those who has wound dehiscense were 2 (10%). Chest infection was present in 5 (25%) cases. Renal function impairment in 6 (30%) and GI hemorrhage was found in 2(10%).

Post op complications:

	Benign	Malignant	Total
Wound sepsis	4	5	9
Wound dehiscence		2	2
Chest infection	1	4	5
Real impairment	2	4	6
GI haemorrhage		2	2

DISCUSSION

The common belief that jaundice is caused by some sort of increased heat in the body and that the use of some medicines and cold food could correct

Operations performed	CBD Stones	Pancreatitis	Ca Pancreas	Ca Gall Bladder	Periampulary Ca	Ca CBD	Metastatic Ca
No. of patients	16	1	11	6	2	3	1
CBD exploration+cholecystectomy	14						
Cholecystectomy			1			1	
Choledochotomy	2						
Choledochodudenostomy			4		1		
Cholecystojejunostomy			2				
External drainage			1		1		
Whipple			1				
Pancreatojujunostomy		1					
Biopsy alone			2	6		1	1
Portoenterostomy						1	

the jaundice leads to maltreatment and very late presentation'. Most patients are afraid of operation and they try all the non-operative alternatives before coming to the hospital. Moreover, the time spent in referrals also contributes to late presentations. These are the reasons why majority of patients with malignant obstructive jaundice come to the hospital when is growth is far advanced and even surgical palliation is not even possible in most cases.[8] This fact is evident from our study as in many patients with malignant disease no palliation was possible and only biopsy was performed 13, The commonest cause of extrahepatic biliary obstruction in our case series was malignancy (60.5%). This is a high incidence that is reported in literature 37.2%, 42.4% ,48% , 59%, 19.3%. But a local study done by Munawar Jamil quoted an incidence of 75%.The presentation of obstructive jaundice is very high in the 5th and 6th decade of life[10]. The mean age of 50.49 years, median being 49.75 years. The number of females suffering from the disease is more than the males (58% vs 42%). [9]

The carcinoma of gallbladder had a very high female preponderance and male to female ratio was 1:5 in our study, while the reported ratio is 1:3 and 1:54. The carcinoma of pancreas and CBD stones is more prevalent amongst the females. The male to female ratio being 5:6 and 5:9 respectively. The carcinoma of CBD and periampullary carcinoma on the other hand is commoner in males. The ratio being 2:1 and 2:0 respectively. Most patients with malignant extrahepatic biliary obstruction has advanced disease at presentation , which was inoperable.[10]

CONCLUSIONS

Extra-hepatic biliary obstruction is a challenging disease from both diagnostic and management points of view. Multiple diagnostic and therapeutic modalities are available and almost all patients can have their obstruction relieved through curative or palliative treatment options.

Endoscopic, radiologic and surgical approaches remain as complementary techniques and not as competitive modalities. Choice of procedure should ideally be selected based on the location and type of biliary obstruction, local expertise.

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COMPARISON OF THE RESULTS OF ANTERIOR NASAL PACKING VERSUS WITHOUT ANTERIOR NASAL PACKING FOR BETTER MANAGEMENT OF SEPTOPLASTY

Zubair Iqbal Bhutta,[1] Ali Husnain Sheikh,[2] Muhammad Dawood Saleem,[3] Shuman Roy[4]

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Abstract

Objective: The rationale of this study was to compare the results of anterior nasal packing versus without anterior nasal packing for better management of septoplasty.

Methods: This study was conducted in the department of ENT, Akhtar Saeed Trust Hospital Lahore on 220 patients who were randomly divided in two equal groups. Septoplasty was performed by a single team of surgeons and patients were followed till 6 weeks for evaluation of post-septoplasty complications like pain, septal hematoma and bleeding. Data was collected on a specially designed proforma (attached) and analysed on SPSS version 20.

Results: In this study of 220 patients, there were 139 males and 81 females with age range from 18 to 45 years. The mean age of 139 (63.2%) male patients and 81 (39.1%) female patients was 25.90 ± 5.974.The female to male ratio was 1:1.7. In group "A" consisting of 67 (60.9%) male and 43 (39.1%) female patients the mean age was 25.89 ± 5.97. Similarly, group "B" consisting of 72 (65.5%) male and 38 (34.5%) female patients the mean age was 25.92 ± 6.194. In group "A" (with anterior nasal packing) after septoplasty 51 (46.4%), 45 (40.9%) and 14 (12.1%) patients described mild, moderate and severe pain respectively on visual analog scale. In group "B" (without anterior nasal packing) 18 (16.4%) had no pain and 92 (83.6%) patients had mild pain during the first 24 hours post-operatively (P-value < 0.05). During septoplasty 03 (2.75) patients from each group developed primary heamorrhage of grade I. Reactionary haemorrhage was noted in 27 (24.5%) patient in group A and 8 (7.30%) in group B. Secondary heamorrhage was noted in 26 (23.6%) patients in group A and 04 (3.6%) in group B with statistically significant difference (P-value < 0.05).

Conclusion: On the basis of results in two groups, post-septoplsty complications rate of pain, primary & secondary haemorrhage was less in group B (without anterior nasal packing) than in group A (with anterior nasal packing). Septal hematoma formation was rare in both groups and statistically was not significant. On the basis of result obtained from this study, it is recommended that septoplasty operation without anterior nasal packing can be used confidently to achieve best surgical results.

Key words: Deviated nasal septum, anterior nasal packing, septal haematoma, visual analog scale.

It is a common and traditional practice to do anterior nasal packing after septoplasty to prevent bleeding, septal haematoma, synechiae and to get a midline position of septal cartilage and coaptation of the muco-perichondrial & mucoperiosteal flap. Anterior nasal packing causes nasal pain, headache, epiphoria, dryness of mouth, disturbed sleeping pattern, blocked ears, ear ache, gag and difficulty in swallowing, and also may prolong hospital stay.[1] Although these are temporary sufferings and revert after removal of anterior nasal packing but still are a cause of considerable nuisance to the patient during the period of anterior nasal packing and its removal after 24 - 48 hours[2]. Considerable bleeding may start during anterior nasal packing removal due to injury to the nasal mucosa and becomes difficult to control and may require anterior

1. Zubair Iqbal Bhutta 2. Ali Husnain Sheikh
3. Muhammad Dawood Saleem 4. Shuman Roy
1-4. Akhtar Saeed Medical and Dental College

Correspondence:
Dr. Zubair Iqbal Bhutta, *Professor Akhtar Saeed Medical and Dental College, Lahore*

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nasal packing to be done again. Even if no bleeding is encountered during removal of packing patient may complain of severe discomfort and patient may induce a request for removal of packing under general anaesthesia. The injured mucosa of the septum and turbinates may adhere together to form synechiae formation in the nasal cavities in the post-operative period.[3] These adhesions (synechiae) cause nasal obstruction, crusting, nasal pain, pooling of nasal secretions, ultimately infection and bleeding from the nasal cavities. Patient may return with initial symptoms and consequent failure of surgery.[4] Paraffin granuloma formation may result by anterior nasal packing on the nasal septum. Tight nasal packing to prevent septal haematoma, bleeding and stabilization of septal cartilage, in the midline position increases chances of septal cartilage necrosis due to reduced blood supply leading to septal perforation.[5]

A rare condition, toxic shock syndrome, may occur after septal surgery with nasal packing. It is caused by staphylococcal (sometimes streptococcal) bacteremia and the patient develops nausea, vomiting, purulent secretions, hypotension and body rash[6,7]. Pragmatic benefits without nasal packing septoplasty, do not cause nasal obstruction, nasal pain, headache, dryness of mouth, blockage of ears, earache, gag, difficulty in swallowing, epiphoria and disturbed sleeping pattern.[8,9]

In this context, different studies and literature suggest that anterior nasal packing is not necessary after septoplasty to prevent the post-operative nasal bleeding and septal haematoma.[10,11,13,14] Therefore the routine use of anterior nasal packing following septoplasty is not justified.

The pain was measured on visual analog scale.

1. Visual Analog Scale (VAS)

0	1	2	3	4	5	6	7	8	9	10

Pain was classified as

No Pain = 0

Mild Pain 01 - 03

Moderate Pain = 04 - 06

Severe Pain 07 - 10

2. Post - operative haemorrhage

- Primary haemorrhage
  - Bleeding at the time of injury or operation is known as primary haemorrhage.
- Reactionary haemorrhage
  - Bleeding that may occur within 24 hours is known as reactionary haemorrhage. It starts with the slippage of ligature, dislodgement vasospasm.
- Secondary haemorrhage
  - of a clot or cessation of reflex

Bleeding that occurs after 7 - 14 days is known as secondary haemorrhage. Infection and sloughing off a part of the wall of an artery are the causative factors. In this study, haemorrhage was estimated on grading scale (World Health Organization bleeding scale).

- Grade I

The bleeding is labeled Grade I, when total time intervals of all bleeding events are less than 30 minutes in last 24 hours.

- Grade II

The bleeding is labeled Grade II, when total time intervals of all bleeding events are more than 30 minutes in last 24 hours.

- Grade III

The bleeding is labeled Grade III, when RBC transfusion is essential over routine transfusion requirements.

- Grade IV

The bleeding is labeled Grade iv, when bleeding is accompanying severe haemodynamic instability as below

Fall of blood pressure

> 50 mm / Hg or

> 50% decrease in sysitolie or diastolic blood pressure

Associated tachycardia (Heart rate increases > 20% for 20 minutes)

When RBC transfusion is essential over routine transfusion requirements.

3. Septal haematoma

Blood collection between the septal cartilage and the overlying mucoperichondrium is known as septal haematoma. It usually presents with fluctuating septal swelling within first 03 post-operative days.

METHODS

This study was conducted in ENT department of Akhtar Saeed Trust Hospital from July 2017 to June 2019. It was randomized control trial. Non- probability purposive sampling technique was used.

1. Sample size

The sample size has been calculated (Maeed and Al-Shehri., 2011) using expected percentage of post-operative pain in group A (with anterior nasal packing) 28.60% and 11.40% in group B (without anterior nasal packing) at 90% power of study and 5% level of significance.

In this study, 220 patients were allocated randomly into group A and B comprising 110 patients in each group.

2. Sample selection

- Inclusion criteria

Regardless of the type of septal deviation, patients of either sex between the ages of 18 to 45 years were incorporated in this research work.

- Exclusion criteria

The following patients were excluded from the study if they

- Were submitted to revision surgery.
- Were planned with other associated nasal surgeries (e.g.; Septo-Rhinoplasty).
- Were hypertensive.
- Had coagulation disorders.

PT > 14sec., APTT> 35sec., INR> 1.2

Randomization

Each patient was randomly allocated into two groups as Groups A (110 patients) and group B. (110 patients) by using balloting method.

All collected data was analyzed using SPSS version 20.

- Descriptive statistics, mean and ± S.D was used for quantitative data like age (years).
- Frequencies and percentages were calculated for qualitative data like gender and post-operative complications.

Independent sample t-test was applied to compare intensity of post-operative pain on visual analog scale in both groups.

- Chi-square test was applied to compare presence of post-operative haemorrhage & septal haematoma in both groups.

RESULT

In this study, the average age of patients was 25.90 ± 5.974 years. Minimum age of patients was 18 and maximum age of patients was 45 years. The mean age of patients in Group A and Group B was 25.89 ± 5.773 and 25.92 ± 6.194 years respectively. There was no statistical difference of age in group A and group B, p - value > 0.05 (0.793). In group A with anterior nasal packing, there were 67 (60.90 %) males and 43 (39.10 %) females and in group B without anterior nasal packing, 72 (65.5% %) males and 38 (34.5 %) female patients. The female to male ratio was 1:1.7. There was no statistical difference of gender in 'group A and group B, p-value > 0.05(0.793). Gender distribution. 139 (63.2%) patients were male and 81 (36.8%) were female. Male patients were dominating female patients.

After septoplasty, 51 (46.4%), 45 (40.9%) and 14 (12.7%) patients described mild, moderate and severe pain respectively in group A (with anterior nasal packing), Table 1.

While in group B. 18 (16.4%) patients were free of pain and mild pain complained by 92 (83.6 %) after septoplasty. There was a statistically significant difference between group A and group B (p - value < 0.05). After 24 hours pain intensity shifted from mild to moderate and severe levels 10 (9.1%), 18 (16.4%) and 82 (74.5%) respectively in group A. on the other side in group B, 93 (84.5%) were free of pain and 17 (15.5%) complained mild pain on visual analog scale. There was a statistically significant difference between

Table 1: *Comparison Of Pain In Group A And Group B*

			Pain					
Time	**Group**		**No Pain**	**Mild Pain**	**Moderate Pain**	**Severe Pain**	**P- Value**	**Total**
After	A	Frequency	0	51	45	14	0.448	0.00*
		Percent	0%	46.4%	40.9%	12.7%		
	B	Frequency	18	92	0	0	0.448	
		Percent	16.4%	83.6%	0%	0^0 A)		
After 24 Hours	A	Frequency	0	10	18	82	0.200	0.00*
		Percent	0%	9.1%	16.4%	74.5%		
	B	Frequency	93	17	0	0	0.200	
		Percent	84.5%	15.5%	0%	9%		
During pack removal after 48 Hours	A	Frequency	0	0	38	72	0.285	0.00*
		Percent	0%	0%	34.5%	65.6%		
	Ba	Frequency	100	10	0	0	0.285	
		Percent	90.9%	9.1%	0%	0%		
01 Weeks	A	Frequency	14	96	0	0		0.00*
		Percent	12.7%	87.3%	0%	0%		
	B	Frequency	110	0	0	0		
		Percent	100%	0%	0%	0%		
02 Weeks	A	Frequency	43	67	0	0		0.00*
		Percent	39.1%	60.9%	0%	0%		
	B	Frequency	110	0	0	0		
		Percent	100%	0%	%	0%		
03, 04, 05 & 06 weeks	A	Frequency	110	0	0	0		0.00*
		Percent	100%	0%	0%	0%		
	B	Frequency	110	0	0	0		
		Percent	100%	0%	0%	05		

* p - value < 0.05
Ba = Pain measured in group B (without anterior nasal packing)

group A and group B (p - value < 0.05).

After 48 hours, anterior nasal packing was removed in group A patients and pain levels dramatically shifted towards moderate and severe pain in 38 (34.5%) and 72 (65.5%) patients respectively. While 100 (90.9%) patients in group B were free of pain and only 10 (9.1%) patients had mild pain. There was a statistically significant difference between group A and group B (p - value < 0.05).

After one week 110 (100%) patients were free of pain in group B (without anterior nasal packing). 14 (12.7%) patients in group A were free of pain and 67 (60.9%) patients had mild pain. There was a statistically significant difference between group A and group B (p - value < 0.05).

After two weeks, all patients in group B (without anterior nasal packing) and 43 (39.1%) in group A (with anterior nasal packing) were free of pain while 67 (60.9%) patients had mild pain in group A (with anterior nasal packing). There was a statistically significant difference between group A and group B (p - value<0.05). After 03, 04, 05 & 06 weeks all patients in group A and group B were free of pain.

Table 2: *Septal Haematoma Formation In Group A And Group B*

		Septal Haematoma		
		No Haematoma	**Haematoma**	**Total**
Group A	Frequency	107	03	110
	Percent	97.3	2.7	100.0
Group B	Frequency	106	04	110
	Percent	96.4	3.6	100.0
P- Value		0.083	0.045	0.320

*p - value > 0.05

In group A (with anterior nasal packing) 03 (2.7%) patients and in group B (without anterior nasal packing) 04 (3.6%) patients developed septal haematoma, table 2. There was no statistically significant difference between group A and group B (p - value > 0.05).

During septoplasty, 03 (2.7%) patients from each group developed primary haemorrhage of grade I, table 3. Reactionary haemorrhage was noted in 27 (24.5%) patients in group A and 8 (7.3%) in group B. Secondary haemorrhage was noted in 26 (23.6%) patients in group A and 04 (3.6%) in group B. There was a statistically significant difference between two groups in, reactionary and secondary haemorrhage (p - value < 0.05).

DISCUSSION

In this study, the total number of patient was 220. Patients were between the age ranges of 18 - 45 years. The mean age of patients was 25.90 ± 5.974 years with 139 (63.2%) male and 81 (36.8%) female patients. There was no statistically significant difference between age and gender in group A and group B (p -- value > 0.05). In this study, the female to male ratio was 1: 1.7. This higher proportion of male patients is also reported in literature.[3]

Table 3: Bleeding In Group A And Group B

	No Bleeding	Grade I Bleeding	Grade II Bleeding	Grade III Bleeding	Grade IV Bleeding
Primary (Group A)	107	3	0	0	0
Reactionary (Group A)	83	27	0	0	0
Secondary (Group A)	84	26	0	0	0
Primary (Group B)	101	3	0	0	0
Reactionary (Group B)	102	8	0	0	0
Secondary (Group B)	106	4	0	0	0

In this study, all (220) patients were randomized into two equal groups by balloting method. Group A comprised of 110 patients and was subjected to pack with anterior nasal packing after septoplasty. While group B also comprising of 110 patients was managed without anterior nasal packing post-operatively. We documented and correlated post-operative data in terms of pain, bleeding and septal haematoma in group A and group B. Data of Pin description was collected from patients on visual analog scale reading from 0 to 10 level at 24 and 48 hours, then on 7, 14. 21, 28, 35 and 42 days after procedure.

After septoplasty, nasal pain at 24 and 48 hours was higher in group A (Patients with anterior nasal packing) on VAS than group B (Patients without anterior nasal packing). In group A, mild, moderate and severe pain complained by 31 (46.4%), 15 (40.9%) and 14 (12.7%) patients respectively in first 24 hours after septoplasty. At the end of 48 hours during the removal of anterior nasal packing pain level in group A shifted from mild, moderate and severe stage to moderate and severe level in 38 (34.5%) to 72 (65.6%) patients respectively reporting a value greater than 7 on visual analog scale - severe pain on visual analog scale. On the other side, after 48 hours 100 (90.9%) patients in group B were free of pain and remaining 10(9.1%) had mild pain. In literature, similar results are present in which high grades of post-operative pain were narrated by patients in first 24 hours and higher upon removal of the pack in the anterior nasal packing group 4. Their stated grades on visual analog scale were significantly more than those without anterior nasal packing septoplasty. Patients with anterior nasal packing septoplasty ominously showed more tears, headache and complained disturbed sleep patterns. One more study depicts similar data in which post-operative pain was evaluated after septoplasty in 697 patients 5. This study exhibited that patients packed with anterior nasal packing complained more pain than those without anterior nasal packing after. septoplasty. In our study, patients without anterior nasal packing were 90.9% free of pain and no pain recorded in a single patient after 1 week. However, patients in group A with anterior nasal packing complained nasal pain till the end of 3rd week. Statistically

significant differences persisted throughout the study till the end of 3 weeks between two groups (p — value > 0.05).

In this study, patients in group A (with anterior nasal packing) had minor oozing after septoplasty and more oozing upon removal of anterior nasal packing after 48 hours. This oozing was managed conservatively by nose pinching and vasoconstrictor drops in 83 (75.3%) patients. Remaining 27(24.7%) patients had grade 1 reactionary haemorrhage and 6 patients were repacked with anterior nasal packing for next 12 hours. On the other hand, in group B, reactionary haemorrhage of grade I was noted in 8 (7.2%) patients. They were managed with vasoconstrictor drops and anterior nasal packing was not done even in a single patient. Such observations are also described in the literature.[7] Post-operative reactionary haemorrhage up to 7.7% had been reported. Half of these patients were managed with conservative treatment and remaining half were repacked to control the reactionary haemorrhage. Their statistical data was significant with and without anterior nasal packing after septoplasty.

In addition, 26 (23.6%). cases of secondary haemorrhage in group A and 04 (3.6%) cases in group B came back on 7th and 9th day and all were packed with anterior nasal packing for next 12 hours.

In group B without anterior nasal packing, post-operative oozing was minimal on the first day compared to patients with nasal packing. Five patients came back with minor oozing within 24 48 hours on 3rd day of operation. This oozing was managed with nose pinching and vasoconstrictor drops and send back to home with assurance.

In group A and group B, patient did not come back with secondary haemorrhage of grade II, Ill and IV after septoplasty.

