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## Editorial

# Risk of Infections During Monsoon in Children

Mohsin Masud Jan

Editor

Children are at the greatest risk of contracting gastroenteritis, diarrhoea, cholera and other monsoon related health threats from July to September and the main reason behind outbreaks of certain infections reported every year in monsoon is consumption of contaminated water and foodstuff.

It is time for parents to take proper preventive measures to avoid water and food borne infections and if they do not give due attention to the matter well in time, the monsoon might cause great rise to certain infections among children and infants.

The trend of infections among children is endemic; however, it may take shape of an epidemic with continuous rain spells expected ahead. The risk is greater due to rain spells because rainwater contaminates drinking water reservoirs at source and in supply lines even if there is no leakage at the lines. It is important to mention that the monsoon causes a great increase in number of child patients across country every year with increase in incidence of viral and bacterial diarrhoea, gastro and cholera.

The increase in rainfall in the coming days may pose greater threats to health of children and infants and it is time to make parents aware that they need extra care in case of children from July to September.

It is alarming that in Pakistan, nearly 250,000 children under the age of five die each year due to diarrhoea, mainly because of the use of untreated and contaminated water and unhygienic food. The water-borne illnesses account for nearly 60 per cent of child deaths in Pakistan with approximate 630 children dying daily from diarrhoea.

It is time to sensitize public on the issue and convince them to take extra ordinary care in handling children and infants. Awareness should be created among parents on the health hazards of monsoon asking parents to take extra care of their children for at least two months from now onwards.

To avoid diarrhoea, children should be given water for drinking after boiling while boiled water should be used for preparing milk for infants. Water to be used for children and infants must be brought to

'rolling boil' for 5-10 minutes otherwise it might not be safe for a child to consume.

On hygiene, mothers should wash hands with soap before preparing milk for infants while children should be made habitual of washing hands with soap before and after eating and after going to toilet. Fresh milk and food should be given to infants and small children each time and consumption of leftover food should be avoided.

There is a need of educating mothers on how to prevent monsoon related infections and how to react in case a child gets infection. Mothers should be informed that immediately after the incidence of diarrhoea (motion), a child should be given ORS (Oral Rehydration Salt) which certainly puts a patient out of danger. However as soon as a patient's stool gets consistent, the ORS should immediately be stopped as greater percentage of Sodium in ORS might harm a healthy child.

Studies reveal that in cholera, the watery motion resembles that of rice water and dehydration is much rapid as compared to diarrhoea. Health experts say that such a patient should immediately be taken to the nearest healthcare facility for treatment.

Cholera is an acute infectious disease caused by the bacterium *Vibrio cholerae* that lives and multiplies its colonies in the small intestine. Massive watery diarrhoea is the major symptom of the infectious disease that results in dehydration.

Such dramatic water loss, if left untreated, causing severe dehydration leads to thickening of blood, circulatory collapse (shock) and death. Studies reveal that a good number of cholera victims die six hours after onset of symptoms if not treated in time. Nearly 60 per cent of untreated patients die of the disease.

Cholera can be avoided by giving safe water (boiled water) to children for drinking and avoiding unhygienic conditions. The families should have a clean and functioning lavatory and open defecation on ground, in or near water sources should be avoided.

# Frequency of Asymptomatic Spontaneous Bacterial Peritonitis in Outdoor Patients with Liver Cirrhosis

Muhammad Mumtaz Ather<sup>1</sup>, Malik Muhammad Arif<sup>2</sup>, Mehboob Qadir<sup>2</sup>, Humayun Riaz Khan<sup>2</sup>, Sheik Abdul Khaliq<sup>2</sup> and Talha Rasheeq<sup>1</sup>

## ABSTRACT

**Objective:** Investigate the incidence of asymptomatic spontaneous bacterial peritonitis in patients with liver cirrhosis.

**Study Design:** Prospective study.

**Place and Duration of Study:** This study was conducted at the Gastroenterology Department of Bakhtawar Amin Hospital and Nishtar Hospital Multan from May 2018 to May 2019.

**Materials and Methods:** Eighty six patients of liver cirrhosis were included in the study. Main variables were serum albumin, prothrombin time, ascitic fluid protein, serum bilirubin, child class B, child class C. SPSS version 23 was used for data analysis. Test of significance student t-test and chi square test were applied. P value  $\leq 0.05$  was taken as significant.

**Results:** S. Albumin, PT (s), Ascitic Fluid Proteins, S. Bilirubin, TLC, ESR and CRP of SBP negative patients was  $29.55 \pm 2.95$  (g/dL),  $28.97 \pm 1.25$ ,  $1.87 \pm 0.22$  (g/dL),  $54.21 \pm 2.15$  mmol/L,  $11.91 \pm 2.21$  ( $\times 10^9$  /L),  $34.37 \pm 2.18$  (mm/h) and  $56.47 \pm 2.33$  (mg/ L), respectively. Child class C and child class B was observed as 64.5% and 31.6%, respectively.

**Conclusion:** High frequency of spontaneous bacterial peritonitis is associated with liver cirrhosis; early diagnostic parenthesis should be performed in all outdoor patients for detection of silent cases of peritonitis. Antibiotic prophylaxis reduces the incidence of SBP.

**Key Words:** Liver cirrhosis, spontaneous bacterial peritonitis, ascites, Child pugh, viral hepatitis.

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## INTRODUCTION

Chronic liver disease is a rising economical burden on healthcare facilities worldwide. In European population about 0.1% suffer from liver cirrhosis a deadly adverse situation of chronic liver disease<sup>1,2</sup>. According to a survey 14-26 cases/ one lac and chronic viral hepatitis is the main cause among other major causes of the liver disease are reported. Chronic viral hepatitis is an most instant end stage complication accounting for 78% hepatocellular carcinoma and 57% cirrhosis<sup>3,4</sup>.

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Both of these conditions are preventable among early signs of cirrhosis, ascites is the most common which may lead to bacteria peritonitis a life threatening complication specifically in hospitalized patients<sup>5</sup>. Spontaneous bacterial peritonitis may develop hepatic encephalopathy, sepsis, renal failure, worse condition of liver disease and reduced survival rate. It's percentage is 10 to 30% in hospitalized patients<sup>6</sup>. This rate is also reported 34% in recent studies. Prevalence rate of liver cirrhosis in outdoor department is unknown if spontaneous bacterial peritonitis can help to control the complication like hepatic encephalopathy, hepato renal syndrome, sepsis, and worsening of liver disease<sup>7</sup>. That's why ascitic tap analysis is mandatory in every patient for the analysis of SBP<sup>8</sup>.

There are some restrictions in developing countries like financial and procedural limitations<sup>9</sup>. These limitations hinder the exact practice and incidence rate of SBP in the cirrhotic patients due to chronic viral hepatitis<sup>10</sup>. In this present study we aimed to investigate the incidence characteristics and natural background of SBP in cirrhotic patients who present with chronic viral hepatitis so that local statistics of the disease and their cost ratio then the estimated in local population.



## MATERIALS AND METHODS

This prospective study was carried out at gastroenterology department of Bakhtawar Amin Hospital and Nishtar hospital Multan from 1<sup>st</sup> May 2018 to 1<sup>st</sup> May 2019. Study was approved by ethical committee of hospital and informed written consent was obtained from patients. Non probability consecutive sampling technique was used. Patients with diagnosed cirrhosis and asymptomatic ascities were included in the study. Clinical symptoms of hepatic encephalopathy, upper GI bleed, infection, antibiotic treatment at the time of admission and de ranged renal function and previous history of SBP were excluded from the study.

Diagnosis of cirrhosis was made on laboratory radiological and clinical parameters. Severity of disease was accessed on model of end stage liver disease (MELD) score and child pugh score. Complete physical examination was done to rule out the chronic liver disease, hepatic encephalopathy and prescence of ascities and after that paracentesis was performed. Routine laboratory investigation like CBc , ESR, C reactive protein, AST, ALT, serum bilirubin, gamma GT, albumin, INR, prothrombin time, renal function test and serum electrolytes were performed. Paracentesis was performed with aseptic techniques without ultrasound guidance and 30mm of ascitic fluid was drawn. Diagnosis of SBP was based on absolute neutrophilic count in the absence of intra abdominal infection. Culture positive neutrocytic ascites was considered as positive when culture positive with absolute neutrophilic count  $>250/\text{mm}^3$  while culture negative neutrocytic ascites considered when culture negative with absolute neutrophilic count  $>250/\text{mm}^3$ . Culture positive with absolute neutrophilic count  $<250/\text{mm}^3$  were termed as Bacterascites.

SPSS version 23 was used for the data analysis. Mean and standard deviation was calculated for numerical variables like age serum albumin, prothrombin time, ascitic fluid protein, serum bilirubin and frequency percentages were calculated for qualitative variables like gender, child class B and child class C. Student t-test and chi square test were applied to see the association among variables. P value less than or equal to 0.05 was considered as significant.

## RESULTS

Eighty six patients were included in this study. n=10 patients had SBP positive and n=76 had negative SBP status. The mean age, S. Albumin, PT (s), Asc. Fluid Proteins, S. Bilirubin, TLC, ESR and CRP of SBP positive patients was  $50.91 \pm 4.08$  years,  $30.40 \pm 2.83$  (g/dL),  $29.22 \pm 1.31$ ,  $0.71 \pm 0.002$  (g/dL),  $48.54 \pm 4.54$  mMol/L,  $8.56 \pm 2.11 (\times 10^9 /\text{L})$ ,  $46.93 \pm 1.24$  (mm/h) and  $63.19 \pm 6.39$  (mg/L), respectively. Child class C and child class B was observed as n=7 (70%) and n=1 (10%),

respectively. While, the mean age, S. Albumin, PT (s), Asc. Fluid Proteins, S. Bilirubin, TLC, ESR and CRP of SBP negative patients was  $50.91 \pm 4.08$  years,  $29.55 \pm 2.95$  (g/dL),  $28.97 \pm 1.25$ ,  $1.87 \pm 0.22$  (g/dL),  $54.21 \pm 2.15$  mMol/L,  $11.91 \pm 2.21 (\times 10^9 /\text{L})$ ,  $34.37 \pm 2.18$  (mm/h) and  $56.47 \pm 2.33$  (mg/ L), respectively. Child class C and child class B was observed as n=49 (64.5%) and n=24 (31.6%), respectively. P-value  $\leq 0.05$  considered as significant. (Table. I).

**Table No. I: Different characteristics of the SBP positive and negative patients**

Variable	Positive n=10	Negative n=76	P- value
Age (years)	$50.91 \pm 4.08$	$50.91 \pm 4.08$	0.549
S. Albumin (g/dL)	$30.40 \pm 2.83$	$29.55 \pm 2.95$	0.394
PT (s)	$29.22 \pm 1.31$	$28.97 \pm 1.25$	0.595
Asc. Fluid Proteins (g/dL)	$0.71 \pm 0.002$	$1.87 \pm 0.22$	0.000
S. Bilirubin mMol/L	$48.54 \pm 4.54$	$54.21 \pm 2.15$	0.000
TLC ( $\times 10^9 /\text{L}$ )	$8.56 \pm 2.11$	$11.91 \pm 2.21$	0.000
ESR (mm/h)	$46.93 \pm 1.24$	$34.37 \pm 2.18$	0.000
CRP (mg/ L)	$63.19 \pm 6.39$	$56.47 \pm 2.33$	0.000
Child class C	n=7 (70%)	n=49 (64.5%)	0.730
Child class B	n=1 (10%)	n=24 (31.6%)	0.158

## DISCUSSION

In literature available on this study reported different ratio of spontaneous bacterial peritonitis in hospitalized cirrhotic patients. Its frequency was reported upto 50% in studies. In a study conducted by Gunjaca et al<sup>11</sup> reported 21% spontaneous bacterial peritonitis and 14.1% per annum prevalence rate. His results were statistically significant. In our study child class C was positive in 70% cases and class B found to be positive in 10% of cases.