84 (76.4%) patients in group A and 106 (96.4%) patients in group B did not report any problem till the end of this study. Similar results also have been reported in literature.[8]

After septoplasty, patients in group B (without nasal packing) were discharged on the same day compared to patients in group A (with anterior nasal packing) who were discharged on second and third day.

In this study. septal haematoma was a rare complication after septoplasty. Only 03 (2.7%) patients in group A and 04 (3.6%) patients in group B developed septal haematoma (p-value > 0.05). The septal haematoma was drained and nasal cavity packed for 12 hours. These results show that anterior nasal packing has no substantial role to prevent the septal haematoma after septoplasty. These results correlate with a study[13] in which only one patient with anterior nasal pack 1H, developed septal hematoma post-operatively. A meta-analysis study conducted by Ranglawala[3] reported that 10' and 07 out of 948 patients developed septal haematoma in packed and non - packed groups respectively. Consequently, if anterior nasal packing is certainly effective then there should be no septal haematoma formation in anterior nasal packing septoplasty and definitely should have septal haematoma formation in all patients without anterior nasal packing.

CONCLUSION

On the basis of findings in this study, group B (without anterior nasal packing) had early pain free rate (at day 1) and less complications (such as primary & secondary haemorrhage) compared with group A (with anterior nasal packing). The septal hematoma formation is statistically insignificant in both groups. In future, we can perform septoplasty without anterior nasal packing to achieve early pain - free rates, fewer complications, less hospital stay and may be higher satisfaction of our patients.

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LIFE ISN'T ABOUT FINDING YOURSELF, IT'S ABOUT CREATING YOURSELF.

COMPARATIVE STUDY OF ENDOSCOPIC VS EXTERNAL DACRYOCYSTORHINOSTOMY

Zubair Iqbal Bhutta,[1] Ali Husnain Sheikh,[2] Muhammad Dawood Saleem,[3] Shuman Roy[4]

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Abstract

Objective: To compare the success rate of external and endoscopic dacryocystorhinostomy(DCR) in patients with nasolacrimal duct obstruction

Methods: Total 80 patients were divided into two groups of 40 patients in each group. Group 1 underwent external DCR while group 2 underwent endoscopic DCR in Akhtar Saeed Trust hospital from 1/2/2017 to 31/1/2020.

Results: The success rate of endoscopic group was compared with the external group in regular followup after 7th post-op day, one month, 3 months, 6 months and one year. All the data was entered and analyzed with SPSS version 20. Quantitative variable like age was presented by calculating mean and standard deviation. Qualitative variables were presented by calculating frequencies and percentages

Conclusion: The success rate in terms of relief of epiphora was found better in endoscopic group (92.5%) as compared to external group (85%)

Key words: Nasolacrimal duct, Epiphora, Dacryocystorhinostomy.

Lacrimal drainage pathway starts from the lacrimal puncta and ends in the inferior meatus in the lateral wall of nose. It constitutes lacrimal puncta, lacrimal canaliculi, lacrimal sac, and nasolacrimal duct which ends in an opening in the inferior meatus. Obstruction at any level in the above pathway can cause epiphora(watery eyes). The primary acquired nasolacrimal duct obstruction is believed to occur due to chronic inflammatory process resulting in fibrosis, stenosis, and closure of the duct ostium.[1,2] Nasolacrimal duct obstruction is the most common cause which can be relieved by a surgical operation dacryocystorhinostomy (DCR) which is used to create a fistula that bypasses the obstruction and restores the tear flow.[3] The operative approach can be external or endoscopic. External DCR was the gold standard method even after the endoscopic approach had been described, because of limited technology at that time with a success rate ranging between 80 and 100 %.[2,4] However, the improvements in endoscopic visualisation & instrumentation have made the endoscopic DCR a better choice these days. In addition, endoscopic DCR has several benefits over external DCR i.e no external scar mark, quicker recovery time, and lower postoperative morbidity.[4] Various studies describe different success rates of endoscopic endonasal DCR that range from 89% to 98%.[5] This study was conducted to analyze the difference between the success rate of external and endoscopic dacryocystorhinostomy (DCR) in patients with nasolacrimal duct obstruction. Success being defined as complete relief of epiphora plus patency on syringing at 1 year follow up. Epiphora is overflow of tears onto the face

METHODS

Eighty lacrimal systems of 80 patients coming to Akhtar Saeed Trust Hospital from 1/2/2017 to 31/1/2020 were selected. The patients were selected after detailed ENT examination and opinion from the

1. Zubair Iqbal Bhutta
2. Ali Husnain Sheikh
3. Muhammad Dawood Saleem
4. Shuman Roy
1-4. ENT Department, Akhtar Saeed medical college, Lahore

Correspondence:
Dr. Zubair Iqbal Bhutta, *Professor, ENT Department, Akhtar Saeed Medical College, Lahore*

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ophthalmology department. Patients fulfilling the inclusion criteria with isolated lacrimal duct obstruction were included in the study. The patients were randomly divided into two groups 1 and group 2. Informed consent was taken from the patients. Group 1 underwent external DCR while group 2 underwent endoscopic DCR. Silicone lacrimal tube was removed 12 weeks after surgery. Outcome was compared at 7th postoperative day, 1st month, 3rd month, 6th month and 1 year. S. A standard Performa was used for data collection and the following variables were recorded including age, gender, relief of epiphora on 7th post operative day, 1 month, 3 month, 6 month and one year consecutively. Success rate of either of the procedures in terms of relief of epiphora and patency of syringing at interval of one year was labeled and charted in the table. Demographic profile and relevant data was recorded on research tools.

RESULTS

Data was entered and analyzed with SPSS version 20. Quantitative variable like age was presented by calculating mean and standard deviation. Qualitative variables were presented by calculating frequencies and percentages.

DISCUSSION

In this study out of the 80 patients, 47 (68.75%) were females and 33 (41.25%) were males. we compared two groups of lacrimal sac surgery. Group 1 underwent external dacryocystorhinostomy and group 2 underwent endoscopic dacryocystorhinostomy. On 7th postoperative day, 36(90%) lacrimal systems in group 1 showed relief of epiphora whereas 38 (95%) lacrimal systems in group 2 showed relief of epiphora. On 1 month follow up the values for relief of epiphora in group 1 were 35(87.5%) and 38(95%) in group 2. On 3rd month follow up, the values for relief of epiphora in group 1 remained same as 35(87.5%) whereas in group 2 the values were reduced but still much higher than group 1 at 37(92.5%). The values for relief of epiphora at 6 months were reduced to 34(85%) in group 1 and were stable at 37(92.5%) in group 2. On 1 year follow up the values were further reduced to 33(82.5%) in group 1, while in group 2, values remained stable at 37(92.5%). 1 year follow up patency of the lacrimal

Table 1: *Gender Ratio*

Sex	Frequency	Percentage %
Male	33	41.25%
Female	47	68.75%
Total	80	100

Table 2: *Age*

Total number	Mean	Std. deviation	Minimum	Maximum
80	41.3	13.192	12	64

Table 3: *Relief of Epiphora on 7th Post-op Day*

			Type of procedure		
			External	Endoscopic	Total
Relief of epiphora on 7th day	Relief	Count	36	38	74
		Percentage	90%	95%	92.5%
	No relief	Count	4	2	6
		Percentage	10%	5%	7.5%
Total			40	40	80

Table 4: *Relief of Epiphora At 1 Month*
P Value: <0.5

			Type of procedure		
			External	Endoscopic	Total
Relief of epiphora at 1 month	Relief	Count	35	38	73
		Percentage	87.5%	95%	91.25%
	No relief	Count	5	2	7
		Percentage	12.5%	5%	8.75%
Total			40	40	80

Table 5: *Relief of Epiphora At 3 Months*
p value: <0.5

			Type of procedure		
			External	Endoscopic	Total
Relief of epiphora at 3 months	Relief	Count	35	37	72
		Percentage	87.5%	92.5%	90%
	No relief	Count	5	3	8
		Percentage	12.5%	7.5%	10%
Total			40	40	80

Table 6: *Relief of Epiphora Aat 6 Months*
p value: <0.5

			Type of procedure		
			External	**Endoscopic**	**Total**
Relief of epiphora at 6 months	Relief	Count	34	37	71
		Percentage	85%	92.5%	88.75%
	No relief	Count	6	3	9
		Percentage	15%	7.5%	11.25%
Total			40	40	80

Table 7: *Relief of Epiphora at 1 Year*
p value: <0.5

			Type of procedure		
			External	**Endoscopic**	**Total**
Relief of epiphora at 1 year	Relief	Count	33	37	70
		Percentage	82.5	92.5%	87.5%
	No relief	Count	7	3	10
		Percentage	8.75	7.5%	12.5%
Total			40	40	80

Table 8: *Patency on Syringing at 1 Year*

		Type of procedure		
		External DCR	**Endo DCR**	**Total**
Patency on syringing at 1 year	Patent	37(92.5%)	40(100%)	77(96.25%)
	Not patent	3(7.5%)	0(0%)	3(3.75%)
Total		40	40	80

systems in both groups was assessed by syringing and while 40(100%) lacrimal systems in group 2 were found to be patent, in group I 37(92.5%) lacrimal systems were found to be patent. This difference is statistically significant (P 0.007) and is comparable to the figures that are given in the international studies.[5,6,7]

CONCLUSION

Endoscopic dacryocystorhinostomy(DCR) not only provides significantly better results than External DCR in terms of relief of epiphora, but it is also cosmetically more acceptable to the patient with no external scar mark on the face after surgery. We suggest using this technique more commonly for the patients of nasolacrimal duct obstruction.

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OUTCOME OF SURGICAL PROCEDURES IN PATIENTS SUFFERING FROM PERFORATED PEPTIC ULCER DISEASE

Waqas Husain Qureshi,[1] Zahid Sattar,[2] Aakif Yousaf,[3] Muhammad Ashraf,[4] Akhtar Mahboob,[5] Sajid Mukhtar[6]

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Abstract

Objective: To investigate the mode of presentation and outcomes of surgical procedure along with prognosis of perforated peptic ulcer disease.

Methods: Patients presented with peritonitis having history of peptic ulcer disease in outpatient or emergency department were enrolled in study. X-Ray abdomen and chest were obtained for all patients for diagnosis of pneumoperitoneum. Primary repair and laparotomy was done for all patients and biopsy sample was taken. SPSS software was used to determine the statistical values of variable. P value ≤ 0.05 considered as significant.

Results: In this study 71.7% had perforated duodenal ulcer and 28.3% had perforated gastric ulcer with duodenal, 60% had previous history of peptic ulcer disease and 40% had history of taking NSAIDs. Pain in abdomen revealed in all the patients i.e. 100% patients. Vomiting, fever, constipation and abdominal distension were observed in 63.3%, 40%, 30% and 96.7%, respectively.

Conclusion: Presentation of duodenal perforation is more common as compare to gastric perforation and more in male patients. Reason behind late presentation at health care facilities is unemployment and lack of education. Simple closure and Graham's patch give excellent results and associated with minimum mortality rate.

Keywords: Perforated peptic ulcer, Duodenal ulcer, Surgery, H. Pylori, Abdominal pain.

Perforation of peptic ulcer is a common and critical emergency among typhoid, gastrointestinal and tuberculous perforations.[1] Helicobacter pylori (H. Pylori) is the causative organism of peptic ulcer. Other causes include burns, sepsis, stress, use of non steroidal anti inflammatory drugs (NSAIDS) and multiple injuries.[2] NSAIDS not only cause perforations but bleeding episodes may occur as a result of overuse. Another contributing factor use of steroids isunclear[3].

1. Waqas Husain Qureshi
2. Zahid Sattar
3. Aakif Yousaf
4. Muhammad Ashraf
5. Akhtar Mahboob
6. Sajid Mukhtar

1-6. Department of Surgery Sahiwal Medical College / Sahiwal Teaching Hospital Sahiwal.

Correspondence:
Dr. Waqas Husain Qureshi, *Assistant Professor of Surgery Sahiwal Medical College / Sahiwal teaching Hospital Sahiwal.*
E-mail: waqashusain@hotmail.com

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Aggregation and distribution of mucosal elements and imbalance between them is the cause of gastric perforation.[4] Erosion of 3mm wide and 0.5cm deep mucosal cells may cause duodenal ulcer. In gastrointestinal system colon first perforating site and duodenum is 2nd most[5]. Lesser curvature and anterior of duodenum develops perforation and on other hand posterior wall of duodenum present with bleeding episodes. Prevalence of duodenal ulcer is much higher than stomach ulcer.[6,7]

Perforations occur in 2-14% of cases in peptic ulcer otherwise managed consecutively.[8] There were no usual symptoms of perforation in acute cases but in chronic cases dyspepsia observed before few days of perforation.[9] About 400000 people affected worldwide every year. Closer procedure of perforations was invented by Mikulicz Radecki. Perforation in both organs (duodenal and stomach) spreads the gastric contents in abdomen and patient presents with sudden

onset of excruciating epigastric pain with increasing intensity.[10]

Aim of this is to find out the presentation mode and outcome of surgical management in patients of perforated peptic ulcer disease.

METHODS

This prospective study was conducted on 60 patients presented with acute abdomen from peptic ulcer disease. The study was conducted in surgical ward at DHQ Teaching HospitalSahiwal from 1st Feb 2020 to 31st January 2021 after permission from ethical committee of hospital. Non probability consecutive sampling technique was used. Patients treated conservatively, having abdominal pain due to any other cause not from perforated peptic ulcer and who are fail to give consent were excluded from the study.

After shifting in ward from emergency department and outpatient department, bilateral large bore intravenous cannula were inserted on dorsum of hands. Complete investigations radiological and biochemical were done. Radiological investigation includes x-ray abdomen/ chest to clear the diagnosis of pneumoperitoneum.

Consent was taken from patients after obtaining cardiac and anaesthesia fitness. After arrangement of blood patients were shifted to Operation Theatre where planned procedure was performed. Antibiotics were given prophylactically. Omentopexy was done for duodenal ulcer mad simple closure was done in perforation of gastric mucosa. Six to ten litres normal saline was used to wash peritoneal cavity.

Data determination was done with SPSS computer software. Numerical data like age was presented and frequency (percentages) were calculated for qualitative data like vomiting and abdominal pain. Tests of significance (chisquare test and t tests) were applied. P value less than or equal to 0.05 was considered as significant.

RESULTS

Sixty patients were included in this study, both genders. Gender distribution revealed as n=47 (78.3%) males and n=13 (21.7%) females. The mean age of the patients was 46.21±3.54 years. There were n=24 (40%) farmers, n=9 (15%) traders, n=7 (11.7%) students, n=6 (10%) teachers and n=14 (23.3%) were others. (Table. I).

n=43 (71.7%) had perforated duodenal ulcer and n=17 (28.3%)had perforated gastric ulcer with duodenal. n=36 (60%) had previous history of peptic ulcer disease and n=24 (40%) had taking NSAIDs. Pain in abdomen revealed in all the patients i.e. n=60 (100%) patients. Vomiting, fever, constipation and abdominal distension were observed in n=38 (63.3%), n=24 (40%), n=18 (30%) and n=58 (96.7%), respectively. (Table. II).

DISCUSSION

Duodenal and stomach perforations are the common sites with high incidence rate. In our study duodenal perforations found higher in ratio as compare stomach perforation and ulcer. In a study conducted by Bert leff et al[11] also reported duodenal perforations higher than stomach ulcers which may lead to perforation. Another study was conducted by Nuhu et al[12] and observation was given that ileum is the most common site of perforation in south Asian population and common causes are typhoid and tuberculosis disease.

In our study we observed professional contribution is common. Farmers have greater proportion of peptic ulcer disease about 40% of total number of patients and traders are the second one with 9%. Nasio et al[13] in his study reported similar findings that uneducated and unemployed persons have higher incidence of

Table 1: *Demographic characteristics of the patients*

Variable	n, (%)
Age (years)	46.21±3.54
Gender	
Male	n=47 (78.3%)
Female	n=13 (21.7%)
Occupation	
Farmers	n=24 (40%)
Traders	n=9 (15%)
Students	n=7 (11.7%)
Teachers	n=6 (10%)
Others	n=14 (23.3%)

Table 2: Clinical presentations of the patients

Variable	n, (%)
Gastric ulcer	
Perforated duodenal ulcer	n=43 (71.7%)
Perforated gastric ulcer with duodenal	n=17 (28.3%)
Therapy	
History of peptic ulcer disease	n=36 (60%)
NSAIDs	n=24 (40%)
Clinical presentations	
Pain in Abdomen	n=60 (100%)
Vomiting	n=38 (63.3%)
Fever	n=24 (40%)
Constipation	n=18 (30%)
Abdominal distension	n=58 (96.7%)

peptic ulcer disease. Cause of this factor in unawareness of degenerative food and health care facilities as well.

In our study we observed age difference among perforation and its causes. A study was conducted on Rohikland population by William et al[14] and concluded that perforation due to peptic ulcer mostly occur in 4th decade of life. But this observation is not supported in all studies confirmation needs with multiple studies on large sample size. A similar study was conducted by K. Thossen et al[15] and reported 6th decade is the richest one. These two studies were supportive to our study.

Another study was conducted on Nigerian population by Shah et al[16] and reported contrast results to our findings that stomach perforations are common as compared to duodenum and other sites of infected perforation with H. Pylori. Satapathy et al[17] also reported same results that stomach ulceration are common that ends with perforation. A study was conducted by Jamali et al[18] in 2019 and reported 96% cases presented with abdominal pain and treatment given was surgical management that was associated with surgical site infection as commonest complication.

In our study male presentation is much higher as compared to female gender because male are more prone to causative factors like alcohol consumption and smoking. Türkdoğan et al[19] conducted a similar study and reported alcohol is common cause because of its mucosal degenerative property. Other risk factors may include NSAID and other ulcerogenic drug use. Collier et al[20] conducted a study on risk factors and reported use of NSAIDs is the common contributing factor for peptic ulcer disease. It was reported in 10.7% of patients.

CONCLUSION

Presentation of duodenal perforation is more common as compare to gastric perforation and more in male patients. Reason behind late presentation at health care facilities is unemployment and lack of education. Simple closure and Graham's patch give excellent results and associated with minimum mortality rate.

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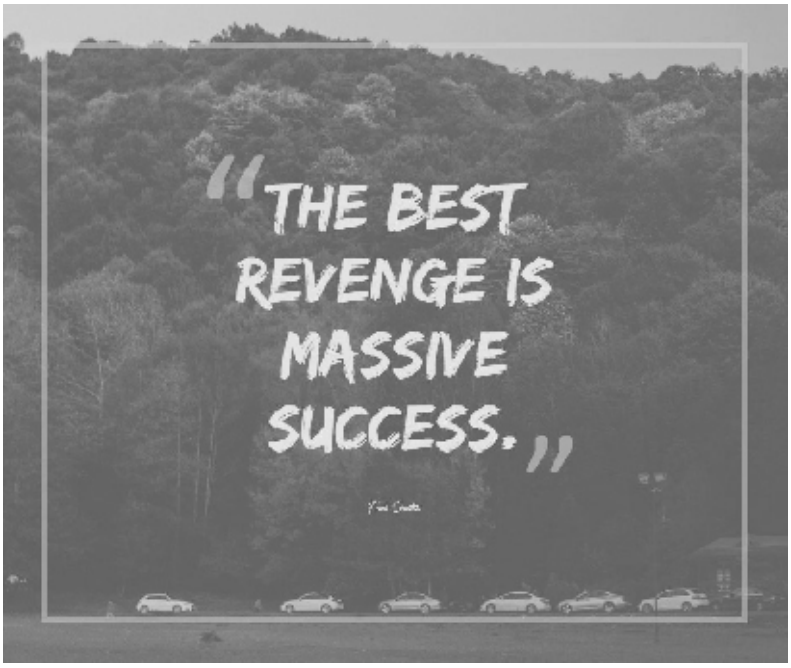

EFFECT OF PLATLETPHERESIS ON HEMATOCRIT HAEMOGLOBIN AND ERYTHROCYTE COUNT OF DONOR AFTER ONE HOUR OF DONATION

Naghmana Mazher,[1] Nazish Saqlain,[2] Seema Mazher,[3] Ghana Babar[4]

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Abstract

Background: Plateletpheresis is a procedure by which platelets are extracted from a single donor by a device while returning the remaining contents of the blood back to the donor's body. By this procedure the yield of platelets is 8 times greater than those separated from whole blood unit.

Methods: It was a cross-sectional study, conducted at the Hematology & Transfusion medicine department of the University of Child Health Sciences & the Children's Hospital, Lahore from December 2020 to July 2021 after Institutional Ethical committee approval and taking informed consent from 68 randomly selected plateletpheresis donors. After donor had been considered eligible for the procedure as per blood donor's selection criteria, the details of procedure of plateletpheresis were explained to each donor and % the questionnaire was filled. Plateletpheresis was done using COM. TEC Cell Separator instrument. Hematological parameters such as hemoglobin (Hb), hematocrit (HCT), and erythrocyte count were analyzed before and after 1 hour of plateletpheresis procedure using SYSMEX XP-100 automated analyzer.

Results: In this study, 68 donors were included; all were healthy male donors, with mean weight 69.29 ± 10.59 Kg. Pre donation HCT levels showed that 60.8% donors had HCT level > 45%, 32.1% had 42-44% and 7.1% had HCT<42%. Regarding pre donation hemoglobin (Hb) levels, 21.4% had 16-18 g/dL, 60.8% had 14-15 g/dL and 17.8% had 10-13 g/dL Hb levels. Whereas, 46.5% had RBCs count between 5.0-6.3 ×1012 /l, 35.7% had 4.0-4.9 ×1012 /l and only 17.8% had 3.2-3.7 ×1012 /l. After 1 hour of donation, changes in HCT were observed as 35.7% donors had >42%, 53.6% had 35-40% and 10.7% donors had HCT <35%. Regarding Hb after donation, 14.3% had 16-18g/dL, 67.9% had 13-15g/dL and 17.8% donors had 11-12g/dL. Post donation count of RBCs (×1012/l) among 42.9% donors was 5-6.3, 32.1% had 4-4.9 and 25% had 3.2-3.7 levels. Mean pre and post donation HCT levels of donors was 40.71±6.03 and 38.09 ±8.25 respectively. Mean pre and post donation Hb levels of donors was 14.44 ±1.85 and 13.84 ±1.90 respectively. Mean pre and post donation RBC levels of donors was 4.83 ± 0.79 and 4.56 ±0.85 ×1012/l respectively. The difference was statistically significant (p-value<0.05) for HCT levels but insignificant for mean RBCs and Hb counts (p-value>0.05).

Conclusion: The decrease in hemoglobin level and red cell count was not so significant while the decrease in hematocrit was statistically significant.

Key Words: Plateletpheresis, Hematocrit, Hemoglobin, red cell Count.

The worldwide used criteria used for blood donations have been devised for safe blood transfusion by obtaining blood products with high-quality standards, and ensuring that donations do not causes health hazards to the either donor or the patient. Plateletpheresis is a procedure by which platelets are extracted from the donor by a device while returning the remaining contents of the blood back to the donor's body[1]. By this procedure the yield of platelets is 8 times greater than those separated from whole blood unit. With the recent advancement in the more frequent clinical uses of blood components has shown great improvement in the field of therapeutic apheresis.[2,3] Platelet trans-

1. Naghmana Mazher 2. Nazish Saqlain
3. Seema Mazher 4. Ghana Babar
1. Fatima Jinnah Medical University, Lahore, Pakistan
2,4. The University of Child Health Sciences & The Children's Hospital, Lahore, Pakistan
3. Allama Iqbal Medical College, Lahore

Correspondence:
Dr. Naghmana Mazher, *Fatima Jinnah Medical University, Lahore, Pakistan*

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fusions are required not only for patients receiving cancer therapy but also for the treatment of various bleeding disorders, during cardiac surgeries and organ transplant. So the plateletpheresis procedure in comparison with manual blood donations has the advantages like shorter time period between the donations, less adverse effects in patients like refractoriness and alloimmunization, along with more controlled doses with good platelet yield and volume collection.

Keeping in view of safe blood transfusion for the highest patient care substantial efforts were put to support the widespread use of single donor plateletapheresis (SDP) instead of platelet concentrate (PC), and is extremely beneficial for the patients of various hematological diseases.[4-6] Major advantages of SDP are economic use of blood due to selective components collection, more frequent donations as compared to whole blood unit, reduced donor exposures and so leading to reduced risk of alloimmunization.[7,8] Although platelets apheresis procedure is safe and well tolerated, however, it can cause some adverse local or systemic reactions to the donors.[9] Apheresis may cause alterations in donor's hematological parameters due to the anticoagulant used and extra-corporeal circulation.[10,11]

METHODS

A cross-sectional study was conducted involving 68 healthy plateletpheresis donors selected with the following criteria: weight > 60 kg; age between 18 and 50 years; hemoglobin > 12.5 gm/dl and platelets count > 200×10^9/L.On screening negative serological tests for HIV, hepatitis B, hepatitis C, syphilis and malaria, absence of any illness; none of them had used anti-inflammatory drugs and should have suitable venous accesses. This study was conducted at the Department of Hematology and transfusion Medicines at university of Children health, Lahore. Procedure details were explained to each donor and informed consent was taken before the procedure.

Ante-cubital veins were used for the venipuncture in all the donors. Vital signs were monitored at the beginning and at end of each procedure; donors were also monitored for adverse events during the procedures. 3ml venous blood sample was drawn twice from the donors; (at the time of donor selection before the apheresis procedure and after the completion of the apheresis procedure), from a vein that was not to be used during the procedure, with minimum stasis through a 21-gauge needle into EDTA Vacutainer, (FCM)). All samples were processed within 10 min of collection for complete blood count (CBC).

The calibrated haematology analyzer, SYSMEX XN-1000 was used for analyzing the red cells parameters i.e. Hb, red blood cells count and HCT. Screening was done using ELISA. After 1 hour of donation again sample was collected in EDTA vial and analysis for the same parameters was done.

Plateletpheresis was done using COM.TEC Cell Separator instrument; single-needle system used as per the manufacturer's standard operating procedure with a whole blood (WB)/acid citrate dextrose (ACD-A) ratio of 11:1, interface set point 0.60 and blood flow rate 60-75 ml/ min. The donors' data (weight, sex, Hb, and pre-apheresis P/B PLT count) were entered into the cell separator program to determine the blood volume processed to reach the target platelets yield (3×10^{11}/L).

The descriptive analysis was done using SPSS 23.0. Frequency was calculated and difference between mean hematocrit, hemoglobin and erythrocyte count were analyzed using paired sample t-test.

RESULTS

The study was conducted at hematology department of university of Child Health, Lahore. In this study 68 donors were included; all were healthy male donors, with mean weight 69.29 ± 10.59 Kg.

Among 68 donors, pre donation HCT levels showed that 41 (60.8%) donors had HCT level > 45, 22 (32.1%) had HCT levels of 42-44 and remaining 7.1% had HCT <42. Regarding pre donation hemoglobin (Hb) levels, 15 (21.4%) had Hb levels in the range of 16-18 g/dL, 41 (60.8%) donors had Hb level of 14-15 g/dL and 12 (17.8%) had 10-13 g/dL Hb levels. Among all the donors, 32 (46.5%) had RBCs

count between 5.0-6.3 g/dL, 24 (35.7%) had RBCs count of 4.0-4.9 $\times 10^{12}$ g/dL and only 12 (17.8%) had 3.2-3.7 $\times 10^{12}$ g/dL. After 1 Hour of donation HCT, Hb and RBC count of donors were measured. Changes in HCT were observed as 24 (35.7%) donors had >42, 36 (53.6%) had HCT of 35-40 and 08 (10.7%) donors had HCT <35. Hb after donation of 10 (14.3%) donors was between 16-18g/dL, 46 (67.9%) had 13-15g/dL Hb and 12 (17.8%) donors had 11-12g/dL. Post donation count of RBCs among 29(42.9%) donor was between 5-6.3$\times 10^{12}$/l, 22 (32.1%) donors count was between 4-4.9$\times 10^{12}$/l and 17 (25%) donors had 3.2-3.7$\times 10^{12}$/ µl RBC count. Table 1

Mean pre and post donation HCT levels of donors was 40.71±6.03 and 38.09±8.25 respectively. Mean pre and post donation Hb levels of donors was 14.44 ± 1.85 and 13.84 ±1.90 respectively. Mean pre and post donation RBC levels of donors was 4.83 ± 0.79 and 4.56 ±0.85 $\times 10^{12}/l$ respectively. The difference was statistically significant (p-value=0.036) for HCT levels but insignificant for mean RBCs and Hb counts (p-value=0.057 & 0.064). Figure 1 and Table 2.

Table 1: *Frequency distribution of pre-post HCT, Hb and RBCs Values (n=68)*

Variables		Frequency	Percentage
Pre HCT	**<42**	05	7.1
	42-44	22	32.1
	>45	41	60.8
Post HCT	**<35**	08	10.7
	35-40	36	53.6
	>42	24	35.7
Pre Hemoglobin	**10-13**	12	17.8
	14-15	41	60.8
	16-18	15	21.4
Post Hemoglobin	**11-12**	12	17.8
	13-15	46	67.9
	16-18	10	14.3
Pre RBCs	**3.2-3.7**	12	17.8
	4.0-4.9	24	35.7
	5.0-6.3	32	46.5
Post RBCs	**3.2-3.7**	17	25.0
	4.0-4.9	22	32.1
	5.0-6.3	29	42.9

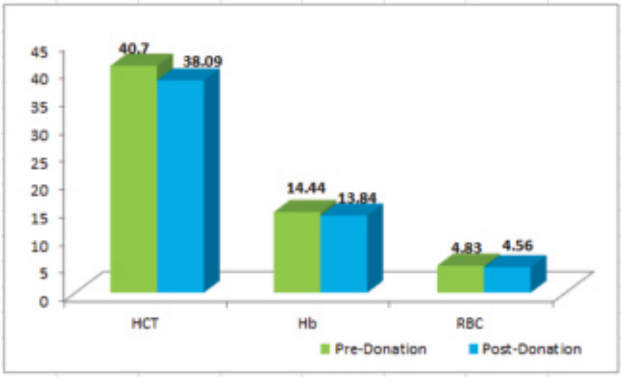

Figure 1: *Mean Change in HCT, Hemoglobin and RBCs among donors.*

DISCUSSION

Among 68 donors, pre donation HCT levels showed that 41(60.8%) donors had HCT level > 45%, 22(32.1%) had HCT levels of 42-44 % and remaining 7.1% had HCT <42%. Regarding pre donation hemoglobin (Hb) levels, 15(21.4%) had Hb levels in the range of 16-18 g/dL, 41 (60.8%) donors had Hb level of 14-15 g/dL and 12(17.8%) had 10-13 g/dL Hb levels. Among all the donors, 32 (46.5%) had RBCs count between 5.0-6.3$\times 10^{12}/l$, 24 (35.7%) had RBCs count of 4.0-4.9 $\times 10^{12}/l$ and only 12 (17.8%) had 3.2-3.7 $\times 10^{12}/l$. After 1 hour of donation HCT, Hb and RBC count of donors were measured. Changes in HCT were observed as 24(35.7%) donors had >42%, 36(53.6%) had HCT of 35-40% and 08 (10.7%) donors had HCT <35%. Hb after donation of 10 (14.3%) donors was between 16-18g/dL, 46(67.9%) had 13-15g/dL Hb and 12(17.8%) donors had 11-12g/dL. Post donation count of RBCs among 29 (42.9%) donor was between 5-6.3 $\times 10^{12}/l$, 22 (32.1%) donors count was between 4-4.9 $\times 10^{12}/l$ and 17 (25%) donors had 3.2-3.7$\times 10^{12}/l$ RBC count.

Mean pre and post donation HCT levels of donors was 40.71±6.03 and 38.09 ±8.25 respectively. Mean pre and post donation Hb levels of donors was 14.44±

Table 2: *Mean Comparison of HCT, Hemoglobin and Red Blood Cells (n=28)*

Variables	Pre-donation	Post-donation	p-value
Hematocrit	40.71 ±6.03	38.09 ±8.25	0.036
Hemoglobin	14.44 ±1.85	13.84 ±1.90	0.064
RBCs Count	4.83 ± 0.79	4.56 ±0.85	0.057

1.85 and 13.84 ±1.90 respectively. Mean pre and post donation RBC levels of donors was 4.83 ± 0.79 and 4.56 ±0.85 $\times 10^{12}/l$ respectively. The difference was statistically insignificant (p-value >0.05).

Platelet donation by plateletpheresis caused all three parameters i.e. hematocrit, hemoglobin, and erythrocyte count values to decrease.[13,14] In another study blood loss in apheresis procedures was mentioned to be small and insignificant; it even proposes that the 20-30mL of blood loss that the procedure entails is not significant in comparison with total blood donations, which lead to the loss of approximately 450 ml.[15,16] In our study, post donation parameters, i.e., Hb, Hct, RBC count, decrease is comparable with the studies conducted by Keklik et al., Tendulkar et al, Rajaddhyaksha et al, Das et al, Suresh et al and Garg et al.[15-19]

Seventy-eight (78%) of studies was published after 2000, showed that in countries like Colombia, as this type of donation has become more frequent in recent years, unmet demand has decreased from 10.9% in 2017 to 9.8% in 2018. This demonstrates both the current importance of apheresis donation and the need for research focused on its safety, given that it is one of the procedures that may be most often conducted in transfusion medicine. Pakistan is an emerging country in new technology so it is essential to educate people about its benefits and ensure them that this has no effect on them.

CONCLUSION

The plateletpheresis causes decrease in hemoglobin level and red cell count which is not so significant while decrease in hematocrit is significant statistically.

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VERESS NEEDLE VERSUS DIRECT TROCAR ENTRY FOR LAPAROSCOPY: A RETROSPECTIVE STUDY

Rehana Kanwal,[1] Shehla Baqai,[2] Iffat Hamid,[3] Quratulain Mushtaq,[4] Shazia Tufail,[5] Salma Sadia[6]

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Abstract

Background: The aim of this study is to compare the outcomes of veress needle entry versus direct trocar for laparoscopy in gynaecological surgery in relation to the complications encountered during each technique.

Methods: The present study was conducted on a retrospective basis from September '2017 to September 2020, in the dept of Obstetrics and Gynecology, in Hameed Latif Hospital. All the cases who underwent laparoscopic procedure during this time were taken into account including diagonostic laproscopy and operative both. In those patients traditional technique of veress needle entry was used for access were labeled as group -1 and in which direct trocar entry was dome were labeled as group-2. These two groups were compared in terms of the demographic profile, duration of procedure, previous h/o surgical interventions ,ease of performance and various complications encountered during the procedure.

Results: The total number of patients who underwent laproscopy during this period were 426, which were divided into two groups ,(veress needle entry group,group-1) 213 patients(50%), (direct trocar,group -2) 213 patients(50%).Duration of procedure was 4.5±1.2 min in group 1 which was significantly higher than group 2,2.2±0.8 min(p-value <0.001).Amount of gas required was greater in group 1, 4.9 ±1.3 lts as compared to group 2,2.4.0 ±0.3lts.

Conclusions: Direct trocar entry is as reliable as traditional technique for pneumoperitoneum establishment with veress needle in relation to complications time duration and ease of performance

Keywords: Pneumoperitoneum, Surgical Interventions, Veress needle

Over the last decade, a rapid increase has occurred in the laproscopic surgeons and operative laproscopic techniques although the complications of the laproscopic surgery range from minor injuries to major injuries[1)] access to the peritoneal cavity via small incision is challenging for a laproscopic surgeon. Creation of the pneumoperitoneum is the first and most critical step of laproscopic surgery as fifty percent of the injuries occur during the entry procedure into to the pneumoperitoneum cavity. Table 1 depicts the incidence of the major complications associated with the various techniques of the abdominal entries as reported in a review of different studies.[1-7]

1. Rehana Kanwal
2. Shehla Baqai
3. Iffat Hamid
4. Quratulain Mushtaq
5. Shazia Tufail
6. Salma Sadia

1,2,4,5. Department of Obs/Gynae, CMH Lahore Medical College,
3,6. Department of Obs/Gynae, Sharif City Medical College Lahore,

Correspondence:
Dr. Rehana Kanwal, *Associate Professor Obs/Gynae Dept. CMH Lahore Medical College, E-mail: drrehanakanwal136@yahoo.com*

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METHODS

The present study was conducted on a retrospective basis from September '2017 to September 2020, in the dept of Obstetrics and Gynecology, in Hameed Latif Hospital. All the cases who underwent laparoscopic procedure during this time were taken into account

Table 1: *Complication Rates Based on Technique of Abdominal Entry*

Technique	Complication Rate per 1 Thousand
Direct Trocar	0.61-1.1
Veress Needle	0.3-2.7
Open Laproscopy	0.6-12.0
First Trocar	1.9-2.7
Accessory trocar	0.8-6

including diagonostic laproscopy and operative both. In those patients traditional technique of veress needle entry was used for access were labeled as group -1 and in which direct trocar entry was dome were labeled as group-2. These two groups were compared in terms of the demographic profile, duration of procedure, previous h/o surgical interventions, ease of performance and various complications encountered during the procedure.

The total number of patients who underwent laproscopy during this period were 426, which were divided into two groups ,(veress needle entry group, group-1) 213 patients(50%), (direct trocar, group -2) 213 patients(50%).

Direct Trocar Entry Technique; after induction of general anesthesia patient is placed in the dorsal supine position with her legs in the Allen stirrups after draping incision is made in the umblicus wide enough 5mm to accommodate the diameter of sharp trocar 5mm. Anterior abdominal wall is elevated with left hand and trocar is held in right hand and the trocar is inserted at 90 degree angel with the controlled force and is moved forward in semi circular motion. Trocar is removed and in the canula laproscopy is inserted then intra peritoneal entry ascertained the pneumoperitoneum is created with CO_2. Then telescope is inserted by 2nd blind entry through the umbilicus with veress needle insito.

Veress Needle entry technique: In the same position and same setting as for trocar entry veress needle is inserted from the palmers point at 90 degree angel but no elevation of the anterior abdominal wall palmers test is applied to confirm intraperitonial entry then pneumoperitoneum created.

Pre op evaluation included age of the patient body mass index (BMI), prior surgical interventions, intra operative data collection included the time of umbilical incesion to the time of telescope removal in minutes , amount of gas required is in ltrs and all the major and minor complications during the procedures.

Statistical analysis was done between the two groups for all variables and P value was calculated and P value less than 0.05 was considered significant

RESULTS

Results were comparable in both techniques with less use of insufflation (CO_2) and less time duration so double blind entry is not superior to single blind entry and no difference of complication.

DISCUSSION

It is documented that significantly higher number of attempts are encountered in veress needle group compared to direct trocar insertion group and significant higher number of failed attempts in veress needle group compared to direct trocar insertion group where as complication rate is same.[8] So both methods are equally effective, safe and feasible for creation of Pneumoperitoneum during laproscopic surgery.[9]

Direct trocar entry is quick but comparable to

Table 2: Age Distribution of Patients

Age (Years)	Group 1	Group 2
20-25	42(19.7%)	30(14.0%)
26-35	62(29.1%)	60(28.1%)
36-45	85(39.9%)	96(45.0%)
>45	24(11.2%)	27(12.6%)
Total	213(100%)	213(100%)

Mean BMI of the patients in the both the groups was almost similar

Table 3: Distribution of patients according to BMI

MBI(Kg/m^2)	Group 1	Group 2
125-24.9	146(68.5%)	137(64.2%)
25-29.9	55(25.5%)	68(32.1%)
>30	12(6.0%)	8(3.7%)
Total BMI	213(100%)	213(100%)

Table 4: Duration of Procedure and gas use

	Group 1 Mean plus/minus SD	Group 2 Mean plus/minus SD	P - Value
Whole duration of procedure(min)	4.5±1.2	2.2±0.8	<0.0001
Gas use (liters)	4.9±1.3	2.4±0.5	<0.0001

Table 5: Previous Surgeries in both groups

Previous surgery	Group 1	Groups 2
LSCS	88(77.8%)	88(77.8%)
Previous Laparotomy	25(22.2%)	25(22.2%)
Total	113(100%)	113(100%)

Table 6: Minor complications encountered

Minor Complications	Group 1	Group 2	P Value
Periumbilical bruising	2(0.8%)	2(1.1%)	0.48
Port Site Bleeding	1(0.4%)	1(0.6%)	0.40
Multiple attempts	6(2.9%)	0(0%)	<0.001
Preperitoneal Insufflation	5(2.4%)	0(0%)	<0.001

veress needle technique in terms of complications.[10]

In one study the mean time required for veress needle technique technique was 6.92 minutes while by direct trocar entry it was 4.36 minutes. Complication rates was 18% in direct trocar entry and 16% with veress needle technique.[11]

Zakherah MS reported higher incidence of minor complications in Veress group as compared to Direct trocar entry group giving an incidence of 14% and 0.4% respectively which is comparable to Gunenc et al who reported complication rates of 15.7% and 3.3% with Veress and Direct trocar groups.[12,17] On the other hand, Jacobson M.T et al reported increased incidence of late minor complications such as abdominal wall ecchymosis, wound infection/discharge, granulation tissue formation, delayed healing, minor oozing or bleeding in the direct trocar entry group (2.04%) in contrast to (0.75%) in Veress needle group.[12-17]

CONCLUSION

In conclusion, direct Trocar entry is a safe alternative to the Veress needle entry technique for the creation of pneumoperitoneum. One of the main advantages of this technique is the reduced number of the blind insertions required to gain abdominal access. Other benefits are rapid creation of pneumoperitoneum, less gas use and decreased operating time. In laparoscopic surgeries, it is a more reliable and less time-consuming method.