Use of prophylactic antibiotic therapy reduced the incidence of SBP, this conclusion was reported in some studies our observation was also similar during study. Alaniz et al<sup>12</sup> conducted a study in 2009 and observed the role of prophylactic antibiotics in prevention of SBP. He reported that prevention of SBP is possible in cirrhotic patients if proper and early treatment was started with antibiotic prophylaxis.

Zaman et al<sup>13</sup> also conducted a similar study in 2011 and reported 56% SBP in cirrhotic cases. He labeled SBP as main complication of chronic liver disease and E. coli is most common and frequent offending organism involved in SBP. His conclusion about its prevention is similar as previous reported that antibacterial therapy of early disease and time can prevent prevalence rate of SBP.

Except these, few studies were conducted on incidence of spontaneous bacterial peritonitis in outdoor patients. Castellote et al<sup>14</sup> conducted a study on outdoor patients

and reported culture-negative neutrocytic ascites in 0.5% and bacterascites in 3% of patients. Most common organism was gram positive cocci in his study. In outdoor patients this prevalence rate is much lower when compared with other patients.

Evans et al<sup>15</sup> also conducted a similar study on this topic and concluded that reassessment criteria for outdoor patients required for cases of spontaneous bacterial peritonitis. He observed neutrocytic ascites in 3.5% patients but hepatorenal syndrome was not observed in a single case. Similarly Kasztelan-Szczerbinska et al<sup>16</sup> reported bacterascites in 16.2% cases and neutroascites was observed in 2.7% cases.

Another study was conducted by Khalid M et al<sup>17</sup> and reported neutrocytic ascites as 10% and without culture positive studies. His assessment criteria is also same as in our study, severity was determined with child class B and C. not only hepatitis C is involved but hepatitis C have equal contribution worldwide. Its prevalence increasing day by day from 1991 (6.4 million) cases which increased to 8.5 million in 2005<sup>18</sup>.

Development of bacterial peritonitis is the major morbidity and mortality related factor in liver cirrhosis. Romney et al<sup>19</sup> conducted a study on use of routine laboratory investigations in diagnosis of early peritonitis and its role in patient's survival. He concluded a major role of timely investigations. In our study we also performed daily investigations and treat the intensity of disease accordingly.

## CONCLUSION

High frequency of spontaneous bacterial peritonitis is associated with liver cirrhosis; early diagnostic parenthesis should be performed in all outdoor patients for detection of silent cases of peritonitis. Antibiotic prophylaxis reduces the incidence of SBP.

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# Management of Acute Sinusitis; Don't Forget Orbital Involvement

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## ABSTRACT

**Objective:** To study the results of management of acute sinusitis and early detection and prevention of devastating orbital complications.

**Study Design:** Experimental study

**Place and Duration of Study:** This study was conducted at the Lahore General Hospital Lahore and Red Crescent Medical & Dental College Dina Nath, Kasur in the Departments of ENT and Eye from May 2016-May 2019.

**Materials and Methods:** Study included 50 cases presented with symptoms and signs of acute sinusitis as well as symptoms and signs of orbital complications or threatened orbital complications of acute sinusitis. The cases who presented with acute sinusitis were treated by antibiotics, analgesics, local nasal decongestant and systemic nasal decongestants after taking proper history and ENT examination, blood C/E, ESR, nasal swab for C/S and x-ray PNS occipitofrontal and occipitomenthal views. Those presenting with acute sinusitis along with symptoms and signs of threatened orbital complication were examined by Ophthalmic Surgeon and CT Scan of nose and PNS were requested to type the orbital complications of acute sinusitis according to Chandlers classification. The patients aged 18-60 years were included in the study.

**Results:** Among 50 patients, 76.0% were males and 24.0% were female patients. They were diagnosed as having acute sinusitis clinically. Among them, 92% were treated on conventional lines. There were 8% patients suspected of threatened orbital complications as they developed odema of eyelids. Ophthalmic consultation and CT Scan showed that they had type-I orbital complication according to Chandlers classification for orbital complications. They were given i/v Augmentin along with Metronidazole infusion along with the other treatment modalities given in acute sinusitis generally. Early diagnosis and aggressive medical management resulted in their recovery.

**Conclusion:** Acute sinusitis with orbital complications are threat to patient vision and life but are uncommon. Ophthalmic consultation and urgent CT scan are mandatory if suspicion of orbital complication is arising. CT scan of nose, paranasal sinuses and orbit give guidance for surgical intervention or medical management. If acute sinusitis is diagnosed early and treated promptly and adequately, orbital complication are unlikely and orbital complications even if threatening are picked early. In collaboration with ophthalmic surgeon along with CT scan, they will also not progress to ophthalmoplegia, blindness and cavernous sinus thrombosis if treated aggressively.

**Key Words:** Acutesinusitis, orbital, complications, Chandlers classification.

**Citation of articles:** Enver T, Hussain A, Mahmood N. Management of Acute Sinusitis; Don't Forget Orbital Involvement. Med Forum 2019;30(7):6-9.

## INTRODUCTION

Sinusitis is the inflammation of paranasal sinuses and nasal mucosa. It is a frequent medical problem affecting over 24 million individuals yearly. The sinusitis could be acute (about < 4 weeks), sub-acute (4 to 8 weeks) or persistent (almost for 8 or more weeks). All 3 kinds of sinusitis have same symptoms and hence are mostly difficult to differentiate.

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Several factors are responsible for sinusitis chronicity including mucus recirculation, osteitis and ostial blockage.

Generally the acute sinusitis occurs due to common cold but dental extraction, dental infectivity, diving and swimming, trauma and nose operation are also responsible for it. The influencing factors comprise any anatomical anomalies, polyps, septal deviations, enlarged adenoids, foreign body or allergic rhinitis. Bacterial infectivity promptly follows any viral insult while streptococci, pneumococci, escherichiacoli, H. influenza and staphylococci are the bacteria held responsible.

Acute sinusitis orbital complications are rare but comprise abscess and orbital cellulites both among adults and children but remain comparatively infrequent.

Orbital septum begins from periosteum and coming up from periosteum anterior extension from orbital boundary in the eyelids, detaches eye superficial

portion (preseptal region) from deeper structures of orbit (postseptal region).<sup>1,2</sup>

Acute sinusitis orbital complications are categorized through Chandler 1970 based upon medical evaluation alone like pre- & post-septal contaminations and put patients in 5 groups. The Grade-1 is Preseptal cellulitis (inflammatory edema), Grade-2: OC (orbital cellulitis), Grade-3: SPA (subperiosteal abscess), Grade-4: OA (orbital abscess), and Grade-5: CST (cavernous sinus thrombosis).<sup>3</sup> Though, identifying the grades among children with painful and/or swollen eyes could be further vague.<sup>1</sup> To make classification criteria simple, orbital septum complications comprising inflammatory edema and postseptal contaminations have been suggested. Once the sinusitis is main cause, infectivity spread mostly through ethmoid sinuses; though, infectivity can spread via maxillary antrum roof or frontal sinus floor.<sup>1</sup> Orbital complications could be an outcome of development of infectivity through destruction of osteitic bone, bony defects or via communicating veins thrombophlebitis.<sup>4</sup>

Several and varied sinus pathologies can show with orbital involvements.<sup>5</sup> The most frequent reason of OC is primary sinus infectivity.<sup>6</sup> Orbital complication comprises 74 to 85 percent of complications emerging from the acute rhinosinusitis and generally it is inferior to the acute ethmoidal sinusitis because ethmoid sinus is detach from orbit just via lamina papyracea.<sup>7</sup> Among developing states, sinusitis is not well treated<sup>8</sup> and believed a major reason regarding orbital complications.<sup>9</sup> Antibiotics introduction has changed the sinusitis course as well as its problem. During pre-antibiotic period, among patients mortality and morbidity caused by orbital problems secondary to the sinusitis were 17 percent and 20.5 percent, respectively. With stronger antibiotics advent and novel surgical modalities, mortality and morbidity rates have been decrease to 1-2.5% and 3-11 percent, respectively.<sup>10</sup>

Management plan regarding sinusitis orbital complications depends upon affection severity at early presentation.<sup>11</sup> Medical therapy is encouraged among mild cases with neither visual affection nor the ocular mutility restriction. Treatment failure mandate surgical intrusion managing both nearby orbit or affected sinuses.<sup>12</sup> Acute sinusitis is believed a serious problem due to orbital complications. Delay in diagnosis as well as proper management could affect patient vision and even it becomes most dangerous disease.<sup>13</sup> Therefore, present study aims to determine the modes of presentation and the outcome of different management strategies and early detection and prevention of orbital complication.

## MATERIALS AND METHODS

The study was conducted in Department of ENT, Lahore General Hospital Lahore and Department of

Eye and ENT in Pak Red Crescent Medical and Dental College, Dina Nath, Kasur from 2016 to 2019.

All patients aged 18 to 60 years with acute sinusitis were included in this study. Diagnosis was based on history, physical examination and investigation such as x-rays paranasal sinuses, blood C/E, ESR and nasal swabs for culture sensitivity. CT scan of nose paranasal sinuses and orbits were requested in selected cases in which there was suspicion of threatened orbital complications.

These patients were treated with antibiotics, nasal decongestant locally and systemically, steam inhalation and saline irrigation.

In four patients with acute sinusitis, where there was suspicion of threatened orbital complications as odema of eyelids developed and were brought under consultation of ophthalmic surgeon and CT scans ordered to type the orbital complication of acute sinusitis according to Chandlers classification and vigorous treatment was started with addition of i/v Augmentin Metronidazole infusion along with conventional treatment.

## RESULTS

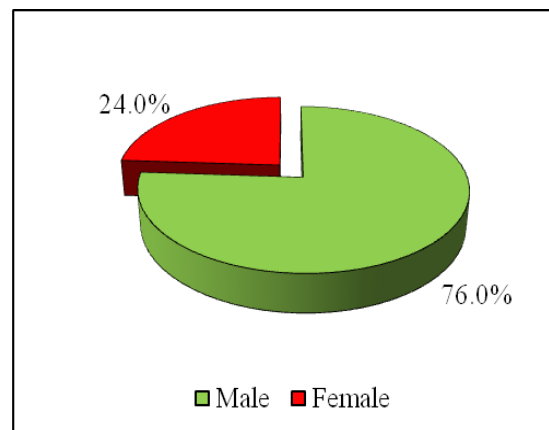
**Table No.1: Gender of patients**

	Frequency	Percentage
Male	38	76.0%
Female	12	24.0%
Total	50	100.0%

**Table No.2: Age of patients**

	Frequency	Percentage
20-25 years	13	26.0%
25-30 years	2	4.0%
40-45 years	32	64.0%
50-60 years	3	6.0%
Total	50	100.0%

Result shows that among 50 patients, 38 (76.0%) were males and 12 (24.0%) were female patients.