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EFFICACY OF RISPERIDONE FOR THE TREATMENT OF PATIENTS PRESENTING WITH FIRST EPISODE OF SCHIZOPHRENIA AFTER UNSUCCESSFUL TREATMENT WITH OLANZAPINE

Maahin Rizwan,[1] Farasat Ali Dogar,[2] Fur Haider,[3] Shajeel Akhter[4]

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Abstract

Background: Schizophrenia is a mental illness in which early control of symptoms with antipsychotic treatment may yield better outcomes clinically. Several previous reports have suggested that olanzapine is efficacious and tolerated well by patients who are drug naive and have first episode schizophrenia. However, it has also been seen that some patients fail to respond to an initially prescribed olanzapine in first episode schizophrenia.

Objective: To determine the efficacy of risperidone for the treatment of patients presenting with first episode of schizophrenia after unsuccessful treatment with olanzapine.

Methods: 100 patients who fulfilled inclusion criteria were enrolled. Risperidone was started on a dose of 2mg and 4mg once at night and was increased to a maximum of 12mg in divided dose in 4-6 weeks' time. Patients were observed at 3 months interval for a change in BPRS scores and efficacy was labeled. Data was stratified for age, gender, socioeconomic status and educational status. Post stratification chi square test was applied and it was seen that none of these had any association with efficacy of risperidone as indicated by a p value of >0.05.

Results: The mean age was 34.99±11.21 years, 66% males and 33% females. Risperidone was efficacious in 55% patients. mean risperidone dose 5.82 ±2.226 mg and BPRS score 76.48±17.281 respectively. Risperidone was efficacious in 55% patients. 58% had low, 31% had middle and 11% had high socioeconomic status.

Conclusion: Risperidone is effective in treating patients with first episode schizophrenia.

Key Words: Anti psychotics, olanzapine, risperidone, schizophrenia, efficacy

Schizophrenia is a mental disorder involving abnormalities of thought, perception and changes in personality. Individuals suffering from schizophrenia are at high risk of having morbidity and mortality.[3] Effective treatment of first episode schizophrenia is very necessary because a rapid response to the treatment that has a good safety profile, can help in improving drug adherence.[1-7]

Literature has shown that schizophrenia progression occurs early and the plateau is reached during the first five years after first acute episode of psychosis[1]. Therefore, it has been seen that early control of symptoms with antipsychotic treatment during the initial stage of disease may yield better outcomes clinically, leads to shorter time to reach remission, greater quality of improvement, a decrease in the risk of relapse of psychosis, lesser negative symptoms and less cognitive impairment[2].

Usually it is seen that those patients who have first episode of schizophrenia are likely to respond well to the pharmacological agent compared to those

1. Maahin Rizwan
2. Farasat Ali Dogar
3. Fur Haider
4. Shajeel Akhter

1-3. Department of Psychiatry, Fatima Jinnah Medical University, Lahore.

Correspondence:
Dr. Maahin Rizwan, *Fatima Jinnah Medical University, Lahore.*

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who have chronic multiple episodes[4]. Apart from this, it has been seen that a lot of patients with first episode of schizophrenia stop their medication due to lack of efficacy or side effects related to the medication. Previous literature has shown that the rates of discontinuation of medication due to lack of efficacy are 9-48%.[1] These findings increase the need for the information about the treatment options in patients with first episode schizophrenia who had failed to respond to an initial trial of antipsychotic that has been prescribed. Frequency of efficacy of risperidone is 56.8%.[8]

Several previous reports have suggested that olanzapine is efficacious and tolerated well by patients who are drug naive and have first episode schizophrenia.[4] However, it has also been seen that some patients fail to respond to an initially prescribed olanzapine in first episode schizophrenia. A study conducted in the past revealed that 60% of the treating clinicians select risperidone as a second antipsychotic drug when olanzapine at optimal dose and for optimal duration fails to provide sufficient response.[5]

A lot of international research is being carried out for the evaluation of effectiveness of risperidone and a lot of comparison studies have been done too with other antipsychotics.[1-7] However, no such study has been conducted so far in Pakistan. Therefore, the rationale of the current study was to evaluate the efficacy of this antipsychotic i.e. risperidone in patients presenting with the first episode of schizophrenia who had failed to respond to an initial trial of olanzapine so that awareness can be created among treating psychiatrists regarding the effectiveness of a drug that will help in improving compliance, thus reducing the morbidity associated with schizophrenia. The objective of the study was to determine the efficacy of risperidone for the treatment of patients presenting with first episode of schizophrenia after unsuccessful treatment with olan-zapine.

METHODS

A descriptive case series was carried out at psychiatry department of Sir Ganga Ram Hospital Lahore from 24th May 2019 till 23rd February 2020. A sample size of 100 subjects were calculated from WHO sample size calculator keeping 95% confidence level and 10% margin of error and keeping expected percentage of efficacy of risperidone as 56.8%.[8] Subjects age 16-60 years of either gender of schizophrenia diagnosed by the presence of Hallucinations (any one of these i.e. auditory, visual, tactile, olfactory, gustatory), Delusions (any one of these i.e. persecutory, reference, control), Irrelevant talk for the last 1 month (presenting for the first time) were included in study through a non-probability / consecutive sampling. Patients who had other psychotic illnesses on multiple psychotropic medications, a serious medical illness or pregnant or lactating females were excluded from the study. The patients were assessed by adequate history at baseline. Risperidone was started on a dose of 2mg and 4mg once at night and was increased to a maximum of 12mg in divided dose in 4-6 weeks' time depending on the condition of the patient. Patients were observed at 3 months interval for a change in BPRS scores and efficacy labeled by an improvement in the Brief Psychiatric Rating Scale (BPRS) score of ≥40% from baseline at 3 months interval as assessed clinically. The data was be analyzed through SPSS version 17. Quantitative variable such as age, dose of risperi-done, BPRS score at baseline were presented as mean and standard deviation. Qualitative variable such as gender, efficacy, educational status and socioeconomic status were presented as frequency and percentages. Data was stratified for age, gender, socioeconomic status and educational status. Post stratification Chi square test was applied to deal with the effect modifiers and a p value of ≤0.05 was considered as significant.

RESULTS

A total of 100 patients who filled the inclusion criteria were enrolled. The mean age of the patient was 34.99 + 11.21 years. 66% males and 33% females (table 4). Risperidone was efficacious in 55% of the patients with first episode schizophrenia (Table no:1).

58% patients were of low socioeconomic status, 31% patients were of middle socioeconomic status

and 11% patients were of high socioeconomic status (table 6). Out of 100 patients, 33% were illiterate, 45% had studied till middle and 22% were educated till matric or higher (table 7). The mean dose of risperidone was 5.82+2.226 mg. The mean BPRS score was 76.48 +17.281.

Data was stratified for age, gender, socioeconomic status and educational status. Post stratification chi square test was used to assess statistical significance with demographic variables. There was no statistical association between demographic variables and efficacy for age, gender, education and socioeconomic status. ($p > 0.05$). (Table no:2).

DISCUSSION

The current study evaluated the efficacy of risperidone in patients who presented with first episode of schizophrenia and had previous failed treatment response to olanzapine. This study showed that risperidone was efficacious in 55% of the patients. The effect of age, gender, socioeconomic status and educational status was assessed on efficacy of risperidone and it was found that none of them had any significant effect on the efficacy.

Table 1: *Demographic and Clinical Profile of Subjects*

VARIABLES n=100	FREQUENCY	PERCENTAGE
Age Mean =34.99 ± 11.21 years		
18-30 years	51	51.0
31-45 years	35	35.0
46-50 years	41	41.0
Gender		
Male	66	66.0
Females	33	33.0
Educational status		
Illiterate	33	33.0
Middle	45	45.0
Matric/ Higher	22	22.0
Socioeconomic status		
Low	58	58.0
Middle	31	31.0
High	11	11.0
Efficacy		
Yes	55	55.0
No	45	45.0

Table 2: *Efficacy and Demographic Variable Cross Tabulation*

Variables n=100	Age groups	Efficacy		Total	P value
		YES	NO		
Age	18-30 years	30 (30.0%)	21 (21.0%)	51 (51.0%)	0.732
	31-45 years	18 (18%)	17 (17%)	35 (35.0%)	
	46-60 years	7 (7.0%)	7 (7.0%)	14 (14.0%)	
Gender	Male	37 (37.0%)	29 (29.0%)	66 (66.0%)	0.534
	Female	18 (18.0%)	16 (16.0%)	34 (34.0%)	
Education status	Illiterate	20 (20.0%)	13 (13.0%)	33 (33.0%)	.539
	Middle	25 (25.0%)	20 (20.0%)	45 (45.0%)	
	Matric / higher	10 (10.0%)	12 (12.0%)	22 (22.0%)	
Socio-ecnomic status	Low	34 (34.0%)	24 (24.0%)	58 (58.0%)	.652
	Middle	15 (15.0%)	16 (16.0%)	31 (31.0%)	
	High	6 (6.0%)	5 (5.0%)	11 (11.0%)	

The adherence to treatment of patients with schizophrenia is affected by the efficacy as well as tolerability of different atypical antipsychotics. It is still under debate that which antipsychotic is effective more compared to the others and have a good safety profile. In view of this, a study was carried out by Wang C et al.[7] to evaluate differences in efficacy, acceptability and safety profile of five atypical antipsychotics in patients who presented with first episode schizophrenia[7]. The authors enrolled 200 patients with first episode of schizophrenia who were drug naïve. The patients were assigned randomly one of the atypical antipsychotic for 6 to 8 weeks. The atypical antipsychotics that were included were aripiprazole, risperidone, quetiapine, olanzapine or ziprasidone. Brief Psychiatric rating scale was used to assess the efficacy of the drug after 6 to 8 weeks. The results revealed that there was significant decline in the score of Brief psychiatric rating scores by the use of all atypical antipsychotic. However, major decline in scores was seen in patients who received risperidone for 6 to 8 weeks in comparison to other drugs. There was no difference between all five atypical antipsychotics in terms of treatment discontinuation. Extrapyramidal side effects were noticed less in the groups receiving olanzapine and quetiapine also reported by several studies.[7,12-15] So, the authors concluded that risperidone

was more effective than other antipsychotics in the treatment of first episode schizophrenia. There was no difference in terms of discontinuation of treatment and adverse effects other than extrapyramidal side effects between all five groups. The current study revealed similar results in terms of efficacy of risperidone i.e. it was effective in treating patients with schizophrenia, who previously had a failed trial of olanzapine.[7,16,18-20]

Another study conducted by Cheng Z, et al[9,17] investigated the effectiveness and tolerability of aripiprazole, olanzapine and risperidone in patients who presented with first episode of schizophrenia. It was a randomized trial conducted in 6 medical centers of China[9]. Efficacy of risperidone, olanzapine and aripiprazole was assessed using the Positive and Negative Syndrome Scale (PANSS). Apart from it, tolerability and functioning was assessed too. The results showed that all of the three atypical antipsychotics were able to improve the score of PANSS at the end of the study. Risperidone in comparison to other two atypical antipsychotics had superior efficacy in lowering down scores of PANSS from baseline.[23-25] Largest weight gain was associated with olanzapine. Functioning and social performance was improved more with risperidone than with olanzapine and aripiprazole.[26] So, the authors concluded that due to improved efficacy and improvement in functionality and a good tolerability profile risperidone is a better choice than the other two atypical antipsychotics. Similar efficacy results were yielded by current study of risperidone.[9]

LIMITATION OF STUDY

The study had few limitations; firstly it was conducted at a single center so the results cannot be generalized, Secondly, the sample size was small so it cannot be applied to whole general population and lastly, the efficacy was assessed only in first episode of schizophrenia patients, however, it was not assessed in those presenting with chronic schizophrenia.

CONCLUSION

The current study concluded that risperidone was effective in treating patients who presented with first episode schizophrenia. Future studies must be carried out to evaluate the efficacy in patients with chronic schizophrenia and treatment resistant schizophrenia to reduce further morbidity. Comparison studies with other antipsychotics on a large number of sample population must be conducted to make recommen-dations for a single drug for treatment of schizophrenia.

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SCORING THE SEVERITY OF PULMONARY INVOLVEMENT IN COVID-19 PATIENTS DURING THE SECOND WAVE OF PANDEMIC BY USING HRCT

Rafia Irum,[1] Aneeza Qayyum,[2] Hira Bushra,[3] Saba Durrani[4]

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Abstract

Background: Covid-19 with its fast spread has been declared as a global medical emergencyaffecting almost the entire world including Pakistan. The World Health Organization (WHO) officially announced it as a pandemic in March 2020. In Pakistan the disease came under control in July 2020, when the Government on October 28, 2020 notified the nation about the second wave of Covid-19, keeping in view the rise in the number of cases among the local population.

Objective: The aim of our study was to determine the disease severity among the local population of Punjab during this second wave of pandemic by using this 25-point CT severity score, which can not only benefit the infected patientswithtimely effectivedisease management, but also ensure appropriate use of medical resources for this purpose.

Methods: This was a descriptive, Observational, Cross sectional study conducted in the Department of Radiology, Sharif Medical City Hospital, Lahore for 3 months after the approval by ethical review board. Cases of COVID 19 were included in the study as per the set inclusion criteria using 'Non-probability, consecutive sampling' technique.All patients of both genderfalling in the definitional criteria of 'Suspected', 'probable' or 'confirmed' case of COVID-19 Pneumonia irrespective of the age were included in the study.

Results: All 65 patients were classified as per the definitional criteria of 'Suspected', 'probable' or 'confirmed' case of COVID-19 Pneumonia irrespective of the age after written consent,and were sent for High Resolution CT scan of the chest – HRCT chest. The primary outcome was the severity of disease using HRCT scoring criteria. Difference of severity of COVID as per HRCT 25 point scoring was significant for age ($p < 0.0001$), gender ($p<0.001$), socioeconomic status of patients ($p=0.034$), fever ($p =0.013$), cough ($p=0.009$) and shortness of breath ($p < 0.0001$).

Conclusion: The aim of our study was to determine the disease severity among the local population of Punjab during this second wave of pandemic by using this 25-point CT severity score, which can not only benefit the infected patients with timely effective disease management, but also ensure appropriate use of medical resources for this purpose. Side by side our study can guide the medical and government authorities to take suitable steps for the local population depending upon the lethality of disease in the second wave. Moreover, this study will be additive to literature and will serve as a reference study for such more such episodes in future.

Key Words: Pulmonary, Covid-19, Second wave, HRCT

1. Rafia Irum
2. Aneeza Qayyum
3. Hira Bushra
4. Saba Durrani

1,2,4. Department of Radiology, Sharif Medical City Hospital, Lahore

3. Department of Radiology, Ch. Pervaiz Ilahi Institute of Cardiology Multan

Correspondence:
Dr. Rafia Irum, *Assistant Professor, Department of Radiology, Sharif Medical City Hospital, Lahore.*

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Covid-19 with its fast spread has been declared as a global medical emergency affecting almost the entire world including Pakistan. The World Health Organization (WHO) officially announced it as a pandemic in March 2020.[1] In Pakistan the disease came under control in July 2020,[2] when the Government on October 28, 2020 notified the nation about the second wave of Covid-19, keeping in view the rise in the number of cases among the local population.[3]

Pakistan being a third world country with limited resources and medical facilities this disease has posed a major threat among the local population. Although Covid-19 can affect any of the body organs, Pulmonary involvement has been identified as a main cause of morbidity and mortality in effected individuals.[4] HRCT Chest CT plays a key role in the diagnosis of Pulmonary disease in infected patients and also helps in determining the disease severity based on the proportion of Pulmonary involvement.[5] RSNA Consensus statement has described GGO with or without consolidation in a peripheral, posterior, and diffuse or lower lung zone distribution as typical CT findings in Covid-19 Pneumonia patients.[6] Several CT severity scores have been formulated to assess the burden of Pneumonia among Covid-19 patients, thus supporting the clinicians in their clinical judgment and ensuring effective timely management of patients.[7] Recently a study has found that 25-point CT severity score have positively correlated with the clinical severity of Pneumonia in Covid-19 patients.[8]

Table 1: Showing the Definitions of a 'Suspected', 'Probable' and 'Confirmed' Case of COVID 19

DEFINITION OF SUSPECTED CASE:[9]
Clinical Criteria:
Acute onset of fever (axillary temperature of more than 100.6 °F), cough and shortness of breath
Epidemiological Criteria:
Residing or working in an area with high risk of transmission of the virus anytime within the 14 working days prior to symptoms onset.
Or
Working in health setting, within health facilities anytime within 14 days prior to symptoms onset
DEFINITION OF PROBABLE CASES:
A person who meets the clinical criteria above and/or is a contact of a probable or confirmed case with **HRCT Chest** showing Multiple bilateral ground glass opacities, often bilateral peripheral and lower lung distribution.
DEFINATION OF CONFIRMED CASES:
A person with laboratory confirmation of Covid-19 Infection i.e PCR positive for COVID 19.

The aim of our study was to determine the disease severity among the local population of Punjab during this second wave of pandemic by using this 25-point CT severity score, which can not only benefit the infected patients with timely effective disease management, but also ensure appropriate use of medical resources for this purpose. Side by side our study can guide the medical and government authorities to take suitable steps for the local population depending upon the lethality of disease in the second wave.

METHODS

This was a descriptive, Observational, Cross sectional study conducted in the Department of Radiology, Sharif Medical City Hospital, Lahore for 3 months after the approval by ethical review board. Cases of COVID 19 were included in the study as per the set inclusion criteria using 'Non-probability, consecutive sampling' technique. All patients of both gender falling in the definitional criteria of 'Suspected', 'probable' or 'confirmed' case of COVID-19 Pneumonia irrespective of the age were included in the study. The primary objective of this study was to determine the degree of pulmonary involvement by using HRCT in suspected and diagnosed cases of COVID-19 patients that admitted directly from the OPD or Emergency in our setup during the second wave of pandemic.

Table 2: Showing 25-Point CT Severity Scoring for COVID 19 using HRCT

25-Point CT severity Score:	
Objective visual assessment by two observers of each lung lobe for the degree of involvement and classified as:	
0 or <5% involvement- score of 0	0
5–25%	1
26–50%	2
51–75%	3
>76% score	4
Total severity score will be then calculated by summing scores of all five lobes scores ranging from 0–25	
Total score:	**Severity**
7 or less	Mild
8-17	Moderate
18 or more	Severe

Covid-19 Pneumonia was defined as an acute viral pneumonia caused by corona virus. All those patients with an HRCT Chest not suggestive of Covid-19 Pneumonia as per reporting of an unbiased consultant radiologist were excluded. Similarly, those patients of pneumonia who are diagnosed as a Non-Covid-19 Pneumonia or those previously diagnosed with Covid-19 Pneumonia and still coming on follow up were also excluded.