**Figure-1: Gender of patients**

Among 50 patients, majority 32 (64.0%) was 40-45 years old, 13 (26.0%) were 20-25 years old and 3 (6.0%) were 50-60 years old while 2 (4.0%) patients were 25-30 years old.

Orbital manifestation as swelling of eyelid in 4 (8%) patients was encountered on right side.

Forty six patients responded to antibiotic augmentin, local nasal decongestant xylometazoline, systemic nasal decongestant pseudoephedrine, steam inhalation and saline irrigation.

Four patients who developed odema of eyelids and ophthalmic consultation and CT Scan placed them in Stage-I of Chandler classification of orbital complications of acute sinusitis were treated aggressively by adding metronidazole infusion and i/v augmentin in addition to treatment given for sinusitis already.

All patients recovered with the treatment given. Their symptoms and signs disappeared, leukocyte count returned to normal, ESR returned to normal and follow up x-ray PNS showed disappearance of opacity of sinuses and return of radiolucent sinuses one month after.

## DISCUSSION

In acute sinusitis the organism found are *H. influenzae*, *staphylococcus*, *streptococcus* while in adult aerobic and anaerobic bacteria are important.<sup>14,15,16</sup> Inflammation of paranasal sinuses is one of the commonest medical problem.<sup>17</sup> Orbital complications not only threat vision but also life from complications such as meningitis, brain abscess and cavernous sinus thrombosis.<sup>18</sup>

However, orbital complications remain relatively uncommon. The location of orbital infection is described with respect to orbital septum either as preseptal (periorbital) or postseptal (orbital).<sup>19</sup> The distinction between these two is important because post-septal infection are treated vigorously to prevent devastating complications.

Conventional plain x-rays or paranasal sinuses can tell if one sinus is involved or there is pansinusitis. CT Scan of orbit and sinuses can help in diagnostic differentiation as well as determining which patient will benefit from surgical interference.<sup>20</sup>

It is to be noted that CT Scan may identify the abscess and Krohelet al. reported that an abscess developing within 24 to 38 hours may produce non specific inflammatory signs on CT and not identify as abscess.<sup>21</sup> Demetrios et al. found that CT Scans were to be accurate predictors of sub periosteal abscess among 80% patients.<sup>22</sup>

It is well known that i/v antibiotics can penetrate the abscess,<sup>23</sup> but without drainage their anti-bacterial activity within the abscess is poor, probably because the purulent milieu protects the micro organism by enzymatic degradation of antibiotics.<sup>24</sup>

In our study 4 patient belonging to stage Type-I Chandler Classification for orbital complications were treated successfully by i/v antibiotics and role of surgery was limited to those patient who did not respond to antibiotics.

Other 46 patients presenting with acute sinusitis were diagnosed early and managed adequately and did not proceed to any orbital complication.

It was noted that orbital complication can occur in acute sinusitis when there is delay in diagnosis of acute sinusitis, delay in starting proper treatment, improper selection of antibiotic, underdose, antibiotic not given according to schedule but irregularly and also not given for a proper duration. Secondly, the complications will arise if along with antibiotic, local and systemic nasal decongestant, steam inhalation and saline irrigation are not given to allow free drainage.

It was found that orbital inflammation is secondary to sinusitis in around 70% of cases<sup>[14,25]</sup> and maxillary, frontal, ethmoid sinuses may be involved.<sup>[26]</sup>

## CONCLUSION

Orbital complications secondary to acute sinusitis are threat to patient vision and life but they are uncommon. Complete examination of ENT and eyes is required to diagnose acute sinusitis and its orbital complications. Radiology of sinuses show the sinus/sinuses affected and can be of value in follow up of cases to see whether resolution has taken place and radiolucency has restored.

CT is mandatory if orbital complications are suspected and earlier the better because it will guide that surgery is required or not. Orbital complications of sinusitis are due to ignorance, lack of awareness, under treatment on part of the patient and doctor and delayed/missed diagnosis on part of clinician.

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# Co-Infection of HBV in Partially/Non-Vaccinated Diagnosed HCV Positive Patients

Raza Muhammad Khan<sup>1</sup> and Asmatullah Khan<sup>2</sup>

of HBV in Partially/Non-Vaccinated Diagnosed HCV Positive

## ABSTRACT

**Objective:** To determine the frequency of co-infection of HBV in partially/non-vaccinated diagnosed HCV positive patients.

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

**Place and Duration of Study:** This study was conducted at the Department of Medicine, DHQ Teaching Hospital Bannu, Khyber Pakhtunkhwa from Feb 2015 to Aug 2015.

**Materials and Methods:** Data was collected from 371 patients already diagnosed as HCV positive for more than 1 year, through a preset questionnaire, to note their vaccination status against HBV. Those patients who were partially or non-vaccinated, were screened for HBsAg by ELISA, to document the co-infection.

**Results:** Out of 371 HCV positive patients, 201 patients were males (54.2%) and 170 (45.8%) were females. Only 89 (23.99%) patients were vaccinated (49 males and 40 females) while the rest 282 were either non-vaccinated (260 patients) or partially vaccinated (22 patients). So overall 282 (76.01%) HCV positive patients were lacking proper vaccination against HBV, and merely 89 (23.99%) patients were properly vaccinated against HBV. Out of those 282 HCV positive patients, who were either non-vaccinated or partially vaccinated, 14 (4.96%) patients were found to be HBsAg positive by ELISA (co-infection).

**Conclusion:** The frequency of vaccination against HBV was very low in this high risk adult group patients (18-60 years) already infected with HCV. Only 89 (23.99%) patients were properly vaccinated, which is an alarming situation. Out of these 282 HCV positive patients lacking proper vaccination against HBV, 14 (4.96%) patients were found to be HBsAg positive by ELISA (co-infection). This co-infection can be prevented by proper planing by health care provider to improve vaccination.

**Key Words:** Hepatitis C virus (HCV), Vaccination status (vaccinated/non-vaccinated/partially vaccinated), Hepatitis B virus (HBV), Bannu.

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## INTRODUCTION

Hepatitis C is an infectious disease caused by the hepatitis C virus (HCV), previously called as "non-A non-B hepatitis". It is estimated that 130–170 million people i.e.; 3% of the world's population are living with chronic hepatitis C<sup>1</sup>. About 3–4 million people are infected per year, and more than 350,000 people die yearly from hepatitis C related diseases<sup>1</sup>. Its prevalence is higher in some countries in Africa and Asia e.g.; Egypt (22%), Pakistan (4.8%) and China (3.2%)<sup>1</sup>.

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Hepatitis B (HBV) infection is caused by Hepatitis B Virus (HBV)/ Dane particle, previously called as "Serum Hepatitis". The disease has caused epidemics in parts of Asia and Africa and it is endemic in China<sup>2</sup>. About a third of the world population has been infected at one point in their lives including 350 million who are chronic carriers<sup>3, 4</sup>. National and regional prevalence ranges from over 10% in Asia to under 0.5% in the United States and northern Europe. As of 2010, China has 120 million infected people, India 40 million and Indonesia 12 million. According to WHO, worldwide, an estimated 2 billion people are infected with the HBV, more than 240 million have chronic liver disease and 600,000 people die every year due to acute or chronic consequences of hepatitis B<sup>3</sup>.

Both hepatitis C<sup>1</sup> and B<sup>2,3,4</sup> are becoming a major health challenge for the world in general and government of Pakistan and KPK in specific.

According to one study in Pakistan, prevalence of HBV infection among healthy adults, blood donors and non-donor, was 2.4% and that for HCV infection was 3.0%<sup>5</sup>. The condition is even worse in Khyber Pakhtunkhwa (KPK) and FATA areas. In one study, 224 out of 7148 i.e.; 3.13% blood donors were positive for anti-HCV antibodies by ICT<sup>6</sup>. In another study, 57 patients out of

1269 (4.49%) patients were HBs-Ag positive and 88 patients (6.93%) patients anti-HCV antibodies positive<sup>7</sup>. According to Government of KPK, 1553 Hepatitis B and 6214 Hepatitis C patients were treated in year 2011-12 under Hepatitis Control Programme<sup>8</sup>.

Both hepatitis B and C viruses are hepatotropic and have the same mode of transmission. Co-infection with these two viruses can occur especially in area of high prevalence.

Hepatitis "B" virus co-infection can occur in those HCV-positive patients who are not vaccinated against HBV infection. Dual chronic infection with HCV and HBV is common in areas endemic for either virus like China for HBV<sup>2</sup>.

In one study in Taiwan, co-infection with HBV in active HCV infection was noted in 161 patients (HBsAg positive) out of 321 (50.16%)<sup>9</sup>. Co-infection with HBV or Hepatitis A virus (HAV) in patients with chronic HCV infection is associated with increased morbidity and mortality<sup>10,11</sup>.

Complications like Acute Fulminant Hepatitis, Hepatocellular Carcinoma and Cirrhosis are more common and earlier in those HCV patients who are co-infected with Hepatitis B, HIV and alcoholics<sup>12</sup>.

No local data is available regarding hepatitis B and C co-infection in KPK. Dual chronic infection with HCV and HBV is common in areas endemic for either virus.

Peg-Interferon alfa 2a & 2b along with Ribavirin are antiviral which can be used for co-infection caused by HCV & HBV<sup>1</sup>. It is equally effective in patients with HCV mono-infection and in those with chronic HCV-HBV infection.<sup>9</sup> 9 million U of standard IFN 3 times weekly for 3 months could clear HCV in 31% of patients with HCV-HBV coinfection.<sup>13</sup>

Standard IFN and Ribavirin could cause sustained HCV eradication at rates comparable to those in patients with HCV alone and, interestingly, up to 21% of their patients lost the hepatitis B surface antigen<sup>14</sup>.

## MATERIALS AND METHODS

This descriptive, cross sectional study was conducted at Department of Medicine, DHQ Teaching Hospital Bannu KPK, 6 months from Feb 2015 to Aug 2015.

Sample Size: 371 HCV positive patients who were analyzed for HBV vaccination (taking 40.5%<sup>15</sup> as frequency of true vaccination rate against HBV, keeping 5% margin of error and 95% confidence interval, using WHO sample size calculator). Out of it, the 282 patients not vaccinated were tested for HBV infection. Consecutive, Non-probability Sampling used. Inclusion Criteria: All "HCV" positive patients (Anti-HCV Abs positive by ELISA, diagnosed for last one year, noted from clinical record), not vaccinated for HBV, of Either gender, and aged above 18 and under 60 years.

Exclusion Criteria: Those patients with a history of previous Hepatitis "B" infection (who have cleared the virus either spontaneously or by treatment), vaccinated

patients, patients with End-stage liver disease, patients terminally ill, and patients with dementia/mentally retarded were not included because, as they were either already infected, naturally immunized/vaccinated to HBV, would not benefit from future planned vaccination or would give recall bias.