All patients admitted with suspected COVID were sent for High Resolution CT scan of the chest – HRCT chest, though which 1 to 2 mm thin slices with high spatial frequency algorithm generate exquisite lung details. Typical CT Findings of Covid-19 Pneumonia include: Bilateral, peripheral, and basal predominant ground-glass opacities (GGOs) with or without consolidation. Ground-glass opacification / opacity (GGO) was defined as an area of increased attenuation with preserved bronchial and vascular markings. Consolidation was defined as increased lung attenuation with loss of vascular markings and air bronchogram.

After approval from Institutional Review Board (IRB), all the patients fulfilling the inclusion criteria who presented to the Radiology Sharif Medical City Hospital for HRCT Chest were selected. HRCT were performed using Toshiba Aquilion16 slicer CT, with the patient in prone position.

HRCT images were collected and assessed by two experienced consultant radiologist for the presence or absence of typical findings of Covid-19 pneumonia as described by RSNA Consensus statement. Disease severity score was evaluated using a 25-point CT severity score (table no. 2). Each lung lobes was visually scored as 0 to 5, with 0 indicating no involvement and 5 indicating more than 75% involvement. Total CT score will be determined as the sum of involvement of each lobe, ranging from 0 (no involvement) to 25 (maximum involvement)

Collected data was analyzed by using SPSS 24.0. Data will be stratified in age groups, gender and socio-economic status. Mean and standard deviation was calculated for age, weight, BMI, total severity score. Frequency and percentage was calculated for gender, socioeconomic status and for each CT severity score i.e. mild, moderate and severe. Chi square test was used to compare the CT severity score with gender, socio-

Table 4: *Showing the Severity of the Disease as per HRCT Creteria*

SEVERITY OF DISEASE AS PER HRCT 25-POINT SCORE	Score		N	%
	7 or less	**Mild**	31	47.7
	8-17	**Moderate**	20	30.8
	18 or more	**Severe**	14	21.5

Table 3: *Showing the Details of all the Variables Noted in the study is Relation to the Severity of the Disease*

SR.	VARIABLE		N	%	Mild	Moderate	Severe	P - Value
1	**AGE GROUPS**	20 to 30 yr	2	3.1	2	0	0	0.0001
		31 to 45 yr	9	13.8	9	0	0	
		46 to 60 yr	23	35.4	12	10	1	
		> 60 yr	31	47.7	8	10	13	
2	**GENDER**	Male	48	73.8	28	9	11	0.001
		Female	17	26.2	3	11	3	
3	**SOCIO ECONOMIC STATUS**	Poor Class	2	3.1	0	0	2	0.034
		Middle class	33	50.8	16	13	4	
		Upper class	30	46.2	15	7	8	
4	**FEVER**	Yes	57	87.7	29	14	14	0.013
		No	8	12.3	2	6	0	
5	**COUGH**	Yes	55	84.6	30	13	12	0.009
		No	10	15.4	1	7	2	
6	**SHORTNESS OF BREATH**	Yes	39	60.0	6	19	14	0.0001
		No	26	40.0	25	1	0	
7	**CASE DEFINATION**	Suspected	37	56.9	23	10	4	0.038
		Probable	8	12.3	2	4	2	
		confirmed	20	30.8	6	6	8	

economic status and presence or absence of chronic illness in patients. Student T- test was used to compare CT severity score among the different age groups and gender. A $p<0.05$ was considered statistically significant.

RESULTS

In this descriptive Cross sectional study conducted in the Department of Radiology, Sharif Medical City Hospital, Lahore for 3 months after the approval by ethical review board, 65 cases of COVID-19 were included in the study as per the set inclusion criteria using 'Non-probability, consecutive sampling' technique.

All 65 patients were classified as per the definitional criteria of 'Suspected', 'probable' or 'confirmed' case of COVID-19 Pneumonia irrespective of the age after written consent, and were sent for High Resolution CT scan of the chest – HRCT chest. The primary outcome was the severity of disease using HRCT scoring criteria.

Among these 65 patients, 2 of 65 (3%) were less than 30 years old, 9 of 65 (13.8%) were of age 31 to 45 years, 23 (35.4%) were of 46 to 60 years and 31 (48%) were of old age (more than 60 years). Male to female ratio of patients was 3:1 with 74% males (n = 48) and females 26% (n = 17).

Among the patients coming for HRCT due to COVID enrolled in the study, almost all were of middle or upper socioeconomic class. Fever, cough and shortness of breath was seen in 87.7% (n = 57), 84.6% (n = 55) and 60% (n= 39) out of 65 patients included in study.

At the time of HRCT these patients were categorized into suspected COVID case, probable and confirmed as a per the operational definition by an unbiased attending consultant blinded to the study. Data analysis showed that of 65 patients suspected, probable and confirmed cases were 37, 8 and 20, respectively, as shown in the table no. 3.

Severity of the second wave of COVID -19 was accessed using the 25-point severity score and patients were categorized into mild, moderate and severe disease. Details are shown in table no 4. Mild disease was seen in 31 (47.7%), moderate disease in 20 (30.8%), and severe 14 (21.5%).

Data of the primary outcome was stratified for various age groups, gender, socioeconomic status, and various symptoms like fever, cough and shortness of breath, and post-stratification chi square test was applied. Difference of severity of COVID as per HRCT 25 point scoring was significant for age ($p < 0.0001$), gender ($p<0.001$), socioeconomic status of patients ($p = 0.034$), fever ($p = 0.013$), cough ($p = 0.009$) and shortness of breath ($p < 0.0001$).

DISCUSSION

The COVID-19 pandemic has led to terrible medical and economic implications. The severity of COVID-19 is mostly determined by the degree of pulmonary involvement. Since the beginning of the pandemic, the role of chest CT imaging in the treatment of COVID-19 patients has evolved. The description of CT scan findings, usage of chest CT imaging in various acute and sub-acute situations, and its value in predicting chronic illness have all been improved.[10]

In our study, out of 65 patients, 3% were <30 years of age, 13.8% of 31 to 45 years, 35.4% of 46 to 60 years and 48% of old age. Male to female ratio of patients was 3:1, almost all were of middle or upper socioeconomic class. Fever, cough and shortness of breath was seen in 87.7% (n = 57), 84.6% (n = 55) and 60% (n= 39) patients. At the time of HRCT these patients were categorized into suspected, probable or confirmed case (as shown in the table no. 3). Severity of the second wave of COVID -19 was accessed using the 25-point HRCT severity score into mild, moderate and severe. Mild disease was seen in 47.7%, moderate in 30.8%, and severe in 21.5%. All the patients with severe disease were admitted in the ICU.

In a study done in Bangladesh, Hossain MI, et al[11] revealed that after analyzing data from COVID patients, total lung involvement on HRCT chest of all the patients enrolled in the study was 43.9 ± 19.9%, and half of the total cases had mild to moderate lung involvement. Around 500 cases enrolled, ICU admission rate was only 25%. In a similar study from Bangladesh, lung involvement was reported to be 33.4± 10.5% around 30% cases showed mild lung involvement.[12] Oliveira

et al[13] reported this percentage to be 30% in Florida. Similar studies of our region reported the ICU admission rate of less than 10%.[14,15]

The average age of COVID patients enrolled was 44.2 11.9 years, with just around one-fifth being female. Data analysis revealed that 22 percent of individuals had no lung involvement. According to the HRCT severity score among the total 699 positive cases of COVID, 47 percent of patients had mild illness, 44.2 percent had moderate disease, and 8.8 percent had severe lung involvement. The CT severity score was observed to be associated with lymphopenia, elevated serum CRP, d-dimer, and ferritin levels (p 0.0001). Oxygen needs and length of hospital stay increased as scan intensity increased. They came to the conclusion that this 25-point HRCT severity grading system corresponds well with COVID-19 clinical severity. Our findings imply that a chest CT rating system can help predict COVID-19 disease prognosis and has a strong correlation with lab tests and oxygen needs.[8] A 22 percent ICU admission rate was seen in this study. The greatest results were connected with negative and milder HRCT findings, whereas individuals with more severe HRCT score scans had a higher mortality rate. Around 5% of those scanned in the moderate group died, while 23% died in the severe group.

Similar to that reported in our study, studies have reported that males had severe COVID disease as measured by the HRCT score. According to several researches, this difference of severity between genders might be attributable to a variety of variables, including behavioral differences and the potential protective impact of oestrogen. [16]

In a study done in South Asia on COVID patients, it was concluded that elderly patients were more impacted during the second wave, and the fatality rate was also greater than in reported in earlier studies. Cough and fever were the most prevalent symptoms, while HTN and diabetes were the most common co-morbidities. The percentage of lung involvement was greater than that reported in first wave, and the major characteristics related with death were old age, the co-existence of CKD, and the need for ICU care.[11]

In a local study done during first wave, HRCT scan was done in only confirmed cases of COVID and data collection showed that ground glass opacity was the most common (in 88.5% cases), consolidations in 53%, with majority showing bilateral and peripheral involvement of the lungs. Most commonly superior parts of lower lung lobes were involved. According to the CT-Severity Scoring, 90% were mild 7% were min moderate category, and only around 3 % patients had severe COVID disease.[5] This was different then that reported in our study during the 2nd wve of COVID. They concluded that HRCT scoring can be very helpful in categorizing COVID pneumonia into mild, moderate, and severe, especially in setups of under-developed and developing countries requiring a faster triage process.

This study has significant limitations, including the need for a larger multicenter sample to improve the accuracy of the findings and the fact that assessing disease severity on HRCT scans can be subjective. Finally, additional variables that may influence illness outcome, such as lifestyle and reliance on self-reporting/underreporting of comorbidities, should be evaluated. A future comparative research is needed to investigate the link between increasing lung HRCT participation and increased ICU requirement in management of COVID.

CONCLUSION

The aim of our study was to determine the disease severity among the local population of Punjab during this second wave of pandemic by using this 25-point CT severity score, which can not only benefit the infected patients with timely effective disease management, but also ensure appropriate use of medical resources for this purpose. Side by side our study can guide the medical and government authorities to take suitable steps for the local population depending upon the lethality of disease in the second wave. Moreover, this study will be additive to literature and will serve as a reference study for such more such episodes in future.

Conflict of Interest *None*

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EFFECTIVENESS OF TREATMENT WITH RIFAXIMIN PLUS LACTULOSE VERSUS LACTULOSE ALONE FOR HEPATIC ENCEPHALOPATHY DUE TO CHRONIC LIVER DISEASE

Rana Muhammad Arif,[1] Muhammad Aftab,[2] Muzammal Aslam Kataria,[3] Muhammad Shahid[4]

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Abstract

Background: Hepatic encephalopathy (HE) is the syndrome of disordered consciousness and altered neuromuscular activity that is seen in patients with acute or chronic hepatocellular failure or porto systemic shunting. Rifaximin is an antibiotic drug that is absorbed in small amounts and has high concentration in GI tract, its spectrum of activity is wide.

Objective: To determine the efficacy of treatment with rifixaimin plus lactulose versus lactulose alone for hepatic encephalopathy due to chronic liver disease among patients admitted at a tertiary care hospital.

Methods: One hundred and twenty patients of hepatic encephalopathy were taken. They were divided into two groups of sixty each. Sixty patients labeled as group A were given lactulose plus Rifaximin; Second group of sixty patients labeled as group B and were given lactulose only.

Results: The mean age of patients in Group A (Rifaximin plus Lactulose) was 55.75+ 6.92 years, while the mean age for patients in Group B (Lactulose alone) was 55.82 + 7.32 years. In Group A 60.0%(n=36) and in Group B 55.0% (n=33) were male. In Group A 75% (n=45) patients and in Group B 58.3% (n=35) patients clinically improved. ($p < 0.05$).

Conclusion: Rifaximin Plus Lactulose is better in managing new onset HE in individuals suffering from fibrosis of liver versus conventional treatment by lactulose alone.

Keywords: Cirrhosis of liver, Acute hepatic encephalopathy, Reversal, Rifaximin, Efficacy

Hepatitis B virus (HBV) and hepatitis C virus (HCV) are amongst major causes of hepatic ailments especially of extreme severity, some of these are liver cirrhosis and Hepatocellular carcinoma.[1] According to WHO approximately 350 million individuals with prolonged HBV and 170 million individuals with long-standing HCV are present across the world with annual mortality of 563,000 and 366,000 respectively.[2] Pakistan is one of the countries which are severely affected with these infections in 4.8% population.[2] About 20–30% of patients develop fibrosis in a period of 20 years and on development of fibrosis or scarring, problems like portal hypertension, bleeding from GI tract, Porto-systemic encephalopathy, collection of fluid in abdomen and liver cancer start occurring commonly.[3,4] Reduction in intestinal bacteria that produce ammonia remains the major target in patients with hepatic encephalopathy. Oral metronidazole and neomycin have been effectively used to serve this purpose. Side effect profile of these drugs is major limitation in their use.

Some poorly absorbed antibiotic with no systemic manifestations may be used. Rifaximin is thought to be prototype in this kind. Many researches showed better and fast recovery in signs or symptoms of hepatic encephalopathy during treatment with rifaximin than with disaccharides that cannot be absorbed. Patients who received rifaximin needed less time of admission

1. Rana Muhammad Arif 2. Muhammad Aftab
3. Muzammal Aslam Kataria 4. Muhammad Shahid
1-4. *Allama Iqbal Medical College/Jinnah Hospital Lahore.*

Correspondence:
Dr. Rana Muhammad Arif, *Jinnah Hospital Lahore. Medical Unit 5, E-mail: rana.arif202@gmail.com*

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in hospital, and hence lesser hospital bills than patients who were treated with lactulose.[5] There are contradictory results in other studies. For example, 103 patients in total, having stage I–III new onset hepatic encephalopathy were randomly allocated for having rifaximin (50 patients, 1100 mg/day) or lactulose (53 patients, 60 g/day) for a duration of five to ten days. This study showed that both drugs are having equal i.e. 81.6% patients receiving rifaximin and 80.4% patients being given lactulose exhibited recovery.[6] One more study showed rifaximin to be 58% effective.[9] A meta-analysis of 5 randomized controlled trials compared the effectiveness of rifaximin with other anti-microbial drugs, and concluded that rifaximin (n=68) had same efficiency as of neomycin or paromomycin (n=60, neomycin or paromomycin) (OR=2.77, 95%CI: 0.35-21.83, P=0.21),7 but a current mathematical model has suggested that starting treatment with disaccharide alone and then adding rifaximin to it will help in reducing burden of cost to patient.[8]

Many studies from European population have concluded that rifaximin is effective in treatment of acute hepatic encephalopathy[5] and is highly well tolerated but some studies don't prove the use.[6,7] Similarly scarce data is available for Pakistani population. Pakistani population has its own specific dietary habits, gut flora, and environment. The current study aims to evaluate the role of rifaximin in remission of acute hepatic encephalopathy.

METHODS

A Randomized Controlled Trial was conducted at Medical Unit 1 and 3, Jinnah Hospital, Lahore over a period of one year. Sample size of 120 cases (60 in each group) was determined by 95% confidence level, 5% margin of error and considering anticipated effectiveness of rifaximin plus lactulose as 76% compared to lactulose alone as 50.8% through a purposive non-probability sampling. Subjects with age 30 to 80 years of both gender, Unconscious patients not responding to verbal stimuli or patients with altered sensorium i.e. opening eyes on verbal stimuli but not able to perform simple addition or subtraction and evidence of coarse liver on ultrasonography labeled as hepatic encephalopathy due to chronic liver disease were included in the study. Individuals who are known to have lactulose intolerance, having hypersensitivity to rifaximin determined by history and medical record or patients with Glasgow coma scale < 5 determined by clinical examination were excluded. An informed consent was taken from them before making them part of study. Information regarding their demographic data was noted in the performa. Baseline CBC, LFT's, RFT, Serum Electrolytes, PT INR & Abdominal ultrasound done. MELD score was also estimated. Individuals were randomized in two clusters by using lottery method: Group A patients were given lactulose 30 ml thrice a day and rifaximin 550 mg per oral twice a day while group B was given only lactulose 30 ml per oral thrice a day. They were kept under observation and their mental state was assessed 48 hours after initiation of the therapy. All the patients were asked to give answer of three simple mental mathematical calculations of subtraction and addition. A patient able to perform all the three calculation was labeled as out of encephalopathy and treatment was labeled as effective. The results were noted in the Performa. Data was entered and assessed by the SPSS version 23. Mean with standard deviation was calculated for quantitative variables like age. Frequency and percentages in case of categorical variables like gender and efficacy. Chi square test was used for finding significance of change. A p value less than 0.05 was considered significant.

RESULTS

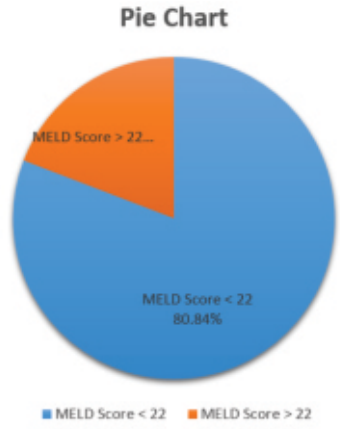
Age distribution of the patients was studied which showed that mean age of all patients in both groups was 55.78+7.09. The mean age of patients in Group A (Rifaximin plus Lactulose) was 55.75+ 6.92 years, while the mean age for patients in Group B (Lactulose) was 55.82 + 7.32 years. (Table no:1) Gender distribution of the patients was carried out and expresses that 60%(n=36) in Group A (Rifaximin plus Lactulose) and 55%(n=33) in Group B (Lactulose) were male and 40%(n=24) in Group A (Rifaximin plus Lactulose) and 45%(n=27) in Group B (Lactulose) were females.

(Table No. 1). In group A (Rifaximin plus Lactulose) fifty-five patients were positive for anti HCV and five patients were positive for hepatitis B surface antigen. In group B (Lactulose) fifty-four patients were found positive for anti HCV and HBsAg was positive in six patients. Patients were also categorized according to MELD Score. Out of total 120 patients, 80.84% (n=97) patients were having MELD score less than 22 and 19.16% (n=23) patients were having MELD score greater than 22. (Figure no:1)

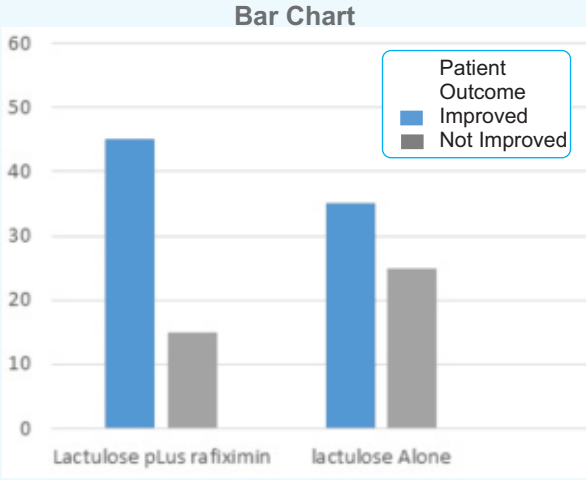
In Group A (Rifaximin plus Lactulose) 75% (n 45) patients and in Group B (Lactulose) 58.3% (n=35) patients clinically improved ($p<0.05$). (Graph No.1). Total patients having MELD Score less than 22 were 80.84% (n=97) and out of these 77.31% (n=75) clinically improved while total patients having MELD score greater than 22 were 19.16% (n=23) and out of these 21.73% (n=5) clinically improved ($p<0.001$). (Graph No: 2)

Table 1: *Age and Gender distribution of the Patients*

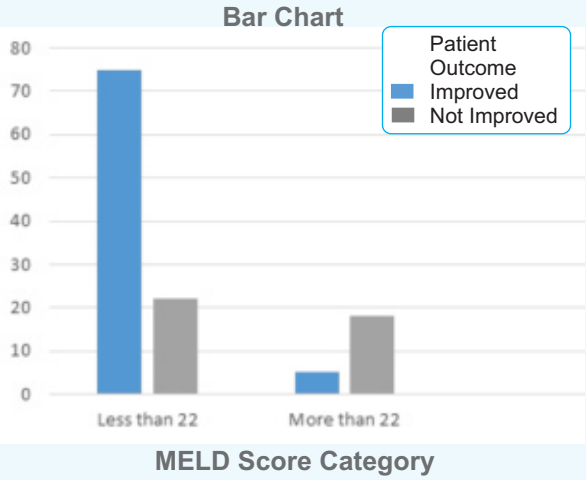
Variables	Group	
	Group A (n=60) Rifaximin Plus Lactulose	Group B (n=60) Lactulose
Age Mean (SD)	55.75 (6.92)	55.82 (7.32)
< 45 years	15 (25.0%)	12 (20.0%)
> 45 years	45 (75.0%)	48 (80.0%)
Gender		
Male	36(60.0%)	33(55%)
Female	24(40.0%)	27(45%)
Total	60(100.0%)	60(100.0%)



Graph 1: *Patient Distribution According to MELD Score*



Graph 2: *Treatment Outcome*



Graph 3: *Treatment Outcome according to MELD Category*

DISCUSSION

Hepatic encephalopathy is a serious condition occurring because of failure of liver to function and affecting central nervous system severely. The pathology involved is not clearly known, although, raised blood levels of ammonia are thought to be associated with causation.[9]

Many therapies are aimed at reduction in number of episodes of hepatic encephalopathy by decreasing concentration of nitrogenous compounds in GI tract like ammonia ,this is in line with hypothesis that HE occurs due to deposition of toxins formed in GI tract

affecting nervous system in body particularly ammonia, in patients suffering from liver failure and portosystemic shunting.[10] Rifaximin is a drug that is absorbed to a small quantity from GI tract, has good antibiotic function, covers wide variety of organisms and concentrates and has low chance of developing resistance.[11]

Many researches for European population have recommended that rifaximin plus lactulose is having good efficacy in treatment of new onset hepatic encephalopathy[5] and is highly acceptable by most authorities but some researches do not found it superior to lactulose.[6,7,12] Similarly scarce data is available for Pakistani population. Pakistani population has its own specific dietary habits, gut flora, and environment, however, the recent research has objective to evaluate the use of rifaximin plus lactulose in remission of acute hepatic encephalopathy.