Data Collecting Procedure: The study was conducted after approval from hospitals ethical and research committee/ board. All the patients who were HCV positive not vaccinated for HBV and meeting the inclusion criteria, as per operational definitions, presented to the Department of Medicine, DHQ Teaching Hospital Bannu, through emergency or OPD, were included in the study. All patients were first counseled for interview. The purpose and benefits of the study were explained to all patients, and a written informed consent was obtained from all who agreed to participate in the study. A detailed medical history (used as a diagnostic tool) was taken from all the patients, regarding duration of HCV infection and hepatitis "B" vaccination status. A structured questionnaire was distributed among patients (study population), as data collection tool having all variables of interest.

All the patients were interviewed on the basis of questionnaire and they were categorized as Vaccinated, Partially vaccinated or Non-vaccinated Hepatitis "B".

Those HCV positive patients who were partially/ non-vaccinated were screened for HBsAg by ELISA from hospital laboratory of DHQ Teaching Hospital Bannu, if they were not screened in the past after 1 year of acquiring HCV infection, to document the co-infection.

All the information including name, age, gender, address, vaccination status and co-infection were recorded in that pre-designed Proforma. Only a complete Proforma was subjected to analysis. Strict exclusion criteria was applied to control confounders and bias in the study results.

Statistical Analysis: Data obtained was entered into SPSS version 10 and analyzed in descriptive statistics. Mean  $\pm$  SD were calculated for numerical/ quantitative variables like age. Frequencies and percentages (%) were calculated for categorical/ qualitative variables such as gender, vaccination status and co-infection. Vaccination status and co-infection were stratified among age and gender to see the effect modifiers. All results were presented in the form of tables, charts.

## RESULTS

A total of 371 patients with HCV positive were included in the study. Among them, 201 (54.18%) were male and 170 (45.82 %) were female, with male to female ratio of 1.18: 1.0. Their age ranged between 18 and 60 years, and the mean age was  $37.15 \pm 14.009$  years. 89 (23.99%) patients were completely vaccinated, while 282 (76.01%) patients were either non-vaccinated (260 patients i.e. 70.08%) or partially vaccinated (22 patients i.e. 5.93%), as per operational definition.



**Table No.1: Summarized descriptive statistics of study population (n=371)**

Vaccination Status	Age Group									Total Patients
	18-25 years			26-55 years			56-60 years			
	M*	F	T	M	F	T	M	F	T	
Vaccinated	16	13	29	27	22	49	06	05	11	89
Non-vaccinated	50	43	93	68	59	127	22	18	40	260
Partially Vaccinated	03	03	06	07	06	13	02	01	03	22
Total Patients	69	59	128	102	87	189	30	24	54	371

\*M= Male F= Female T= Total

Out of 371 (n=371) HCV positive patients, 201 patients were males (54.2%) and 170 (45.8%) were females. Only 89 (23.99%) patients were vaccinated (49 males and 40 females) while the rest 282 were either non-vaccinated (260 patients i.e. 70.08%, 140 males and 120 females) or partially vaccinated (22 patients i.e. 5.93%, 12 males and 10 females) (table 2). So overall 282 (76.01%) HCV positive patients were lacking proper vaccination against HBV, and merely 89 patients were properly vaccinated against HBV.

Out of those 282 (n=282) HCV positive patients, who were either non-vaccinated or partially vaccinated, 14 (4.96%) patients were found to be HBsAg-positive by ELISA (co-infection) and 268 (95.04%) were HBsAg-negative by ELISA (table 3). Cross-tabulation between vaccination status and co-infection is shown in table 4 which showed that all the 14 HBsAg-positive patients (co-infected) were those who were not vaccinated at all (8 males and 6 females). Co-infection in table 3, while combined vaccination status & co-infection in table 4.

**Table No.2: Frequency of vaccination status of patients (n=371):**

Vaccination status	Frequency	Percentage
Non-vaccinated	260	70.1%
Partially Vaccinated	22	5.9%
Vaccinated	89	24.0%
Total	371	100.0%

**Table No.3: Frequency of co-infection of patients (N=282):**

Parameters	Frequency	Percentage
HBsAg -VE by ELISA	268	95.035%
HBsAg +VE by ELISA	14	4.965%
Total	282	100%

**Table No.4: Co-Infection in non-/partially vaccinated patients (N=282):**

Vaccination status	Co-Infection by HBV			Total
	Not checked	HBs Ag-ve by ELISA	HBsAg+ve by ELISA	
Non-vaccinated	-	246	14	260
Partially Vaccinated	-	22	0	22
Vaccinated	89	-	-	89
Total	89	268	14	371

P value= 0.000

## DISCUSSION

Hepatitis C is an infectious disease of the liver. It is a world health problem. It is estimated that 130–170 million people i.e.; 3% of the world's population are living with chronic hepatitis C<sup>1</sup>. Hepatitis C is the

leading cause of liver transplantation and is primary cause of cirrhosis (27%) and Liver cancer (25%)<sup>16</sup>. Novaccine against the hepatitis C is available. Its spread and transmission can be decreased by adopting preventive measures.

If these HCV-positive patients are also co-infected at the same time with HBV, HIV or are alcoholics, then the disease progress is more rapid and accelerated, leading to early hepatic failure, cirrhosis or hepatocellular carcinoma.

Management of chronic HCV patients also include screening of these patients for HBV infection, and if not infected/prior immunized/vaccinated, then proper vaccination of these patients against HBV with standard vaccination schedule<sup>17,18</sup>. This vaccination will protect against HBV as well as HDV infection.<sup>18,19</sup> No local data is available regarding hepatitis B and C co-infection in KPK. Dual chronic infection with HCV and HBV is common in areas endemic for either virus.

This preliminary study presents a detailed survey of 371 HCV-patients, both out patients and in-door patients, who were aged 18-60 years, with mean age 37.15±14.009 years, who were positive for anti-HCV positive by ELISA for >1 year, noted from their clinical records, with compensated liver disease, according to inclusion criteria. Their vaccination status was inquired against HBV infection.

Out of 371, only 89 (23.99%) patients were vaccinated (49 males and 40 females) against HBV. This vaccination rate is slightly higher than the vaccination rate noted in a study in Texas<sup>12</sup>, where it was 21.9% (vs.23.99%). While this vaccination rate is lower than the vaccination rate noted in a study in New York USA<sup>15</sup>, where it was 40.5% (Vs 23.99%).

Out of 371, a large portion of 282 (76.01%) patients were lacking proper vaccination against HBV according to standard schedule, they were either non-vaccinated (260 patients i.e.70.08%) or partially vaccinated (22 patients i.e.5.93%), as per operational definition.

These 282 patients were subjected to screening program for HBV co-infection. The method used was detection of HBsAg by ELISA.

The 22 patients who were partially vaccinated were all negative for HBsAg. It means that none of them has HBV co-infection. Though anti-HBs was not checked to see whether the partial vaccination has mounted some immunity against HBV or not, but it seemed that still they have some immunity against HBV due to this partial vaccination.

The 14 patients, all from 260 non-vaccinated patients (4.96% of 282), were positive for HBsAg by ELISA (Co-infected). This rate of co-infection is very low as compared to that noted in one study in Taiwan<sup>9</sup> (4.96

Vs 50.16), partially because of low prevalence /endemicity of HBV here and use of less sensitive test for screening for HBV infection (HBsAg by ELISA), which can neither detect occult/latent hepatitis B (HBsAg-negative and anti-HBc-positive) nor HBV infection in window period (HBsAg and anti-HBs both negative). This added risk to HCV-positive patients would have been prevented/decreased by proper vaccination against HBV infection, with standard schedule of vaccination.

## CONCLUSION

This study has demonstrated that a large proportion of the HCV-positive patients lacked proper vaccination against HBV, where both the viruses have high prevalence, and HBV infection can occur to these patients (co-infection) when not vaccinated for HBV. Therefore, all those managing HCV-positive patients should also counsel and educate the patients, regarding preventive measures against both HCV/HBV infections, screen these patients for HBV infection, and if not co-infected, then properly vaccinate them against HBV, with standard schedule of vaccination, along with giving standard Treatment including recent antivirals for HCV.

**Recommendations:** In the view of the above study, we recommend:

- The guidelines that all HCV-positive patients should be screened and vaccinated for HBV, must be practiced.
- All the HCV free-treatment programs, which have already been started, should incorporate free vaccination against HBV as well, to prevent co-infection.

## Author's Contribution:

Concept & Design of Study: Raza Muhammad Khan  
 Drafting: Asmatullah Khan  
 Data Analysis: Raza Muhammad Khan  
 Revisiting Critically: Raza Muhammad Khan  
 Final Approval of version: Raza Muhammad Khan

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

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# Spectrum of Causes of Cholestatic Jaundice in Neonates and Infants

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## ABSTRACT

**Objective:** To determine the causes of Cholestatic jaundice in infants and children.

**Study Design:** Analytical study.

**Place and Duration of Study:** This study was conducted at the Department of Pediatrics Naseer Teaching Hospital Peshawar from January 2015 to December 2018.

**Materials and Methods:** A total of 25 patients presented with Cholestatic jaundice to the department of pediatrics were included in the study. All patients of both gender presented with jaundice in infancy. Data collected from all patients was put on a predesigned proforma. Data was analyzed on SPSS version 14.

**Results:** A total of 25 patients diagnosed with Cholestatic jaundice were included in the study. Out of 25 patients 15 (60%) were male and 10(40%) were female. Biliary atresia was the most common cause present in 7(28%) cases, followed by galactosemia and progressive familial intrahepatic cholestasis (PFIC) which were 4(16%) cases each. Cytomegalovirus (CMV) infection was found in 3(12%) cases. Alagille syndrome and choledochal cyst were diagnosed in 2(8%) cases each. Caroli disease, Neonatal sepsis and Neonatal hemochromatosis was present in 1(4%) case each.

**Conclusion:** From this study we concluded that Cholestatic jaundice is a common problem in infants and has diverse causes both medical and surgical. Timely diagnosis is important for the prognosis of disease.

**Key Words:** Cholestatic jaundice. Direct bilirubin. Infants.

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## INTRODUCTION

Cholestatic jaundice is defined as reduced bile formation or excretion resulting in retention of biliary substances within the liver which should be normally excreted into the intestinal lumen in bile<sup>1</sup>. Incidence of Cholestatic jaundice in infants is approximately 1 in 2500 to 5000 live births with different causes<sup>2</sup>. Neonatal jaundice can be due to conjugated or unconjugated hyperbilirubenemia, but conjugated hyperbilirubenemia is always pathological due to cholestasis<sup>3</sup>. Cholestatic jaundice usually presented with prolong jaundice, pale color stool, dark color urine and sometime bleeding disorder<sup>4</sup>.

The first step in diagnosing cholestasis is to find out intrahepatic or extra hepatic cause, and early diagnosis is important for prognosis in some condition as in biliary atresia<sup>5</sup>.

Cholestatic jaundice is usually due to metabolic and canalicular dysfunction of different etiologies such as TORCH infection (toxoplasmosis, herpes simplex, cytomegalovirus, Rubella) idiopathic neonatal hepatitis, neonatal hemochromatosis, galactosemia, tyrosinemia, cystic fibrosis, alpha 1-antitrypsin deficiency, hemophagocytic lympho-histiocytosis (HLH) and extra hepatic diseases (biliary atresia, choledochal cyst gall stones)<sup>3</sup> <sup>6</sup>. Detail history taking is important for diagnosis and it include details of neonatal screening, any medication, passage of first bowel, onset of jaundice, color of stool and urine, consanguinity, pruritus and previous history of miscarriages and other siblings<sup>7</sup>. Hepatomegaly, splenomegaly and acholia (pale color stool) must be observed as these findings indicate significant cholestasis<sup>8</sup>.

Initial approach for diagnosing cholestasis is to do conjugated bilirubin along with aspartate aminotransferase (AST) alanine aminotransferase (ALT) and gamma glutamyl transferase (GTT) level which are variably elevated. Abnormal Synthetic liver functions like prolonged prothrombin time (PT), raised serum ammonia, low albumin level and hypoglycemia shows severe hepatic dysfunction needs urgent referral

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to tertiary care hospital. Urinalysis for reducing substances is important to rule out galactosemia<sup>9</sup>.

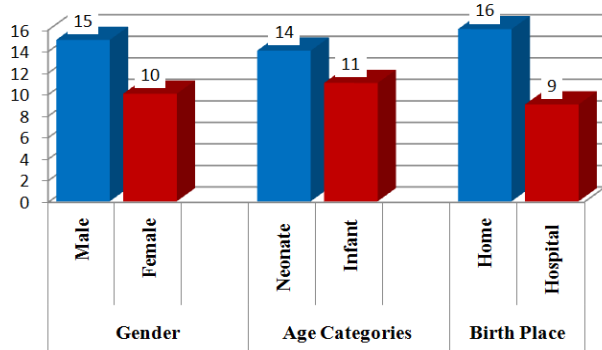
## MATERIALS AND METHODS

The study was carried out in the department of pediatrics Naseer Teaching Hospital, Peshawar from January 2015 to December 2018. Patients included in this study were from ward, nursery and OPD of pediatric department. A total of 25 patients were included in the study. All cases included in the study presented with Cholestatic jaundice in infancy.

The data was recorded on a predesigned proforma including detail history, clinical examination and investigations. All cases included in the study were having Cholestatic jaundice. Investigations have been done to find out the causes by performing Complete blood counts (CBC), Liver function tests (LFTS), conjugated and unconjugated bilirubin levels, serum albumin, prothrombin time(PT), urine for reducing substances, serum ferritin level, TORCH screening test, abdominal ultrasonography, echocardiography, HIDA scan and liver biopsy. The study had necessary approval from the Institutional ethical committee and informed consent was taken from the parents/guardian of the subject. The data was transferred and analyzed using statistical package for social sciences (SPSS) version 14. The results were presented in the form of percentages, chi-square test was applied for comparison of proportions with significance of p value less than 0.05.

## RESULTS

A total of 25 patients diagnosed with Cholestatic jaundice were included in the study. Out of 25 patients 15 (60%) were male and 10(40%) were female.



**Figure No.1: General Characteristics of Neonates and Infants**

Similarly 14(56%) were neonate (< 28 days) and 11 (44%) infants (>28 days) where, minimum age of presentation with jaundice was 21 days and maximum age of 3 months with average of 37.44 days. Biliary atresia was the most common cause present in 7(28%) cases, followed by galactosemia and progressive familial intrahepatic cholestasis (PFIC) which were 4(16%) cases each. Cytomegalovirus (CMV) infection was found in 3(12%) cases. Alagille syndrome and

choledochal cyst were diagnosed in 2(8%) cases each. Caroli disease, Neonatal sepsis and Neonatal hemochromatosis was present in 1(4%) case each (table 1).

**Table No.1: Causes of Cholestatic jaundice in neonates and infants**

Diseases	No of cases	percentages
Biliary atresia	07	28%
Galactosemia	04	16%
PFIC	04	16%
CMV infection	03	12%
Alagille syndrome	02	8%
Choledochal cyst	02	8%
Caroli disease	01	4%
Neonatal sepsis	01	4%
Neonatal hemochromatosis	01	4%

## DISCUSSION

Many disorders in neonates and infants can present with Cholestatic jaundice and early diagnosis and treatment is very important for prognosis. Biliary atresia is one the most common cause of Cholestatic jaundice as reported in our study which is 28%. Hoerning et al study performed in a tertiary care center also revealed biliary atresia the most common cause in 40% of cases<sup>10</sup>. Average age of patients with biliary atresia was 50 days. All patients were referred to specialized unit for surgical management. Galactosemia was the 2<sup>nd</sup> most common cause found in 4(16%) cases. Galactosemia is one of the most common metabolic disease causing Cholestatic jaundice in infants as found in other studies like Gottesman et al which revealed galactosemia in 36.49% of metabolic cases<sup>11</sup>. All patients of galactosemia were put on lactose free milk with significant improvement of jaundice. PFIC is also the 2<sup>nd</sup> most common cause of cholestasis in our study found in 16% of cases. Many studies had near same results as revealed in Kamath BM et al, Fischler B et al and Ruth ND et al found PFIC in 11.75%, 12.9% and 16% respectively<sup>12, 13, 14</sup>. Cytomegalovirus (CMV) infection is present in 3(12%) cases, which were treated with gancyclovir for 6 weeks with significant improvement. CMV infection as a cause of cholestasis are different in other studies ranges from 2 to 7% in some studies and up to 34% in other studies<sup>15, 16</sup>. This high frequency of CMV hepatitis may be due to high incidence in some countries. Alagille syndrome was present in 2 cases which contributes to 8% of all cases. Both patients were having dysmorphic features (triangular face, broad face, hypertelorism, deep set eyes) pulmonary stenosis and Cholestatic jaundice. Gottesman et al found Alagille syndrome in 6% of cases close to our results<sup>11</sup>. Choledochal cyst was found in 2 cases (8%). Hitch et al and bazlul et al found choledochal cyst in 3.5% and 6.5% of cases

respectively which are nearly to our findings<sup>17, 18</sup>. Neonatal sepsis, Caroli disease and neonatal hemochromatosis were present in 01 case each contributing 4% in each case. Rafeey et al found neonatal infection in 3.28% of cases, while Ipek et al found in 9.78% of cases. This high incidence may be due to variation of neonatal sepsis incidence in different areas<sup>19,20</sup>. One patient of neonatal hemochromatosis was admitted with hepatic failure and was died after 3 days of admission.

## CONCLUSION

From this study we concluded that Cholestatic jaundice is a common problem in infants and has diverse medical and surgical causes. Timely diagnosis is important for the prognosis of disease.

**Recommendation:** It has been recommended that infants presented with persistent jaundice must be investigated for cholestasis as many causes are treatable if diagnosed timely.

### Author's Contribution:

Concept & Design of Study:	Rifayat Ullah Afridi
Drafting:	Irfan Khan
Data Analysis:	Sher Bahadur
Revisiting Critically:	Shezad Najeel and Irum Naz
Final Approval of version:	Shadman and Kifyat Ullah Afridi

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

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# Comparison of Efficacy of Latanoprost 0.005% with Bimatoprost 0.01% in Patients with Open Angle Glaucoma

Intraocular Pressure with Latanoprost and Bimatoprost

Nadia Nazir, Zulfiqar Ali, Ejaz Latif, Imran Nazir and Zunaira Alvi

## ABSTRACT

**Objective:** To compare the mean change in intraocular pressure with Latanoprost 0.005% and Bimatoprost 0.01% in patients with open angle glaucoma

**Study Design:** Randomized open clinical trial.

**Place and Duration of Study:** This study was conducted at the outpatient department of Ophthalmology, Bahawal Victoria Hospital, Bahawalpur from December, 2015 to November 2016.

**Materials and Methods:** 60 diagnosed patients of open angle glaucoma age group 20 to 50 years were included coming to eye OPD having intraocular pressure greater than 20 millimeter of mercury at 8:00am. The patients were allotted group A or group B by the lottery method. The group A was considered as Latanoprost group while group B as Bimatoprost group. Group A was treated with Latanoprost 0.005% while the group B with Bimatoprost 0.01% as mono-therapy with one drop daily in conjunctival sac as topical administration at 05.00 p.m for 29 days, beginning on day 0 of the study. Follow up visits were conducted on day 30 at 8 am and IOP of both eyes were measured and mean reduction in IOP was noted.

**Results:** Difference between base line and day 30 IOP right eye of male patients in group A was 6.75 +/- 0.52mmHg while in group B was 7.58 +/- 0.24mmHg (P=0.001) and the difference between base line and day 30 IOP Left eye of male patients in group A was 6.60 +/- 0.70mmHg while in group B was 7.28 +/- 0.38mmHg. (P=0.0031)

The difference between base line and day 30 IOP right eye of female patients in group A was 6.18 +/- 0.01mmHg while in group B was 7.06 +/- 0.06mmHg (P=0.0001) & difference between base line and day 30 IOP Left eye of female patients in group A was 6.36 +/- 0.10 mmHg while in group B was observed 8.0 +/- 0.31mmHg. (P=0.001)

**Conclusion:** Current study showed that mean change in reducing the intraocular pressure with Bimatoprost 0.001% is more significant than Latanoprost 0.005%

**Key Words:** Glaucoma, Intraocular pressure, Latanoprost 0.005%, Bimatoprost 0.01%, Quality of Life, Health related quality of life.

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## INTRODUCTION

It is difficult to define glaucoma precisely, partly because the term encompasses a diverse group of disorders. All forms of the disease have in common a characteristic potentially progressive optic neuropathy that is associated with visual field loss as damage progresses, and in which IOP is key modifiable factor<sup>1</sup>. Three large phase-III clinical trial with Latanoprost 0.005% have been performed in Europe (Scandinavia & UK) and USA<sup>2-4</sup> In the Scandinavian and the U.S studies Latanoprost 0.005% was significantly more effective than timolol.

The IOP lowering activity of Bimatoprost 0.01% has been evaluated in the laser-induced ocular hypertensive monkey model,<sup>5</sup> and the top of the dose response curve was determined to be 0.004%.<sup>6</sup> On the basis of these analysis, prostaglandin analogues are now being used as primary therapy for open angle glaucoma.

Prostaglandin analogues lower intra-ocular pressure by increasing the uveoscleral outflow of aqueous humor.<sup>7</sup> Latanoprost 0.005% is phenyl-substituted prostaglandin analogue. Bimatoprost 0.01% is a topical ocular isopropyl ester prodrug, that is rapidly hydrolyzed by esterases in the cornea to the biologically active, free acid. Bimatoprost 0.01% has greater affinity for the prostaglandin F(P) receptor than either PGF<sub>2</sub>α or Latanoprost 0.005%.<sup>8</sup> Their concentration in aqueous humor peaks at 2 hours and declines over the next 24 hours. Systemically they are rapidly metabolized and have plasma half life of about 17 minutes. These pharmacokinetics are almost ideal for an ocular drug. The intraocular pressure lowering effects of prostaglandin analogue is not only well maintained but an additional effect is seen after 2-4 weeks. This delayed effects may be due to the specific mechanism

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of action of prostaglandins, which increase uveoscleral outflow, and recent studies show that they induce changes in the extra-cellular matrix of the ciliary muscle of the eye.<sup>9</sup> These changes may facilitate aqueous humor outflow through the ciliary muscle (uveoscleral route). This process might possibly not to be completed in 2 weeks, which would explain the additional decrease in IOP after some months of treatment with prostaglandin analogues. An additional benefit is that monotherapy definitely improves patient compliance. There is very little national and local data available to compare the two drugs i.e latanoprost versus bimatoprost in reducing IOP in patients with primary open angle glaucoma.