In this study, Age distribution of the patients was studied which showed that mean age of all patients in both groups was 55.78+7.09. The mean age of patients in Treatment with Rifaximin plus Lactulose was 55.75 + 6.92 years, while the mean age for patients underwent treatment with Lactulose alone was 55.82+7.32 years. The current study concluded that 75 %(n=45) in treatment group and 58.33%(n=35) in control group were treated effectively, while remaining 25%(n=15) in treatment group and 41.66%(n=25) in control group were not managed in an effective manner, p value was determined as < 0.05, which shows statistically significant difference. The above findings are in agreement with a study conducted on 120 patients of HE, out of affected individuals, 76% in Rifaximin Plus Lactulose in comparison with 50.8% on lactulose alone who had total reversal of hepatic encephalopathy, with P Value <0.0466. In another study conducted on 130 patients in Pakistan, there was reversal of hepatic encephalopathy in 58.46% patients in cluster taking only lactulose and 67.69% in Rifaximin plus Lactulose group (P Value=0.035), after ten days of follow-up.[7]

Findings suggest that treatment with rifaxamin in addition to lactulose is better than treatment with lactulose only in reversal of hepatic encephalopathy, and the difference is also statistically significant. Moreover, rifaximin plus lactulose therapy was more effective in patients with MELD Score less than 22.[14-18] Lastly, safety of prolonged use of Rifaximin in individuals having hepatic fibrosis still an issue to be considered. Certainly, the raised Rifaximin absorption in patients with liver cirrhosis remarkably increases its level in plasma and this is associated with a number of side effects.[7] Furthermore, a few cases of C. difficile colitis in patients taking rifaximin treatment for long time are documented,[13] and chances of resistance by other bacteria will recommend that care should be taken for recommendation of prolonged rifaximin treatment in patients with hepatic encephalopathy.[2] In light of the above analysis the hypothesis of the study that "Rifaximin plus lactulose is a better treatment in reversal of acute hepatic encephalopathy in cirrhotic patients versus treatment with Lactulose alone" is well justified as we found statistically important difference with P Value < 0.05. These findings have also been supported by other studies on this at different other hospitals.[19,20]

CONCLUSION

We concluded that Rifaximin plus lactulose treatment is better in reversal of acute hepatic encephalopathy in cirrhotic patients as compared to conventional treatment with lactulose alone and this difference is also statistically significant.

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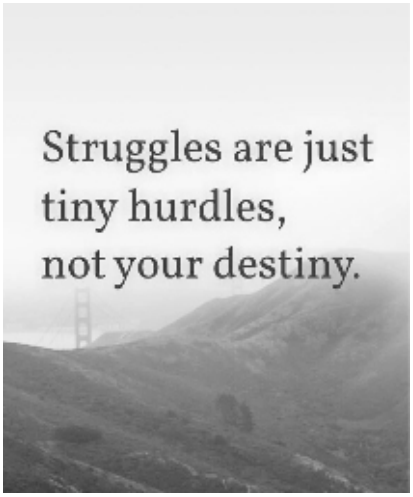

COMPARISON OF DENTAL PHOBIA AMONG PAKISTANI DENTAL STUDENTS WITH & WITHOUT CLINICAL EXPERIENCE, USING CORAH'S DENTAL ANXIETY SCALE

Ayesha Fazal,[1] Faiza Siddiqa,[2] Benish Mehmood,[3] Nazim Farooq,[4] Mariam Babar,[5] Anoosha Tariq[6]

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Abstract

Background: Dental phobia is an obsession also called as dental anxiety or dental fear. Dental phobia may develop by noticing painful procedures or listening about them from other people. It may also affect relationship among dentists and patients. The objective of present study is to compare levels of Dental phobia in dental students with & without clinical experience in dental college of Pakistan using CORAH'S Dental anxiety scale.

Methods: A cross sectional study was conducted, using Non-probability convenient sampling. Sample size calculated was 259 using Cochran's formula for smaller population. Norman's Corah Dental Anxiety Scale (DAS) questionnaires, English version was used to assess different levels of anxiety among dental students. Independent samples t-test was used to determine level of anxiety associated with different dental procedures among non- clinical & clinical dental students.

Results: Total anxiety levels in non- clinical students was found to be high (9.66±3.11) than in clinical students (9.04±3.07). Statistical significance was found between the two groups, with few exceptions like pre-procedural feelings, injection, gagging, RCT, extraction, panic attacks & worried about extensive treatments (P-value <.05). Phobia associated with Root canal treatment & extraction was found to be high in non- clinical as well as clinical students. However, phobia associated with gagging was more in clinical students. Panic attacks was found to be less in non- clinical & clinical students.

Conclusion: Non-clinical students were found to be more phobic to dental procedures. Counselling sessions & training is suggested for non-clinical students regarding different dental procedures.

Key Words: Dental anxiety, dental phobia, clinical students, pre- clinical students

Dental phobia is an obsession also called as dental anxiety or dental fear. Dental anxiety can be defined as unfounded or exaggerated worries or response by an individual when it's time for their appointment for dental treatment and can affect any age, sex or social status.[1] High prevalence of dental anxiety is found in patients & prevalence increases with increase age.[2] Dental anxiety is found in both, dental students and patients and is found to be higher in patients. It may affect dentist as well as it increases the level of dentist's stress during treatment provision[3] Although dental anxiety and dental phobia are the terms which can be used interchangeably, but some studies showed a slight difference between the two. Dental phobia is considered to be more serious and life threatening than the anxiety.[4] Dental anxiety is found to be 20% and is more prevalent in general population than dental

1. Ayesha Fazal
2. Faiza Siddiqa
3. Benish Mehmood
4. Nazim Farooq
5. Mariam Babar
6. Anoosha Tariq

1. *Department of General Pathology and Microbiology Department, Margalla Institute of Health Sciences (MIHS), Rawalpindi.*
2. *Department of Community Dentistry, Margalla Institute of Health Sciences (MIHS), Rawalpindi*
3. *Department of Community & Preventive Dentistry, NUMS, Rawalpindi*
4. *Islamabad College of Physiotherapy, Margalla Institute of Health Sciences (MIHS), Rawalpindi*

5,6. *Margalla Institute of Health Sciences*

Correspondence:
Dr. Benish Mehmood, *Associate Professor, Community & Preventive Dentistry, NUMS, Rawalpindi.*
E-mail: benishmehmood@hotmail.co.uk

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phobia which is 5%.[5] Odontophobia is another term used for dental phobia which is caused by many factors such as sound of drill, fear of being injured, and injection phobia; associated with some past dental experience. The literature review revealed that local anesthetic injection, and then teeth drilling is the most anxious of all dental situations.[6] Dental phobia may develop by noticing painful procedures or listening about them from other people.

Research study, conducted in India reported 94% prevalence of dental phobia among patients.[7] The prevalence was higher compared to studies done by Fotedar et al. (29%),[8] and Madfa et al. (63%).[9] The reason behind distraction from necessary treatment and postponed appointment is fear of the dental appointment, which affect the patient both psychologically and physically leading to more invasive type of treatment.[10,11] Higher anxiety level also leads to lack of cooperation from patient which ultimately affects the treatment procedure.[12] For the behavior management of patient, the reason of fear should be known which has become a difficulty in the administration of the patient, which can also reduce dental prevention, especially in children and young people.[13]

Fear of getting dental treatment is even lesser in senior dental students than the juniors.[14] Due to lack of proper educational sessions on oral hygiene maintenance, dental anxiety rate is considerably high in non- medical students residing in universities.[15] It was found to be more even in students with non-medical background. Local anesthesia and drilling procedures of teeth were most profoundly associated with the dental phobia among the students with non-medical background.[16] Prevalence of dental phobia among both, the medical as well as dental students was found to be high. But astonishingly, it was found to be more in dental students. One of the reason of which could be that the medical students might be unaware of the dental procedures. Dental phobia was found to be more common in female dental students less than 20-year age group.[17] Females were more phobic of different dental procedures, such as local anesthetic procedures.[18] While comparing different dental fears and phobias among the general public, it was found that dental fear was least common with the prevalence of 24.3%, preceding other fears that is, fear of snakes, heights and physical injuries. But while considering phobias, dental phobia was most common among all i.e. 3.4%, followed by others like height phobia and spider phobia.[19]

In Malaysia, dental students were found to be more anxious (96%) than their medical colleagues (90.4%). Overall prevalence rate was found to be 90% which is quiet high.[20] High prevalence of dental anxiety among dental care seekers yielded patients with negative behaviors in their persuasion towards dental treatment and offers dental treatment more difficult to achieve it auspiciously. Dental anxiety may also affect relationship among dentists and patients.[21] Although high prevalence of dental phobia has been found among the dental students as well as the general public, no such literature could be found in the current area of study. Therefore, this cross sectional study was carried out to compare dental phobia among dental students of Pakistan with & without clinical experience.

METHODS

The study was approved by Ethical review committee of Margalla Institute of Health Sciences, Rawalpindi. (Reference number: FS/69/19). An informed consent was obtained by each participant enrolled in the study. A cross sectional study was conducted at Margalla Institute of Health Sciences, Rawalpindi over duration of five months, from May to September 2019. Non probability convenience sampling method was employed. Sample size calculated was 259 using Cochran's formula for smaller population, when $\alpha = 0.05$ at the test level.

Norman's Corah Dental Anxiety (DAS) Questionnaire, English version developed in 1969 was used to assess different levels of anxiety among dental students. This questionnaire comprised of four items. Each question had five options, ranging from 'A' to 'E'. 1 point was given to option 'A', 2 for 'B', 3 for 'C', 4 for 'D', and 5 points for option 'E'. Option 'A' indicated minimum anxiousness, while option 'E'

indicated maximum anxiety. Scoring of different levels of anxiety ranged from: 4-8: no anxiety, 9-12: moderate levels of anxiety, 13-14: high levels of anxiety, 15-20: severe levels of anxiety. The questionnaire was distributed to the participants at the end of the lecture. Data being collected was kept confidential. Socio-demographic data like age, gender and year of education was also included in the questionnaire.

The data was analyzed using SPSS version 21.0. Independent samples t-test was used to determine the level of anxiety among non- clinical and clinical dental students.

Table 1: *Total Anxiety Levels in Non- Clinical and Clinical Dental Students*

	NON- CLINICAL			CLINICAL		
	Mean ± SD	**Mean difference**	**p-value**	**Mean ± SD**	**Mean difference**	**p-value**
Total anxiety levels	9.66±3.11	.62	.10	9.04±3.07	.62	.10

Table 2: *Dental phobia due to different situations in clinic and dental procedures among the two groups*

	NON- CLINICAL			CLINICAL		
	Mean ± SD	**Mean difference**	**p-value**	**Mean ± SD**	**Mean difference**	**p-value**
Feeling about visiting dentist	2.46 ±1.13	.70	.61	2.39±1.06	.70	.61
Feeling before your turn	2.10±1.05	.02	.87	2.08±1.05	.02	.87
Pre procedural feelings	2.67±1.07	.34	.01	2.32±0.97	.34	.01
Feelings before scaling	2.44 ±0.97	.19	.12	2.25±1.01	.19	.12
Total anxiety scores	9.66±3.11	.62	.10	9.04±3.07	.62	.10
Sound of drill	2.06±0.76	.14	.16	1.92±0.83	.14	.16
Not being numb enough	2.22±0.86	.01	.91	2.21±0.80	.01	.91
Dislike numb feeling	1.97±0.79	.04	.68	1.92±0.93	.04	.68
Injection	2.37±0.90	.32	.00	2.05±0.83	.32	.00
Probing	2.18±1.00	.21	.06	1.96±0.80	.21	.06
Feeling of scraping	2.08±0.87	-.03	.97	2.08±0.89	-.03	.97
Gagging	2.07±0.94	-.25	.02	2.32±0.85	-.25	.02
X-rays	1.59±0.91	.08	.41	1.50±0.82	.08	.41
Rubber dam	2.02±1.08	.09	.46	1.92±1.06	.09	.46
Jaws get tired	2.17±0.84	.01	.94	2.17±0.84	.01	.94
Cold air hurts teeth	2.09±0.82	.16	.11	1.92±0.84	.16	.11
Don't know about procedure	2.05±0.94	.03	.77	2.02±0.94	.03	.77
RCT	2.74±0.91	.24	.04	2.50±0.96	.24	.04
Extraction	2.71±0.77	.24	.02	2.47±0.91	.24	.02
Fear of being injured	2.11±0.86	-.00	.99	2.11±0.86	-.00	.99
Panic attacks	1.63±0.80	-.23	.04	1.86±0.99	-.23	.04
Not able to stop dentist	1.86±0.92	-.05	.64	1.91±0.87	-.05	.64
Not able to ask questions freely	1.85±0.87	-.01	.89	1.86±0.89	-.01	.89
Not taking seriously	1.78±0.83	-.14	.19	1.92±0.95	-.14	.19
Being criticized	2.01±1.04	-.10	.43	2.11±0.00	-.10	.43
Smell in the dental office	1.90±0.90	-.16	.14	2.07±0.91	-.16	.14
Worried about extensive treatment	1.66±0.84	-.26	.02	1.92±0.97	-.26	.02
Worried about cost of treatment	1.76±0.87	-.15	.17	1.91±0.88	-.15	.17
Worried about no of visit & miscellaneous factors	2.09±0.84	.09	.35	1.99±0.84	.09	.35
Embarrassed about mouth condition	1.67±0.80	-.01	.96	1.68±0.84	-.01	.96
Not like feeling of being confined	1.93±1.00	.00	.98	1.92±0.87	.00	.98

*RCT: root canal treatment

RESULTS

Total anxiety levels in non-clinical students was found to be high (9.66±3.11) than in clinical students (9.04±3.07). No significant difference was found between the two groups. (p- value .10) as shown in table I.

Significant difference was found between the two groups, with few exceptions like pre procedural feelings, injection, gagging, RCT, extraction, panic attacks and worried about extensive treatments. (Table II).

Phobia associated with RCT procedure was found to be high in non- clinical students (49.2%) as well as clinical students (36.1%). Similarly, phobia due to extraction in non- clinical and clinical students was found to be 56.3% and 48.1% respectively. However, phobia associated with gagging was more in clinical students (42.9%) than in non- clinical students. Panic attacks was found to be less in non- clinical and clinical students. (Table- III)

Table 3: *Intensities of dental phobia due to different dental procedures.*

	Intensity	Non- Clinical		Clinical	
		Frequency	%	Frequency	%
RCT	Low	16	12.7	23	17.3
	Moderate	24	19.0	40	30.1
	High	62	49.2	48	36.1
	Don't know	23	18.3	20	15.0
Extraction	Low	10	7.9	26	19.5
	Moderate	31	24.6	31	23.3
	High	71	56.3	64	48.1
	Don't know	14	11.1	12	9.0
Injection	Low	27	21.4	39	29.3
	Moderate	34	27.0	51	38.3
	High	56	44.4	40	30.1
	Don't know	9	7.1	3	2.3
Gagging	Low	41	32.5	27	20.3
	Moderate	42	33.3	42	31.6
	High	31	24.6	57	42.9
	Don't know	9	7.1	6	4.5
Panic attacks	Low	67	53.2	65	48.9
	Moderate	37	29.4	29	21.8
	High	16	12.7	29	21.8
	Don't know	3	2.4	9	6.8

DISCUSSION

Although Dental technology has been revolutionized, the phobias, fear, anxiety, and pain associated with dental treatment still remain a universal concern that needs be managed and for improvement of oral health related quality of life.[22] In the present study, dental phobia was being assessed and compared between clinical and non-clinical dental students. Means of total anxiety levels among non-clinical and clinical dental students were found to be comparatively high (9.66±3.11 and 9.04±3.07 respectively). Mean difference among both of the variables was found to be same i.e. 0.62. Hence, no significant difference between the two groups, since the p-value was found to be greater than .05. (Table-I) This is also supported from previous studies that non- clinical students tend to show more levels of dental phobia than the clinical students. This difference is also associated with psychological effects in the pre- clinical than in clinical students.[23]

While assessing all variables between the groups, significant difference was found between the two groups. Though there might be no significant difference among all, but some do show significant difference. They include pre procedural feelings, injection, gagging, RCT, extraction, panic attacks and worried about extensive treatments, since p- value was found to be less than .05. Although, probing was found to be not significantly different, but trend is there since p-value was 0.06. (Table-II)

In table-III those variables have been discussed who showed trends of being significantly different. Dental phobia was found to be high in both the groups, non-clinical as well as clinical, while carrying out RCT procedures (49.2% in non-clinical and 36.1% in the clinical group). Phobia of extraction and injection was also high in the two groups. Panic attacks were found to be moderately low in both, non-clinical and clinical groups. However, trends of phobia from gagging were found to be different among the two groups. It was found to be moderately low in non- clinical, and moderately high in clinical dental students.

Dental phobia of getting dental treatment or sight-seeing of dental treatment was lesser in medical and dental students than the students of art and scienc [24].

However, dental phobia reduces by the end of training of dental course.[25] Studies concluded that dental anxiety has an association with age, gender as well as education level even among dental students.[26] Preclinical or junior students have higher level of anxiety than clinical or senior students.[22] Dental fear will lead to delay in getting dental treatment done. Thus, the dental problems will get worsen due to the delay, leads to more decayed and missing teeth and poor oral hygiene. Increased level of Dental Anxiety might be due to oral hygiene behavior of individuals & lack of dental education.[27] Dental education and awareness programs among the dental students and the hygienists showed marked decrease in the dental anxiety levels. Thus, interventional programs can reduce the dental anxiety among the dental students and will improve their performance in studies as well as patient handling.

CONCLUSION

Non-clinical students were found to be more phobic due to different procedures than clinical dental students. Counselling sessions and training is suggested for non-clinical students regarding different dental procedures.

Ethical Approval: None

Conflict of Interest: None

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FREQUENCY OF ELECTROLYTE ABNORMALITIES IN CHILDREN ADMITTED IN PEDIATRIC INTENSIVE CARE UNIT OF A TERTIARY CARE HOSPITAL IN LAHORE

Muhammad Sarwar,[1] Ambreen Aslam,[2] Muhammad Shafqat,[3] Anila Jamil,[4] Fareeha Kausar,[5] Nighat Sultana[6]

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Abstract

Background: Electrolytes are minerals in human body which play a vital role in maintaining homeostasis within the body. The most common electrolyte disturbances involve abnormalities in the levels of sodium, potassium, calcium, magnesium and phosphate. An abnormally low electrolyte concentration is usually defined as a level that may impair a function dependent on that electrolyte

Objective: To determine the frequency of electrolyte abnormalities in children admitted in Pediatrics Intensive Care Unit of The Children's Hospital Lahore.