## MATERIALS AND METHODS

This study was conducted at the outpatient department of Ophthalmology, Bahawal Victoria Hospital, Bahawalpur from December 2015 to November 2016. Approval from the institute's ethical and research committee was taken for this study. Informed consent was sought from all the study participants. By adopting non probability consecutive sampling technique, we enrolled a total of 60 patients newly diagnosed (within a week duration) of both gender and age 20-50 years and divided into two groups (30 in each group) having intraocular pressure greater than 20 millimeter of mercury at 8 am. Patient must be free of ocular medication at the time of enrollment and was not using any parasympathomimetics or carbonic anhydrase inhibitors for the last 4 days, adrenergic agonists for the last 2 weeks and topical beta-blockers for the last 4 weeks. Patients having previous intraocular surgery, secondary glaucomas, primary narrow angle glaucoma, known hypersensitivity to any component in the study medications, any systemic drug affecting IOP, any uncontrolled systemic disease or severe cardiovascular disease and any previous use of latanoprost / Bimatoprost, patients were excluded.

Patients were diagnosed on the basis of ocular and medical history, recording cup disc ratio, visual field examination with automated perimetry and OCT for retinal nerve fiber layer and intraocular pressure with Goldman Applanation tonometry.

The patients were allotted group A or group B by the lottery method. Their demographic data as well as brief history was taken. The group A was considered as Latanoprost group while group B as Bimatoprost group. Baseline IOP measurements were made at 8 am on day 0. IOP was measured in mm Hg with an applanation tonometer affixed to a slit lamp from both eyes and mean IOP values from both eyes were calculated. Group A was treated with Latanoprost 0.005% while group B with Bimatoprost 0.01% as mono-therapy with one drop daily in conjunctival sac as topical administration at 05.00 pm for 29 days, beginning on day 0 of the study. Follow up visits were conducted on

day 30 at 8 am and IOP of both eyes was measured and mean reduction in IOP was noted.

All the information's were entered in the SPSS version 17.0 and analyzed through its statistical package. The mean and the standard deviation were calculated for the age and IOP at baseline and on day-30. Stratification with respect to age, gender, side of eye was done. Chi. Square test was applied to qualitative data (Gender) and t -test was applied to quantitative data (age, baseline IOP, day-30 IOP).

## RESULTS

A total 60 patients were included in two study groups (each consisting of 30 patients), group A was treated with Latanoprost 0.005% and the group B was treated with Bimatoprost 0.01%.

The age varied from 20 to 50 years in group A. The mean age in group A was 32.0 +/- 4.39 years and in group B was 30.4 +/- 4.9 years (P=0.188). Among group A 16 (60%) male and 14 (40%) female and group B 14 (40%) male and 16 (60) female. (P=0.6056)

The Difference of IOP (base line and on day 30) Right Eye of Male Patients as shown in Table 1 is significant (P=0.001). Difference of IOP (base line and on day 30) Left Eye of Male Patients as shown in Table 2 is significant (P=0.0031). Difference of IOP (base line and on day 30) Right Eye of Female Patients as shown in Table 3 is significant (P=0.0001). Difference of IOP (base line and on day 30) Left Eye of Female Patients as shown in Table 4 is significant (P=0.001).

**Table No.1: Difference of IOP (base line and on day 30) Right Eye of Male Patients**

Group	Mean and S.D of Base Line IOP	Mean and S.D. of day 30 IOP	Difference between base line and day 30 IOP and S.D
Latanoprost 0.005%	26.09±0.75	19.34±1.27	6.75±0.52
Bimatoprost 0.01%	26.25±1.12	18.67±1.36	7.58±0.24

**Table No.2: Difference of IOP (base line and on day 30) Left Eye of Male Patients**

Group	Mean and S.D of Base Line IOP	Mean and S.D. of day 30 IOP	Difference between base line and day 30 IOP and S.D
Latanoprost 0.005%	25.81±1.09	19.21±1.79	6.60±0.70
Bimatoprost 0.01%	26.03±1.08	18.75±0.70	7.28±0.38

Difference of IOP (Baseline and on day 30) Rt Eye of Age Group 20-35 years as shown in Table 5 is significant (P=0.0001). Difference of IOP (Baseline and on day 30) Lt Eye of Age Group 20-35 years as shown in Table 6 is significant (P=0.0001).

**Table No.3: Difference of IOP (base line and on day 30) Right Eye of Female Patients**

Group	Mean and S.D of Base Line IOP	Mean and S.D. of day 30 IOP	Difference between base line and day 30 IOP and S.D
<b>Latanoprost 0.005%</b>	25.78±1.41	19.06±1.40	6.18±0.01
<b>Bimatoprost 0.01%</b>	25.75±1.42	18.09±1.36	7.06±0.06

**Table No.4: Difference of IOP (base line and on day 30) Left Eye of Female Patients**

Group	Mean and S.D of Base Line IOP	Mean and S.D. of day 30 IOP	Difference between base line and day 30 IOP and S.D
<b>Latanoprost 0.005%</b>	26.07±1.07	19.71±0.97	6.36±0.10
<b>Bimatoprost 0.01%</b>	26.18±1.42	18.18±1.73	8.0±0.31

**Table No.5: Difference of IOP (Baseline and on day 30) Rt Eye of Age Group 20-35 years**

Group	Mean and S.D of Base Line IOP	Mean and S.D. of day 30 IOP	Difference between base line and day 30 IOP and S.D
<b>Latanoprost 0.005%</b>	25.59±1.06	19.29±1.30	6.30±0.24
<b>Bimatoprost 0.01%</b>	26.04±1.13	18.31±1.46	7.73±0.33

**Table No.6: Difference of IOP (Baseline and on day 30) Lt Eye of Age Group 20-35 years**

Group	Mean and S.D of Base Line IOP	Mean and S.D. of day 30 IOP	Difference between base line and day 30 IOP and S.D
<b>Latanoprost 0.005%</b>	25.72±1.03	19.18±1.58	6.54±0.55
<b>Bimatoprost 0.01%</b>	26.33±1.23	17.93±1.30	8.40±0.07

**Table No.7: Difference of IOP (Baseline and on day 30) Rt Eye of Age Group 36-50 years**

Group	Mean and S.D of Base Line IOP	Mean and S.D. of day 30 IOP	Difference between base line and day 30 IOP and S.D
<b>Latanoprost 0.005%</b>	25.59±1.22	18.62±1.27	6.97±0.05
<b>Bimatoprost 0.01%</b>	26.00±0.89	18.00±0.89	8.00±0.00

Difference of IOP (Baseline and on day 30) Rt Eye of Age Group 36-50 years as shown in Table 7 is significant (P=0.0001). Difference of IOP (Baseline and

on day 30) Lt Eye of Age Group 36-50 years as shown in Table 8 is significant (P=0.0001).

**Table No.8: Difference of IOP (Baseline and on day 30) Lt Eye of Age Group 36-50 years**

Group	Mean and S.D of Base Line IOP	Mean and S.D. of day 30 IOP	Difference between base line and day 30 IOP and S.D
<b>Latanoprost 0.005%</b>	25.37±0.95	19.25±1.00	6.12±0.05
<b>Bimatoprost 0.01%</b>	26.50±0.44	18.00±0.89	8.50±0.45

## DISCUSSION

Glaucoma is a group of eye diseases which result in damage to the optic nerve and cause vision loss. The most common type is open-angle glaucoma with less common types including closed-angle glaucoma and normal-tension glaucoma. Risk factors for glaucoma include increased intraocular pressure in the eye, a family history of the condition, and high blood pressure.<sup>[10]</sup> but intraocular pressure is the only factor can be modified at present. If treated early it is possible to slow or stop the progression of disease with medication,<sup>[10][12]</sup>

The goal of this treatment is to decrease eye pressure<sup>11</sup>. Worldwide, glaucoma is the second-leading cause of blindness after Cataract<sup>11,13</sup>.

Prostaglandin analogs, such as latanoprost and, bimatoprost increase uveoscleral outflow of aqueous humor. Bimatoprost also increases trabecular outflow.<sup>[14]</sup> However, outcome data have been lacking that there is an unequivocally link between lowering of intraocular pressure and preserving vision<sup>15</sup>. A recent randomized trial<sup>16</sup> showed that topical ocular hypotensive medication was effective in delaying or preventing the onset of open-angle glaucoma in patients with elevated intraocular pressure. Two recent trials<sup>17,18</sup> showed that lowering of intraocular pressure decreased glaucoma progression. The current study was designed to compare the effects of drugs Latanoprost 0.005% and Bimatoprost 0.01% as primary monotherapy for open angle glaucoma. The results of this study showed that Bimatoprost 0.01% is better than Latanoprost 0.005% in lowering of intraocular pressure in follow up visits of all patients with open angle glaucoma. The results are similar with international studies as per statistical data analysis.

In this study, a total 60 patients were included in two study groups (each consisting of 30 patients), group A was treated with Latanoprost 0.005% and the Group B was treated with Bimatoprost 0.01%. The mean age in group A was found 32.0 years and in group B was 30.4 years. Difference between base line and day 30 IOP right eye of male patients in group A was 6.75+/-

0.52mmHg while in group B was 7.58  $\pm$  0.24mmHg (P=0.001) and the difference between base line and day 30 IOP Left eye of male patients in group A was 6.60  $\pm$  0.70mmHg while in group B was 7.28  $\pm$  0.38mmHg. (P=0.0031)

The difference between base line and day 30 IOP right eye of female patients in group A was 6.18  $\pm$  0.01mmHg while in group B was 7.06  $\pm$  0.06mmHg (P=0.0001) and the difference between base line and day 30 IOP Left eye of female patients in group A was 6.36  $\pm$  0.10 mmHg while in group B was observed 8.0  $\pm$  0.31mmHg. (P=0.001).

The difference between baseline and day 30 IOP Rt Eye of age group 20-35 years in group A was 6.30  $\pm$  0.24mmHg while in group B was 7.73  $\pm$  0.33mmHg (P=0.0001) and the difference between baseline and day 30 IOP Lt Eye of age group 20-35 years in group A was 6.54  $\pm$  0.55mmHg) while in group B was 8.40  $\pm$  0.07mmHg (P=0.0001).

The difference between baseline and day 30 IOP Rt Eye of age group 36-50 years in group A was 6.97  $\pm$  0.05mmHg) while in group B was 8.00  $\pm$  0.00mmHg) and the difference between baseline and day 30 IOP Lt Eye of age group 36-50 years in the group A was 6.12  $\pm$  0.05mmHg) while in group B was 8.50  $\pm$  0.45mmHg) (P=0.0001).

The same results are highly comparable with the study conducted by Wang K et al,<sup>19</sup> in which  $8.0 \pm 3.7$  mmHg (32.0%) reduction in IOP was observed in treatment-naïve patients after Bimatoprost 0.01% monotherapy.

In another randomized trials done by DuBiner H et al<sup>20</sup>, it was seen that both Bimatoprost 0.01% and latanoprost 0.005% significantly lowered IOP from baseline (p <.001) but Bimatoprost 0.01% lowered IOP more than latanoprost 0.005% at every time point measured (Bimatoprost 0.01%: 25-34% reduction, 5.9-8.9 mm Hg; latanoprost 0.005%: 20-31% reduction, 4.4-7.9 mm Hg).

Faridi and associates found a 9.45 mmHg (36%) IOP reduction at 2 months and a 9.23 mmHg (35%) IOP reduction at 6 months after Bimatoprost 0.01% 0.03% monotherapy in newly diagnosed ocular hypertension and POAG patients.<sup>21</sup> Since previous clinical evaluations suggest that glaucoma or ocular hypertension patients are rarely troubled by temporary ocular side effects, specifically ocular redness,<sup>22</sup> the mild hyperemia after Bimatoprost 0.01% treatment did not represent a clinical safety concern.

The anticipated introduction in China of the new Bimatoprost 0.01% formulation with the same efficacy and improved tolerability as the original Bimatoprost 0.03% formulation, as well as education of patients explaining the importance of IOP lowering and drug efficacy, may further improve their acceptance and compliance.<sup>23</sup>

## CONCLUSION

Current study showed that mean change in reducing the intraocular pressure with Bimatoprost 0.001% is more significant than Latanoprost 0.005%.

### Author's Contribution:

Concept & Design of Study:	Nadia Nazir
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**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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# Determine the Severity of Lower Urinary Tract Symptoms in Middle Aged and Elderly men and Assess the Impact of Lower Urinary Tract Symptoms on Quality of Life according to Severity

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## ABSTRACT

**Objective:** To examine the severity of lower urinary tract symptoms in men with elderly and middle ages and also determine the effect of lower urinary tract symptoms on patients quality of life.

**Study Design:** Observational / Cross sectional study.

**Place and Duration of Study:** This study was conducted at the Department of Urology, Ayub Medical Teaching Institute Abbottabad from January 2018 to June 2018.

**Materials and Methods:** One hundred and eighty patients with lower urinary tract symptoms with ages 35 to 80 years were included. Patients demographic including age, residence, occupation, education and socio-economic status were recorded. Patients with severe urinary tract infection, bladder cancer, age below 35 years were excluded. Severity of lower urinary tract symptoms were examined by IPSS and bother score. Impact of lower urinary tract symptoms severity on quality of life was examined.

**Results:** There were 110 (61.11%) patients were ages 40 to 60 years while 70 (38.89%) patients were ages above 60 years. Majority of patients had urban residency 66.67%. From 110 patients with ages <60 years, 50 (45.45%) had mild symptomatic IPSS score, 42 (38.18%) had moderate symptoms and 18 (16.36%) had severe symptoms. In patients with ages above 60, 20 (28.57%) had mild, 28 (40%) had moderate and 22 (31.43%) had severe symptoms. Very good, good and poor quality of life was associated with mild lower urinary tract symptoms, moderate lower urinary tract symptom was significantly associated with poor quality of life and severe symptoms was significantly associated with good, poor & worst quality of life ( $p < 0.05$ ). Patients with ages above 60 yrs had high IPSS score  $p$ -value  $< 0.05$ .

**Conclusion:** Severity of lower urinary tract symptoms is significantly associated with quality of life of patients. Patients with elderly ages had high rate of severe symptoms with poor quality of life.

**Key Words:** Lower urinary tract symptoms (LUTS), Severity, IPSS, Quality of life (QoL)

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## INTRODUCTION

Lower urinary tract symptoms are the most frequent disorder in all over the world. According to the International Continence Society (ICS) lower urinary tract symptoms were classifies into three groups storage, voiding and post-micturition.<sup>1</sup> Many of studies

reported that lower urinary tract symptoms are usually effects the patients with adult ages.<sup>2-4</sup> The incidence rate of LUTS shows difference in different studies in which some of studies reported that voiding symptoms are commonly found in men that females and storage symptoms commonly found in females than males and overall incidence rate is similar in both genders.<sup>2,3</sup>

Many of previous studies illustrated that age is a most common factor that involves direct impact on patient's quality of life. Patients with increase age had a high risk of poor quality of life.<sup>4</sup>

According to the studies conducted in Europe and Korea, demonstrated that two/third of lower urinary tract symptoms are found in patients with middle aged. However several studies reported that prevalence of LUTS is high in elderly aged patients with highly impairment of quality of life.<sup>5-10</sup>

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In male population there is a high prevalence of LUTS either in elderly or middle aged and there is no significant difference regarding quality of life.<sup>11,12</sup>

The present study was conducted aimed to examine the severity of LUTS among middle aged and elderly aged patients, also determine the impact of LUTS on patient's Quality of Life.

## MATERIALS AND METHODS

Present study was conducted at Department of Urology, Ayub Medical Teaching Institute Abbottabad from 1<sup>st</sup> January 2018 to 30<sup>th</sup> June 2018. A total of 180 patients with lower urinary tract symptoms with ages 35 to 80 years were included. Patients demographic including age, residence, education, socio-economic status and comorbidities were recorded after taking informed written consent. Patients with severe urinary tract infection, bladder cancer, age below 35 years, patients history of surgical treatment of CaP and those who were not interested to participate were excluded from the study. Severity of lower urinary tract symptoms were examined by IPSS and bother score questionnaire on 1<sup>st</sup> visit at urology department. Impact of LUTS on quality of life of patient was examined. Self prepared questionnaire was delivered to patients to examine the QoL as very good, good, poor and very poor. Data was analyzed by SPSS 20.0. P-value <0.05 was set as significant difference. Frequencies and percentages were applied to analyze the total values.

## RESULTS

Out of 180 patients, 110 (61.11%) patients were ages 40 to 60 years while 70 (38.89%) patients were ages above 60 years. Majority of patients had urban residency 100 (55.55%) while 80 (44.44%) had rural residency. 96 (53.33%) patients were literate while 84 (46.67%) were illiterate. Hypertension found in 102 (56.67%) patients followed by diabetes mellitus and alcohol 60 (33.33%) and 18 (10%) respectively. Urethral stricture was found in 6 (3.33%) patients, overactive bladder was found in 13 (7.22%) patients (Table 1).

From 110 patients with ages <60 years, 50 (45.45%) had mild symptomatic IPSS score, 42 (38.18%) had moderate symptoms and 18 (16.36%) had severe symptoms. In patients with ages above 60, 20 (28.57%) had mild, 28 (40%) had moderate and 22 (31.43%) had severe symptoms (Table 2).

From 70 mild symptoms patients 20 had very good QoL, 35 had good QoL and 15 had poor QoL. From 70 moderate LUTS symptoms patients 5 patients had very good QoL, 15 had good QoL, 49 had poor QoL and 1 had very poor QoL. From 40 severe LUTS patients, 1 had very good, 4 had good QoL, 28 had poor QoL and 7 had very poor QoL (Table 3).

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

Variable	No.	%age
<b>Age (years)</b>		
40 – 60	110	61.11
> 60s	70	38.89
<b>Residence</b>		
Urban	100	55.56
Rural	80	44.44
<b>Education</b>		
Literate	96	53.33
Illiterate	84	46.67
<b>Comorbidities</b>		
Hypertension	102	56.67
DM	60	33.33
Alcohol	18	10
Urethral Stric	6	3.33
OAB	13	7.22

**Table No.2: Severity of LUTS by IPSS**

Variable	Age (years)		P value
	40 - 60	> 60	
Mild Symptoms	50 (45.45)	20 (28.57)	<0.05
Moderate	42 (38.18)	28 (40)	<0.05
Severe	18 (16.36)	22 (31.43)	<0.05

**Table No.3: QoL association with severity of LUTS**

QoL	Mild Symptoms	Moderate	Severe
Very Good	20 (28.57)	5 (7.14)	1 (2.5)
Good	35 (50)	15 (21.43)	4 (10)
Poor	15 (21.43)	49 (70)	28 (70)
Very Poor	-	1 (1.43)	7 (17.5)

P-value 0.001

## DISCUSSION

Many of studies have been conducted to examine the severity of LUTS and prevalence of Lower urinary tract symptoms among patients with different ages and to examine the impact of severity of LUTS on patients QoL.<sup>13-15</sup> Present study was conducted aimed to examine the severity of LUTS among elderly aged and middle aged patients also determine the impact of severity of LUTS on patients Quality of Life. In present study there were 61.11% patients were ages 40 to 60 years and considered as middle aged and 38.89% patients were above 60 years and consider as elderly aged patients. A study conducted by Petrick et al<sup>16</sup> reported patients with ages below 65 year as middle aged and above 65 years as elderly aged.



In the present study, 55.56% patients had urban residence while 44.44% patients had rural residence. 96 (53.33%) patients were literate while 84 (46.67%) were illiterate. Hypertension found in 102 (56.67%) patients followed by diabetes mellitus and alcohol 60 (33.33%) and 18 (10%) respectively. Urethral stricture was found in 6 (3.33%) patients, overactive bladder was found in 13 (7.22%) patients. These results were comparable to some other studies in which majority of patients had urban residence and 45 to 55% patients were literate and OAB was found in 8.3% in middle aged patients and 3.5% in patients with ages above 60 years.<sup>19-21</sup>

In the current study, we found that from 110 patients with ages <60 years, 50 (45.45%) had mild symptomatic IPSS score, 42 (38.18%) had moderate symptoms and 18 (16.36%) had severe symptoms. In patients with ages above 60, 20 (28.57%) had mild, 28 (40%) had moderate and 22 (31.43%) had severe symptoms. These results were comparable to some other studies.<sup>22,23</sup> In this study according to the severity of LUTS relation with Quality of life of patients we found 70 mild symptoms patients 20 had very good QoL, 35 had good QoL and 15 had poor QoL. From 70 moderate LUTS symptoms patients 5 patients had very good QoL, 15 had good QoL, 49 had poor QoL and 1 had very poor QoL. From 40 severe LUTS patients, 1 had very good, 4 had good QoL, 28 had poor QoL and 7 had very poor QoL. These results showed that increase in age had significant association with poor QoL p-value <0.05. We found that patients with elderly ages had a high rate of severe and moderate symptoms with poor and very poor QoL level. These results were similar to many previous studies in which patients with elderly ages had a high rate of poor and worst QoL.<sup>24,25</sup>

## CONCLUSION

Lower urinary tract symptoms prevalence is high in all over the world and severity of symptoms had a great impact on patients Quality of Life. From this study we concluded that severity of lower urinary tract symptoms is significantly associated with quality of life of patients. Patients with elderly ages had high rate of severe symptoms with poor quality of life.

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

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# Endoscopic Management of Primary Obstructive Megaureter: Review of 28 Consecutive Cases

Endoscopic  
Management of  
Obstructive  
Megaureter

Tariq Ahmad, Shakir Rahman, Asif Malik, Muhammad Amjad Khan, Ahmad Nawaz, Akhter Nawaz and Ghufuranullah

## ABSTRACT

**Objective:** To determine the importance of endoscopic dilatation in the management of primary obstructive megaureter.

**Study Design:** Cross sectional study

**Place and Duration of Study:** This was conducted at Institute of kidney Diseases Peshawar, Pakistan from July 2017 to June 2018.

**Materials and Methods:** A sample of 28 patients was selected by convenience sampling. Detail history, examination, urinalysis and complete blood count, ultrasonography and MAG3 renography were performed in all patients. Age in months was a ratio data and analyzed for mean, SD, minimum and maximum.