Methods: This descriptive cross sectional study was conducted at Pediatrics Intensive Care Unit of The Children's Hospital & the Institute of Child Health Lahore from July 2019 to June 2020. The non-probability purposive sampling technique was used. All basic demographic information of age, gender, diagnosis and contact was obtained. Blood sample was obtained in 5cc BD syringe. Samples were sent to the laboratory of the hospital for assessment of electrolytes like sodium, potassium, magnesium, phosphorus and calcium. Reports were assessed and levels of sodium, potassium and calcium were noted. If the values were deranged then hyper or hypokalemia, hyper or hyponatremia and hyper and hypocalcemia, hypomagnesemia and hypophosphatemia was labeled. Qualitative variables like gender, diagnosis and electrolyte abnormality like hyponatremia, hypernatremia, hyperkalemia, hypokalemia, hypercalcemia, hypomagnesemia, hypophosphatemia and hypocalcemia was presented in form of frequency and percentage.

Results: There were 171(52.13%) males and 157(47.87%) females. Hypernatremia was noted in 48(14.6%), hypokalemia was in 186(56.7%), hyperkalemia was in 55(16.8%) and hypercalcemia was noted in 22(6.7%) patients.

Conclusion: Electrolyte disturbances in children become obvious during illness and measurement of serum electrolyte is helpful for immediate therapy to avoid serious life threatening situation. In our study the most common electrolyte abnormality was hyponatremia, hypokalemia and hypophosphatemia.

Keywords: Electrolyte abnormalities, Hyponatremia, Hypernatremia, Hypokalemia, Hyperkalemia, Hypophosphatemia, Hypercalcemia, Hypocalcemia, Hypomagnesemia

Electrolytes are minerals in human body which play a vital role in maintaining homeostasis within the body.[1] They help to regulate myocardial and neurological function, fluid balance, oxygen delivery, acid-base balance and much more. Disturbances in fluid and electrolytes are among the most common clinical problems encountered in the intensive care unit. Critical disorders such as severe burns, trauma, sepsis, brain damage, and heart failure lead to disturbances in fluid and electrolyte homeostasis.[2,3]

The most serious electrolyte disturbances involve abnormalities in the levels of sodium, potassium,

1. Muhammad Sarwar
2. Ambreen Aslam
3. Muhammad Shafqat
4. Anila Jamil
5. Fareeha Kausar
6. Nighat Sultana

1-6. Department of Pediatric Intensive Care, The Children's Hospital, Lahore.

Correspondence:
Dr Muhammad Shafqat, *Department of Pediatric Intensive Care, The Children's Hospital, Lahore.*
Email: muhammadshafqatsial@yahoo.com

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calcium, magnesium and phosphate. The frequency of mixed electrolyte imbalance is 7.9% where as hyponatremia is seen in 9.5%-30%, hypernatremia in 15.3%-30%, hyperkalemia in 10%-29%, hypokalemia in 3.6% and hypocalcemia in 68.3%.[4,5] The overall death rate in electrolyte imbalance was 24.2%. In these 41.6% had hyperkalemia, 25% had hyponatremia, 20.8% had hypernatremia and 12.5% had hypokalemia.[6] Aliku found ambiguous results and reported that that in children admitted to PICU, hyperkalemia as most common electrolyte imbalance in 14.3% children, hypokalemia in 13.6%, hypercalcemia in 12.4%, hypocalcemia in 8.1%, hypernatremia in 4.7%, Hypomagnesemia in 0.8% and hyponatremia in 3.5% children.[7] The prevalence of hypophosphatemia is high in the ICU, reported to be observed in about 28% in critically ill patients while Hypomagnesemia in 50% cases.[8]

Rationale of this study is to assess the electrolyte abnormalities in critically sick children admitted in PICU. Critically ill patients tend to retain fluids and ultimately reduce electrolytes like sodium due to increased secretion of anti-diuretic hormone (ADH) and aldosterone. In addition, inappropriate administration of fluid and electrolytes should be considered in the diagnosis and treatment of fluid and electrolyte disturbances. The pattern of nutritional status may have been different in people of developing country like Pakistan as compared to the developed countries where nutritional status of children is much better. Unfortunately, there is no local data available. So through this study we want to find out the frequency of most common abnormalities of important electrolytes in children which enhance the severity of disease in children which causes admission to PICU. This study will help in improving our practice and proper management plans can be developed to manage and reduce the electrolyte abnormality in children which may also reduce the burden of hospital. The objective of the study was to determine the frequency of electrolyte abnor-malities in children admitted in Pediatric Intensive Care Unit.

Operational definition:

Electrolyte Abnormalities

1. Hyponatremia: Serum sodium concentration < 130 mEq/dL
2. Hypernatremia: Serum sodium concentration > 155 mEq/dL
3. Hypokalemia: Serum potassium level <3.5 mEq/dL
4. Hyperkalemia: Serum potassium level >5.5 mEq/dL
5. Hypocalcaemia: Serum calcium level < 8 mg/dL
6. Hypercalcemia: Serum calcium level > 12 mg/dL
7. Hypomagnesaemia: Serum magnesium level <1.5 mg/dL
8. Hypophosphatemia: serum phosphate concentration < 2.5 mg/dL

Serum electrolytes were assessed by chemical analyzer at the time of admission.

METHODS

This descriptive cross sectional study was conducted at Pediatrics Intensive Care Unit of The Children's Hospital & the Institute of Child Health, Lahore from July 2019 to Jan 2020. The non-probability purposive sampling technique was used. All patients of age 2 month to 16 years of either gender admitted to intensive care unit with any disease were included in this study. Patients transferred from other ICUs, and on diuretic therapy excluded from study.

A total of 328 patients who met the inclusion criteria were enrolled in the study from PICU of Pediatrics Department, The Children hospital Lahore. Informed consent was obtained from parents. All basic demographic information of age, gender, diagnosis and contact was obtained. Then blood sample was obtained in 5cc BD syringe. Samples were sent to the laboratory of the hospital for assessment of electrolytes like sodium, potassium, magnesium, phosphorus and calcium. Reports were assessed and levels of sodium, potassium and calcium was noted. Those values which were deranged either hyper or hypokalemia, hyper or hyponatremia and hyper and hypocalcemia, hypomagnesemia and hypophosphatemia was labeled (as per operational definition). All this information was recorded in a pre-designed pro-

forma.

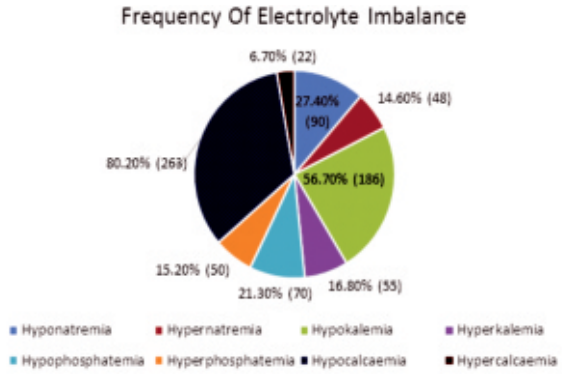
The collected data was analyzed statistically by using SPSS version 22. Quantitative variables like age was presented in form of mean±S.D. Qualitative variables like gender, diagnosis and electrolyte abnormality like hyponatremia, hypernatremia, hyperkalemia, hypokalemia, hypercalcemia, hypomagnesemia, hypophosphatemia and hypocalcemia was presented in form of frequency and percentage. Data was stratified for age, gender, nutritional status and cause of admission. Post-stratification chi-square was applied, taking p-value ≤0.05 as significant.

RESULTS

In our study the hyponatremia was noted in 90 (27.4%) patients while hypernatremia was noted in 49(14.9%) patients. Hypokalemia was noted in 186 (56.7%) patient. Hyperkalemia was noted in 55(16.8%) patients. The hypophosphatemia was noted in 70(21.3%) patients while hyperphosphatemia was noted in 50 (15.2%) patients. Hypocalcaemia was noted in 263 (80.2%) patients. Hypercalcemia was noted in 22(6.7%) patients. (Graph 1)

In children of age <10 years, hyponatremia was present in 72 cases, hypernatremia was found in 38 cases, hypokalemia was found in 155 cases, hyperkalemia in 36 cases, hypophosphatemia in 56 cases, hyperphosphatemia in 41 cases, hypocalcemia in 214 cases while hypercalcemia in 17 cases. In children of age ≥10 years, hyponatremia was present in 18 cases, hypernatremia was found in 10 cases, hypokalemia was found in 31 cases, hyperkalemia in 18 cases, hypophosphatemia in 14 cases, hyperphosphatemia in 9 cases, hypocalcemia in 49 cases while hypercalcemia in 5 cases. The difference was insignificant for all electrolytes imbalance (P>0.05) except hyperkalemia (p<0.05). (Table 1)

In male children, hyponatremia was present in 50 cases, hypernatremia was found in 25 cases, hypokalemia was found in 92 cases, hyperkalemia in 29 cases, hypophosphatemia in 34 cases, hyperphosphatemia in 26 cases, hypocalcemia in 137 cases while hypercalcemia in 12 cases. In female children, hyponatremia was present in 40 cases, hypernatremia was found in 23 cases, hypokalemia was found in 94 cases, hyperkalemia in 25 cases, hypophosphatemia in 36 cases, hyperphosphatemia in 24 cases, hypocalcemia in 126 cases while hypercalcemia in 10 cases. The difference was insignificant for all electrolytes imbalance (P>0.05). (Table 2)



Graph No: 1 *Frequency of Electrolyte Imbalance*

Children presenting with different diagnosis showed statistical significant difference for hyponat-remia,

Table 1: *Comparison of Electrolytes Imbalance with Age*

		Age (years)		Chi-square	p-value
		< 10	⩾ 10		
Hyponatremia	**Yes**	72	18	0.014	0.906
Hypernatremia	**Yes**	38	10	0.006	0.940
Hypokalemia	**Yes**	155	31	3.737	0.053
Hyperkalemia	**Yes**	36	18	6.151	0.010
Hypophosphatemia	**Yes**	56	14	0.010	0.920
Hyperphosphatemia	**Yes**	41	9	0.214	0.644
Hypocalcaemia	**Yes**	214	49	2.633	0.105
Hypercalcemia	**Yes**	17	5	0.077	0.782

Table 2: *Comparison of Electrolytes Imbalance with Gender*

		Gender		Chi-square	p-value
		Male	Female		
Hyponatremia	**Yes**	50	40	0.582	0.446
Hypernatremia	**Yes**	25	23	0.0001	0.994
Hypokalemia	**Yes**	92	94	1.229	0.268
Hyperkalemia	**Yes**	29	25	0.154	0.782
Hypophosphatemia	**Yes**	34	36	0.453	0.501
Hyperphosphatemia	**Yes**	26	24	0.0004	0.984
Hypocalcemia	**Yes**	137	126	0.001	0.975
Hypercalcemia	**Yes**	12	10	0.055	0.815

Table 3: Comparison of Electrolytes Imbalance with Diagnosis

	Hypo-natremia	Hyper-natremia	Hypo-kalemia	Hyper-kalemia	Hypo-phosphatemia	Hyper-phosphatemia	Hypo-calcemia	Hyper-calcemia
Accidental poisoning	7	1	4	3	4	1	11	0
Asthma	4	0	6	3	3	3	7	1
ARF	1	2	3	5	0	3	6	0
Bronchopneumonia	15	6	25	8	15	5	46	2
DKA	9	13	45	10	6	12	58	6
GBS	14	3	19	4	7	5	28	2
Meningoencephalitis	5	10	17	3	7	4	21	5
Sepsis	14	6	32	8	9	9	41	1
Tetanus	4	2	4	3	1	2	6	2
Tuberculosis	2	0	7	2	2	0	7	1
Others	15	5	24	5	6	6	32	2
Chi-square	23.891	19.215	20.975	17.364	5.393	8.153	20.436	13.964
p-value	0.008	0.038	0.021	0.086	0.863	0.614	0.025	0.175

hypernatremia, hypokalemia and hypocalcemia ($p<0.05$) while the difference was insignificant for hyperkalemia, hypo and hyperphosphatemia and hypercalcemia ($p>0.05$). (Table 3)

DISCUSSION

This present descriptive cross sectional study was conducted at Pediatrics Intensive Care Unit of The Children's Hospital & the Institute of Child Health Lahore to determine the frequency of electrolyte abnormalities in children admitted in Intensive Care Unit. According to WHO estimates, in every eight seconds a child dies from a water related disease. In developing countries, 50% of pediatrics hospitalization is due to acute diarrhea. Electrolyte abnormalities are common in children with diarrhea. It may remain unrecognized and may result in raised mortality and morbidity.[12]

In our study hyponatremia was noted in 90(27.4%) patients, hypernatremia was in 48(14.6%) patients, hypokalemia was in 186(56.7%), hyperkalemia was noted 55(16.8%) patients, hypophosphatemia was in 70(21.3%), hyperphosphatemia was in 50(15.2%), hypocalcemia was in 263(80.2%), and hypercalcemia was in 22(6.7%). The common electrolyte disturbance was hyponatremia (56%) followed by hypokalemia (46%).[16] However, about 37% patients had mixed electrolyte disturbance. Different studies showed hypokalemia frequency of around 14%.[14-18]

A study by S.D. Subba Rao showed that the electrolyte abnormalities were observed in 32.4% of children getting admitted to PICU. Hyperkalemia was the commonest, found in 14.4% cases.[21] Pizzoti et al reported hyponatremia in 34% of the hospitalized patients.[19] Subba Rao and Thomas[23] reported hyponatremia in 6.9% of children admitted to pediatric intensive care unit. However, the authors did not include children with diarrhea in their study.

Singhi et al.[26] who found hyperkalemia in 5.4% PICU admissions. This difference could be due to the fact that in their study hyperkalemia was defined as potassium level >6 mEq/L. Hyperkalemia was however, defined as serum potassium levels >5.5 mEq/L. In a study conducted in adults, 6.9% of total admissions had hyponatremia[20]. A higher frequency of 29.8% was observed in the prospective study of 727 sick children[21]. Twenty per cent children in that study had diarrhea. In another study, 34% of the hospitalized patients were classified as hypo-natremic[29].

Aliku found ambiguous results and reported that that in children admitted to PICU, hyperkalemia as most common electrolyte imbalance in 14.3% children, hypokalemia in 13.6%, hypercalcemia in 12.4%, hypocalcemia in 8.1%, hypernatremia in 4.7%, Hypomagnesemia in 0.8% and hyponatremia in 3.5% children.[7] The prevalence of hypophosphatemia is high in the ICU, reported to be observed in about 28% in critically ill patients while Hypomagnesemia in 50%

cases.[8]

Shah GS et al[25] concluded in their study that the hyponatremia, hypokalemia and metabolic acidosis are common electrolyte and acid base abnormalities in children with diarrhea and dehydration and often responsible for mortality.

Kathryn Maitland et al[22] demonstrated in their study that severe hyperkalemia complicated falciparum malaria in 9 children (16%), of whom 7 (78%) died, generally soon after admission. Hypokalemia, hypomagnesemia, and hypophosphatemia were uncommon (<7% of children) at admission but developed in >30% of children within 24h. Hypocalcemia was infrequent (<5% of children) at any time point. Apart from administration of potassium, electrolyte deficiencies were not corrected and were not associated with an adverse outcome. Hypocalcemia, hypophosphatemia, and hypomagnesemia were common at admission to the hospital, appearing in 30%, 70%, and 40% of patients, respectively. Severe hypophosphatemia (phosphate level <0.30 mmol/L) was relatively common, particularly among adults with complicated malaria, and Davis et al. [23]

The finding that hypocalcemia was uncommon at any juncture contrasts with data series for critically ill children[24] and adults.[25] Hypocalcemia is a common complication in sepsis and critical illness and has recently been shown to correlate with disease severity score and mortality risk among patients admitted to the intensive care unit.[26] A study by HA Mohammad et al described that the hypomagnesemia and hypocalcemia were found to be the two most common electrolyte disturbances in patients with chronic stable asthma and also in those with acute asthma exacerbation.[27] Therapeutic agents used to treat patients with chronic asthma have a role on abnormal electrolyte levels.

Memon et al[28] resulted in their study that hypokalemia, hyponatremia and low serum bicarbonate were seen more frequently in patients of group A (with diarrhea) as compared to group B (without diarrhea). In group A hypokalemia was seen in 40 patients (62.5%) while it was observed in 8 patients (22.22%) in group B ($p<0.001$), hyponatremia was seen in 17 patients (26.56%) in group A and in 5 patients (13.88%) in group B ($p<0.001$). In group A 41 patients (64%) had low serum bicarbonate while in group B only 15 patients (41.66%) had low serum bicarbonate value ($p<0.001$).

CONCLUSION

Electrolyte disturbances in children become obvious during illness and measurement of serum electrolyte is helpful for immediate therapy to avoid serious life threatening situation. In our study the most common electrolyte disturbance was hypernatremia, hypokalemia and hypocalcemia.

Limitations of Study: It is among the few studies in our setup about electrolyte abnormalities in children's admitted in Pediatrics ICU Department. Limitation of study is that its results can't be generalized over large geographic area because its data is collected from one Tertiary care hospital.

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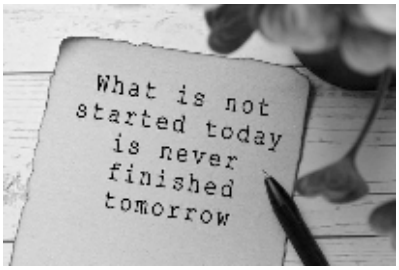

MUCORMYCOSIS

Omair Farooq,[1] Muhammad Usama,[2] Jahanzeb Rasheed,[3] Zia us Salam Qazi[4]

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Abstract

Mucormycosis is one of the most rapidly progressing and fulminant forms of fungal infection which usually begins in the nose and paranasal sinuses following inhalation of fungal spores. It is caused by organisms of the subphylum Mucormycotina, including genera as Absidia, Mucor, Rhizomucor, and Rhizopus. The incidence of mucormycosis is approximately 1.7 cases per 1,000,000 inhabitants per year. Mucormycosis affecting the maxilla is rare because of rich blood vessel supply of maxillofacial areas although more virulent fungi such as Mucor can overcome this difficulty. The common form of this infection is seen in the rhinomaxillary region and in patients with immunocompromised state such as diabetes. Hence, early diagnosis of this potentially life-threatening disease and prompt treatment is of prime importance in reducing the mortality rate.

Keywords: Rhino cerebral mucormycosis, Uncontrolled diabetes, Amphoterecin B, Opportunistic fungal infection.

Mucormycosis is an opportunistic and frequently fulminating fungal infection caused bymembers of the family Mucoraceae, order Mucorales and class Zygomycetes. These are ubiquitous fungi surviving on the decaying vegetation and diverse organic matter. Depending on the immunological status of the patient and site of the body that is affected, the disease may manifest in six different ways as rhinocerebral, pulmonary, cutaneous, gastrointestinal, central nervous system or disseminated forms. Pathophysiology involves inhalation of spores through the nose or mouth or even through a skin laceration. Individuals with compromised cellular and humoral defense mechanisms may generate inadequate response. The fungus may then spread to the paranasal sinuses and consequently to the orbit, meninges, and brain by direct extension. Most healthy people effectively clear fungal elements from their bodies by the innate immune system. However, people with specific risk factors such as diabetes mellitus, immunosuppression, long term corticosteroids, protein- energy malnutrition, hematologic malignancies, renal failure, organ transplant, neutropenia, and high iron overload are more prone to developing fungal infections. However, some patients with mucormysis have no identifiable risk factors. Diagnosis is confirmed by histopathological demonstration of the organism in the tissue. Successful management of this fatal infection requires early identification of the disease and aggressive and prompt medical and surgical interventions to prevent the high morbidity and mortality associated with this disease process. Control of underlying disease needs to be established, metabolic abnormalities corrected and anti fungal therapy should be combined with surgical debriment of all necrotic tissues.

The objective of this report is to shed light on how fast the disease spreads, discuss current management of rhinocereberalmucormycosis and illustrate the radiographic findings to raise clinical awareness for this life threatening disease.

1. Omair Farooq
2. Muhammad Usama
3. Jahanzeb Rasheed
4. Zia us Salam Qazi

1. Akhtar Saeed Medical And Dental College, Lahore
2,3. Medical Officer, Farooq Hospital, West Wood Lahore
4. Federal Post Graduate Medical Institute Shaikh Zayed Hospital Lahore

Correspondence:
Dr. Omair Farooq, Akhtar Saeed Medical And Dental College, Lahore. *E-mail:* omairfarooq@hotmail.com

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CASE PROFILE

Fifty year old gentleman came to us on 6th of may with complains of swelling of left eye, decrease vision and loss of sensation on the cheek and forehead. Patient was being treated previously on the lines of optic neuritis which was the cause of loss of vision in the left eye for which he was being given pulse solumedrol, 2 doses of 1 gram were already given. Patient had a background of Uncontrolled diabetes, Uncontrolled hypertension and had recently recovered from mild COVID 19 Illness.There was no other significant comorbidity. On Initial examination of the patient, he had complete loss of vision in the left eye, complete ophthalmoplegia with 3rd,4th, 6th nerve palsy and loss of sensation in the V1 and V2 distribution of the trigeminal nerve. On the right side there was loss of sensation in the V1 distribution of the trigeminal nerve. On both gross inspection of nasal cavity and anterior rhinoscopy, there was suspicion of some mass which could not be closely appreciated. Taking this further, an Initial diagnosis of mucormycosis with cavernous sinus thrombosis was made. Patient was having recurrent spikes of fever. Patient immediately underwent biopsy under local anesthesia after which he was started on broad spectrum antibiotics including meropenem and vancomycin. In addition to this traditional Amphotericin B deoxycholate (Initially 1 mg /kg /day which was increased slowly to 1.5mg/kg/day). Three days after admission patient developed swelling on the right eye as well along with marked proptosis, ptosis associated with complete ophthalmoplegia resulting in palsies of 3rd 4th and 6th nerves, however the vision was intact in the right eye. FESS (functional endoscopic sinus surgery) was done initially at the time of presentation and repeated after seven days which resulted in bilateral clearing of the nasal cavity and sinuses. The patient had lateral rhinotomy with medial maxillectomy and ethmoidectomy involving clearance of nasal sinuses.

Clinical and laboratory parameters were closely monitored including renal function tests. During the time of administration of Amphotericin B deoxycholate, his serum creatinine and blood urea nitrogen rose to 1.4 and 40 respectively. Because of non Availability of liposomal Amphotericin B , the patient was kept on Amphotericin B deoxycholate. Renal toxicity was managed by renal dose adjustment and aggressive hydration to keep the urine output (more than 1ml/kg/hour). Nasal biopsy result confirmed heavy growth of Mucor and Aspergillus on the specimen. In the third week, patient started complaining of decreased vision in the right eye as well and started to feel a bit drowsy along with headache. CT and MRI of the brain were done which showed no Intracranial extension. Ophthalmologist suggested to give the patient a trial of IV pulse Methylprednisolone therapy due to impending central retinal artery occlusion but this would result in aggravation of Mucormycosis. During the hospital stay of 25 days, a total of 2 Grams of Amphoterecin B deoxycholate were administered. After the first week of treatment, patient was started on Posaconazole syrup (10ml/12 hourly equivalent to 800 mg /day). Moreover, patient also underwent Packed red cell transfusion during the stay due to some blood loss as a result of surgery. On 25th day of hospitalization, he was discharged in good health with no intra cranial extension and preserved vision in the right eye. Patient was discharged on oral Posaconazole tablets (300mg/day). He was medically optimized at time of discharge and all laboratory parameters were within normal range. This is a case of mucormycosis with cavernous sinus thrombosis having a very high mortality of 80% with bilateral eye involvement. This patient showed good signs of recovery. Although he lost vision in his left eye and complete opthalmoplegia but vital organs were prevented from damage. Patient was sent home with a 2 week follow up. Risk factors in this patient were uncontrolled diabetes, previous covid-19 infection.

DISCUSSION

Mucormycosis is rare opportunistic fungal infection characterized by infarction and necrosis of host tissues that results from invasion of the vasculature by hyphae[1]. Any fungi in the Mucorales order can lead to mucormycosis. The most common cause is Rhizopus species, with Mucor species coming in second. Rhizopus species have a high moisture requirement to grow and thus are not typically found inside buildings. Rather, they tend to be found outdoors in soil and decaying material. Normally, these fungi do not cause disease in healthy people.However in people with underlying health conditions or immunosuppression, they may cause

serious rhinocerebral, pulmonary, gastrointestinal, cutaneous, or disseminated infections.

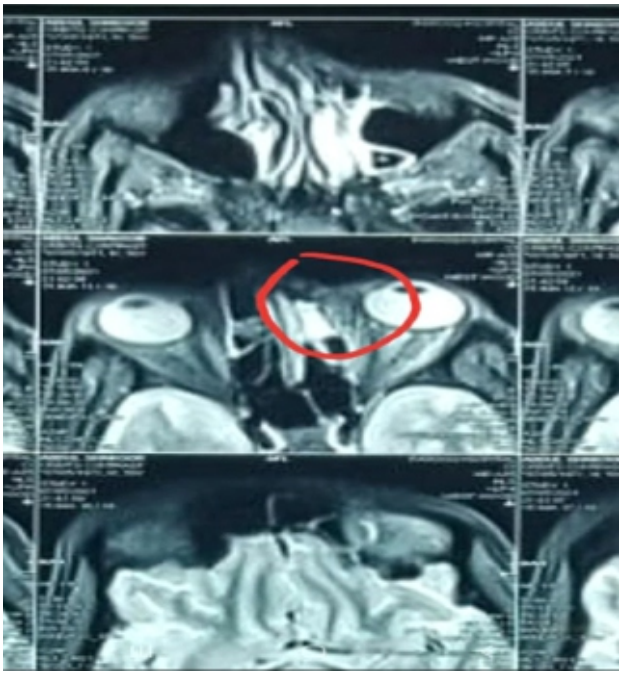
Seventy percent of rhino-orbital-cerebral mucormycosis cases have been found to be in patients with diabetes mellitus, most of whom had also developed ketoacidosis at the time of presentation. Infection usually presents with acute sinusitis, fever, nasal congestion, purulent nasal discharge and headache. All the sinuses become involved, and contiguous spread to adjacent structures such as the palate, orbit, and brain results in clinical symptoms. For example, spread of infection from the ethmoid sinus to the frontal lobe results in obtundation. Clinical suspicion and early treatment with surgical debridement are key to preventing morbidity in this often-fatal condition.[2]

Orbital compartment syndrome (OCS) results from an expansile process within the closed compartment of the orbit leading to increased orbital pressure, and potentially resulting in ischemia and vision loss. It is a true ophthalmologic emergency that requires lateral canthotomy and inferior cantholysis to decompress the orbit. Delay in care can lead to permanent blindness. This diagnosis should be suspected in patients presenting with acute proptosis, elevated intraocular pressure, rapid vision loss, ophthalmoplegia, fixed dilated pupil or afferent pupillary defect. Causes of OCS can be retrobulbar hemorrhage (from trauma, vascular malformations, tumors), cellulitis or other infection, orbital malignancy, or previous orbital surgery.[3]

Diagnosis of mucormycosis starts with having a high clinical suspicion of invasive fungal disease. Patients with diabetes mellitus with signs of rhinosinal disease should have immediate CT imaging. Subtle imaging findings may indicate invasive infection. Imaging methods are of little help during the early stages of rhinocerebral-mucormycosis with thickening of the sinus mucosa or extraocular muscles being described as an early sign suggestive of the disease4. CT scans can be used to evaluate the progression of disease although correlation with the clinical findings may not always be accurate. MRI scans may be more accurate in evaluating the extent of disease due to fungal invasion of soft tissues15. Both CT and MRI scans, however, should be frequently obtained due to the rapidity of disease progression and are indispensible for appropriate planning of surgical interventions. Tissue sampling should also be conducted to confirm the diagnosis. Under direct microscopy, the fungi will have ribbon-like, non-septate hyphae with a diameter ranging from 5 to 25 μm and 90° branching angles. If mucormycosis is still suspected after a negative culture result, molecular identification may be performed. Different techniques such as DNA probe targeting 18S subunit and ITS1 after polymerase chain reaction with pan-fungal primers have been reported.[4]

The treatment of mucormycosis requires a combination of surgical debridement and antifungal therapy. Depending on the extent of the necrosis, surgical debridement of necrotic tissue can involve removing sections of the maxilla, nasal cartilage, palate, mandible, and the orbit.[5] The mainstay antifungal therapy is amphotericin B. In this case study, Amphotericin B deoxycholate (Initially 1 mg /kg /day which was increased slowly to 1.5mg/kg/day). One of the main side effects of amphotericin B is nephrotoxicity. This case study patient was closely monitored including his renal function tests. During the time of administration of Amphotericin B deoxycholate, his serum creatinine and blood urea nitrogen raised to 1.4 and 80 respectively. Renal toxicity was managed by renal dose adjustment and aggressive hydration to keep the urine output (more than 1ml/kg/hour). Liposomal amphotericin B has been shown to have fewer nephrotoxic effects compared to conventional amphotericin B.It is crucial that empiric antifungal treatment is initiated early. Delaying amphotericin B therapy increases mortality. A retrospective cohort study involving 70 patients with hematologic malignancies with mucormycosis showed that patients receiving delayed amphotericin B (six days after symptom onset) had a twofold increase in the mortality rate at four weeks compared to patients receiving earlier treatment.

Reversal of underlying predisposing conditions is of paramount importance. Euglycemia should be restored rapidly and any immunosuppressive conditions reversed if possible. The surgical approach should be based on the clinical state of the patient with timely interventions for appropriate debridement of infected areas.



CONCLUSION

Rhinocerebral mucormycosis still remains a poorly understood disease with high mortality rate. Presently, the triad of clinician's awareness, prompt initiation of treatment and timely surgical intervention represent the effective way of managing the disease.The aim of this report is to bring clinical awareness to the subtle radiographic findings that may help diagnose this aggressive entity. Clinicians must maintain a high index of suspicion for mucormycosis.Further attempts should be made for the early diagnosis of this disease and prompt management of the patient.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflict of Interest: *None*

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Delaying amphotericin B–based frontline therapy significantly increases mortality among patients with hematologic malignancy who have zygomycosis. Clinical Infectious Diseases. 2008 Aug 15;47(4):503-9.

INVASIVE DUCTAL CARCINOMA IN MALE BREAST

Haseeb Mehmood Qadri[1], Fahad Qayyum[2], Zuhaira Chaudhary[3], Muhammad Imran[4]

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Abstract

The male breast develops in a similar manner to that of the female breast until puberty. Owing to absence of pre-pubertal estrogen stimulation, male breast development ceases at this stage, thus normal adult male breast mimics immature female breast. Male breast cancer is 1%, while 99% malignant tumors occur in female breast. Wide variation in the incidence of male breast cancer has been noted in different geographic regions around the world. In Pakistan, much less information is available regarding male breast cancer. We present a case on breast carcinoma in a healthy, fertile middle aged male.

Keywords: Breast, male, invasive ductal carcinoma

Male and female breast has the same pattern of histologic and physiologic development until puberty.[1] The gradual surge in testosterone and a grave decrease in estrogen account for the cessation of breast development in males.[2] Gynecomastia is defined as the benign proliferation of glandular breast tissue in men.[3] It can by physiologic, as occurring in the extreme of ages; or non-physiologic, caused by chronic conditions (e.g. cirrhosis, hypogonadism, renal insufficiency), iatrogenic medications or rarely tumors.[4] Breast cancer in males is usually the result of genetic mutations in BRCA1 or BRCA2.[5] Male breast cancer (MBC) accounts for 1% of all breast cancers and less than 1% of all annual cancer deaths in males.[6] In Pakistan, the prevalence of male breast cancer is attributed as roughly 2 males/100 females.[7] Majority of MBCs are invasive ductal carcinomas with ER positivity.[8] Modified radical mastectomy is considered to be the standard care of choice for MBC.[9] The outcome of breast cancers in males has a less favorable outcome than in females with the same condition.[10]

1. Haseeb Mehmood Qadri
2. Fahad Qayyum
3. Zuhaira Chaudhary
4. Muhammad Imran

1. Department of Surgery, Lahore General Hospital, Lahore
2. RHC Malka, Tehsil Kharian, Gujrat
3,4: Department of Pathology, Allama Iqbal Medical College, Lahore

Correspondence:
Dr. Haseeb Mehmood Qadri General Hospital Lahore.
Email: haseebmehmood18@yahoo.com.

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CASE PROFILE

A 46 year old man of heavy built presented to in surgical outpatient department with the complaint of left sided painless sub-areolar swelling, which he noticed three months back. It gradually increased in size. He was noncompliant hypertensive with positive family history of breast carcinoma in his mother. He was a father of three children. His pubertal and sexual development was normal. He had no other systemic complaint. On examination, there was a 3x3cm palpable sub-areolar lump in left breast, hard in consistency, mobile in all planes and non-adherent to the overlying skin. Testicular examination was unremarkable. Systemic examination was unremarkable, especially for liver disease. No group of axillary, cervical or inguinal lymph nodes was palpable. Workup was completed, revealing a 36x28mm hypoechoic left sided breast lesion, suggestive of gynecomastia. The report of core biopsy stated left invasive ductal carcinoma. Pre-operative hormonal profile including the serum testosterone, FSH, LH, Beta-HCG, Alpha-fetoprotein and LDH levels were within normal range. Modified radical mastectomy with level III axillary lymph node dissection was performed, excising 5x4cm mass and 30 lymph nodes. The patient was admitted to ward for monitoring axillary

and flap drain output. The histopathology report revealed invasive ductal carcinoma, grade III. The Ki67 index was 14%. The receptor status showed positive estrogen and progesterone receptors and equivocal Her2 neu, which was confirmed as negative on fluorescent insitu hybridization (FISH). The peripheral and deep surgical resection margins were free of tumor. Eight out of thirty identified axillary lymph nodes had metastatic deposits. He was referred to oncology for further consultation and management, one week postoperatively, after the surgical wounds were unremarkable on examination. A written consent was obtained by the patient's attendant to publish the case for academic purposes. Ethical letter was taken from the institutional review board.

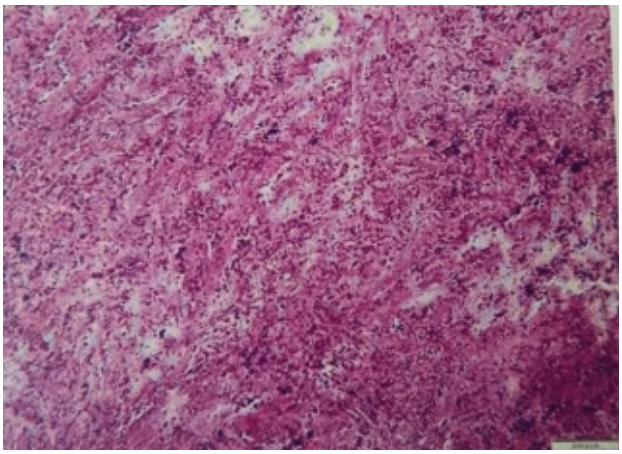

Figure 1: *Invasive Ductal Carcinoma, Grade III with Areas of Necrosis. (x4)*

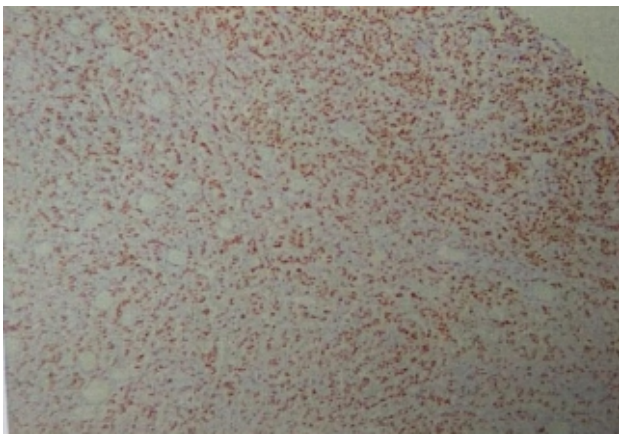

Figure 2: *Estrogen Receptor Positivity*

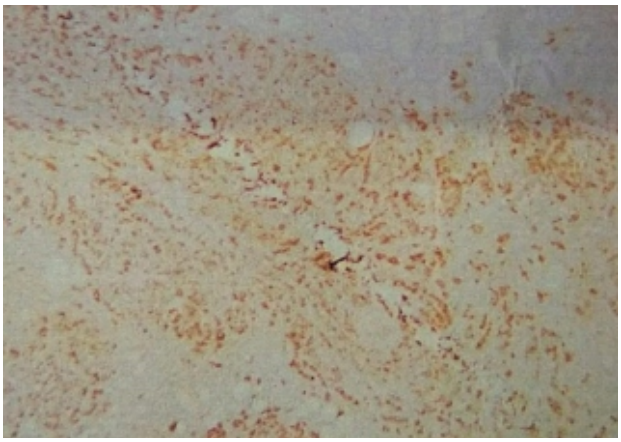

Figure 3: *Equivoval Her2 neu, confirmed negative on FISH*

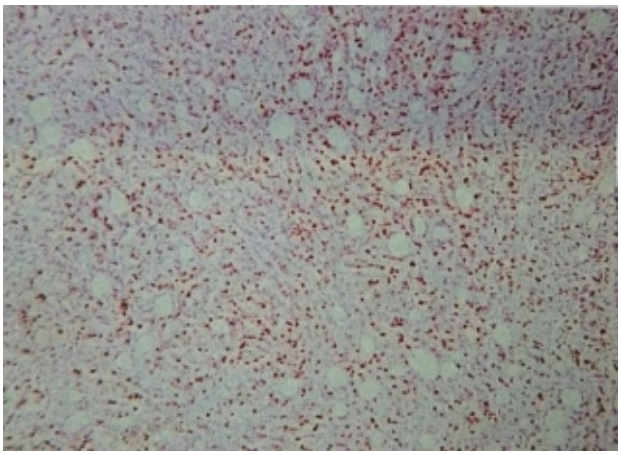

Figure 4: Ki67 index 14%

DISCUSSION

This case report presents a unique case of male breast cancer in a fertile, healthy patient with the only risk factor of positive family history. However, the various risk factors for gynecomastia and male breast cancer documented in other studies, like gondal disorders, chronic conditions (e.g. cirrhosis and renal insufficiency), obesity, alcohol intake, radiation exposure, iatrogenic medications and tumors are absent in our case.[11,12]. The majority of the rudimentary breast tissue in men exists in the sub-areolar region and cancers often present as painless, sub-areolar mass, which was the similar presentation in our patient.[13] Clinically, it may be unilateral or bilateral, with left predominance prevailing as reported in studies, which is similarly in our case. [14] The size of the primary tumors was roughly 3x3cm in this case, which accounts for the delay in seeking

medical advice in Pakistan because of cultural restrains.[1,2] The size of the primary tumor at the time of presentation in Western population is much smaller than in this case.[15,17] The sinister physical examination findings of skin infiltration and ulceration, as documented in other studies, were absent in our patient.[16] There are atypical differences, grossly or microscopically in male and female patients with breast carcinoma, however owing to the underdevelopment of breast tissue in males, the tumor mass invades the underlying chest muscles in cases of late clinical presentation.[18,19] Likewise, the post-operative biopsy report in our patient also states invasive ductal carcinoma with histologic grade III. The worse prognosis for male breast cancer has been attributed to the advanced age at presentation and a higher incidence of lymph nodes metastases. [20,21] Contrastingly, the age of presentation is fifth decade and eight out of the thirty excised axillary lymph nodes were tumor positive. Modified radical mastectomy (MRM) is currently the surgical gold standard treatment of male breast cancer (70% of all cases), followed by radical mastectomy, total mastectomy and lumpectomy with or without irradiation.[22,23] The patient in our case report underwent MRM and was referred to aspecialized hospital for chemotherapyand radiotherapy after consultation from the oncologist.

Limitations of the study: The patient was followed for one month in the surgical outdoor for post-operative follow-up. However, the patient didn't respond to the telephonic contact after a month.

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Author's Contributions:
HMQ: Manuscript writing and data collection
FQ: data collection and bibliography
ZC: Pathology description and photographs
MI: Proof reading and final drafting

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