**Results:** The age range was 4 months to 144 months. The mean age was  $26\text{months} \pm 5.4\text{SD}$ . Male to female ratio was 1.8. Range of Distal ureter diameter on Ultrasound was 9 to 35 mm with average of  $14\text{mm} \pm 6.85\text{SD}$ . Preoperative diuretic MAG3 showed obstruction in all cases with split renal function with range of 18 to 35% on affected side. JJ stent duration was 3 to 12 weeks with Average 9 weeks  $\pm 4.29\text{SD}$ . Reflux was not noted in any patient on postoperative MCUG.

**Conclusion:** Endoscopic treatment of obstructive megaureter is practical and effective therapeutic option. It should be extended to symptomatic cases for which open surgical repair is indicated.

**Key Words:** Megaureter, Primary, Obstructive ureter

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## INTRODUCTION

Caulk in 1923, initially explained congenital megaureter. It was diagnosed in neonates and children<sup>1</sup>. In adults it is rarely diagnosed and present in 3<sup>rd</sup> and 4<sup>th</sup> decade. It is mostly unilateral but in 15 – 25 % cases it is bilateral. Male to female ratio is 1.2 to 4.8. Children with obstructive uropathy usually suffer from obstructive type of ureter. However some are due to reflux and some are normal variety of urinary tract. A ureter is considered as megaureter if the luminal diameter is larger than  $8\text{mm}^2$ . Primary obstructive megaureter is a congenital dilatation of the ureter secondary to an adynamic segment at its terminal portion as a result of an intrinsic disturbance<sup>3</sup>.

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The pathogenesis of obstructive megaureter is due to the expression of transforming growth factor beta which might lead to a lack of post natal dysplasia. It represents 6-8% of all displaced urinary malformation in utero<sup>4</sup>. It can be associated with other genitourinary abnormalities such as duplex system, undescended testes, contralateral hydronephrosis and mega calicosis. King classified megaureter into primary and secondary obstructive megaureter<sup>5</sup>. Majority of the primary megaureter is diagnosed just in advanced stage of gestation<sup>6</sup>. It is confirmed after birth by ultrasound, MAG3 renography with diuretic stimulation and contrast instillation cystography<sup>7</sup>.

The management of congenital megaureter is controversial. Due to growth and maturation, about 80% of prenatally detected primary obstructive megaureter resolve spontaneously<sup>7</sup>, hence conservative management is considered a safe initial approach<sup>9,10</sup>. Surgical intervention even in the setting of some pathology, such as obstruction, is not always warranted. The major challenge in the management of obstructive megaureter is the clinical decision to intervene or not<sup>11,12</sup>. The classical management for the symptomatic primary obstructive megaureter is ureteral re-implantation, usually after ureteral remodelling<sup>13</sup>. Treatment may also be necessary in non-symptomatic

children with impaired renal function on scintigraphy<sup>14,15</sup>.

## MATERIALS AND METHODS

This cross sectional study was conducted at institute of kidney diseases Peshawar, Pakistan from July 2017 to June 2018. A sample of 28 patients was selected by convenience sampling. All pediatric population from 1 year to 12 year was included in the study. Age in months was a ratio data and analyzed for mean, SD, minimum and maximum. Those patients who had distal ureteric diameter more than 8 mm were included in the study. Detail history, examination, urinalysis and complete blood count, ultrasonography and MAG3 renography were performed in all patients. The indications for procedure were cross sectional ureterovesical diameter greater than 10mm, obstructive pattern on radionuclide scan, differential renal function less than 40% and recurrent urinary tract infections. Informed and written consent was taken from all patients. After general anesthesia and appropriate antibiotic cover patient was put in lithotomy position. Cystoscopy was done with 12 Fr, rigid cystoscope. Guide wire was passed in the affected ureter. Teflon ureteral dilators are passed in sequence from 6 Fr to 12 Fr under fluoroscopy guidance. 6 Fr double J stent was left in place. Catheter was kept for bladder drainage. All surgeries were performed by senior and experienced surgeons. All patients were followed up to 1 year. MCUG was performed in all patients after stent removal for secondary vesico-ureteric reflux.

## RESULTS

All of the operations were successfully completed. The age range was 4 to 144 months. The mean age was 26months $\pm$ 5.4SD. There were 18(64.28%) male and 10(35.72%) were female. Male to female ratio was 1.8:1. There were 18 patients presented on left side and 6 on right side. 2 patients had bilateral obstructive megaureter. Range of Distal ureter diameter on Ultrasound was 9 to 35 mm with average of 14mm $\pm$ 6.85SD. 16(57.14%) patients presented were in <24 months of age group followed by 8(28.57%) patients in 25-96months and 4(14.28%) patients in >96 years of age group. Preoperative diuretic MAG3 showed obstruction in all cases with split renal function with range of 18 to 35% on affected side. JJ stent duration was 3 to 12 weeks with Average 9 weeks $\pm$ 4.29SD. No significant postoperative pain, bleeding, incontinence or other major complications noted. Reflux was not noted in any patient on postoperative MCUG.

## DISCUSSION

Megaureter is defined as distal ureteric diameter more than 8mm from 30 weeks gestation onward.

Management of megaureter has evolved for the last 20 years. Open surgery is associated with many complications and as result many surgeons avoid open bladder surgery. The conservative approach has gained popularity. First time shenoy and rance described endoscopic treatment of primary megaureter<sup>16</sup>. Subsequently several authors described balloon endoscopic dilatation<sup>17</sup>. But it is associated with meatal rupture and ureteral stricture. Angulo and coworkers in 1998 described endoscopic dilation of obstructive megaureter in Spain<sup>18</sup>. They operated on 11 patients in whom the problem was resolved with single dilatation in six patients and with second one in the remaining five.

Symptoms, ureteral dilatation on ultrasound and obstructive type emptying curve on renal scintigraphy are three criteria for endoscopic treatment of primary obstructive megaureter<sup>19</sup>. In our study twenty five out of 28(89.28%) patient were treated successfully with endoscopic dilatation. Only 3 patients required open surgical procedure because of inability to negotiate ureteral meatus(n=2) or to pass stent through ureteral meatus(n=1). This result is consistent with the (91%) result in the study of teklali Y et al<sup>13</sup>. In contrast in the study of Castagnetti M et al 50% patient required open surgery at the age of 14 months<sup>8</sup>.

Follow up in our study was short from 6 months to 1 year, but we reported good results and low morbidity. Postoperatively in all patients the excretion pattern on MAG 3 scan was unobstructed. We observed a number of complications. Poor tolerance of stent was noted in 1 patient who was treated with anticholinergic medications. Migration of stent was noted in one patient, which was readjusted at three week time. 3 patients had breakthrough infections, who responded to antibiotics. One patient had Persistent hematuria which was treated with transanemic acid.

Patients having symptomatic megaureter have variety of options such as conservative management with the hope of self-resolution. It can also be endoscopically approached and dilated with serial dilators. It can also be incised endoscopically. Traditionally it can be treated surgically both by laparoscopic and open approach. In open approach ureter is disconnected from the urinary bladder and re implanted in urinary bladder. It can be re implanted both by intravesical and extravesical technique. Some patients who have nonfunctioning kidney undergo nephro ureterectomy.

The potential onset of secondary vesico-ureteral reflux may create controversy. We did micturating cystogram in all patients. Not a single patient developed secondary VUR postoperatively. In contrast Ortiz et al reported secondary VUR in 21.5% patients, which were successfully treated by endoscopic sub ureteral injection<sup>12</sup>. Angulo et al reported reflux in 2 of the 11 patients<sup>18</sup>. One was secondary to neurogenic bladder which was treated successfully by Teflon STING. The

other was with grade I reflux which did not required treatment. It is concluded that endoscopic dilatation of primary obstructive megaureter yielded excellent short term results.

## CONCLUSION

Endoscopic dilatation of vesico-ureteric junction allows effective internal drainage of primary obstructive megaureter. The history, physical examinations and imaging studies are essential for precise diagnosis of congenital obstructed megaureter. It is technically feasible and safe procedure. Although this procedure is associated with few complications such as infection and stent migration, none of the patient is at risk of deterioration that would have outweighed the morbidity of complication. In future more clinical researchis required to prove its convenience. This procedure for the management of megaureter is safe and successful and has moved away children from the risk of unnecessary surgery.

### Author's Contribution:

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# To Determine the Frequency of Pancytopenia in Children Presenting with Malaria

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## ABSTRACT

**Objective:** To determine the Frequency of Pancytopenia in children presenting with Malaria

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

**Place and Duration of Study:** This study was conducted at the Pediatrics Department, DHQ Teaching Hospital, Gomal Medical College, D. I Khan from October, 2015 to April, 2016.

**Materials and Methods:** Before carrying out the research permission was obtained from ethical committee of hospital. Questionnaire was used for collection of data. All children < 18 yrs with malaria were registered in research from OPD. MP and Special smear tests were done for diagnosis of malaria in admitted children with fever. Informed written consent was taken from parents. All the above-mentioned information were recorded in a pre-designed proforma. Strictly exclusion criteria was followed to control confounders and bias in the study results. All the laboratory investigations were done under supervision of single expert pathologist having minimum of five years of experience.

Sample size was 232 while technique used was Nonprobability consecutive sampling.

**Results:** In this study males were 60.34% and females were 39.66%. The female to male proportion was 1:1.6.8.51 years+4.23SD was the average age of the patient. The frequency of pancytopenia among children with malaria was found in 85(36.64%) patients.

**Conclusion:** Pancytopenia is a common problem in clinical practice. The incidence is high in malaria patients. & requires prompt action when patients present with malaria so that one can be managed to decrease illness and prolong survival.

**Key Words:** Pancytopenia, Aplastic anemia, Bone Marrow, Malaria.

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## INTRODUCTION

Pancytopenia refers to a reduction below normal values of all 3 peripheral blood lineages; leukocytes, platelets and erythrocytes. It can be inherited or acquired. It is caused by decrease in or damage to hematopoietic stem cells and their microenvironment, resulting in

hypoplastic or aplastic bone marrow, maturation defects or differentiation defects such as myelodysplasia. Drugs, chemicals, toxins, infections (malaria) and radiations are important causes of pancytopenia<sup>1</sup>. Weakness, fatigue and pallor result from anemia; petechiae, purpura and bleeding occur due to thrombocytopenia and infections occur due to leucopenia<sup>2</sup>.

Many studies have shown its incidence to range from 2 to 14 cases/million/year. Greater frequency is found in Asian countries<sup>3</sup>.

Malaria is caused by Plasmodium of genus (falciparum, vivax, ovale, malariae and knowlesi) & transmitted to human by female anopheles mosquito. Malaria affects about 300-500 million people and causes more than a million deaths per year worldwide<sup>4</sup>. The prevalence of plasmodium in Pakistan among treatment seeking patients with suspected malaria was 6.6% in Pakistan and 10.8% in KPK<sup>5</sup>. In 2010 in Pakistan, 95 million people out of 161 million people roughly 60% live in malaria endemic regions. In 2006, Malaria Disease Surveillance Program in Pakistan, registered 3.5 million slides and 127825 confirmed cases of malaria with an

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annual parasite incidence (API) of 0.8 case per 100 population<sup>6</sup>.

Pancytopenia is a complication of malaria. A study from India observed pancytopenia in 4% of patients with malaria<sup>7</sup>, while a study from K.P.K observed it in 9% of patients with malaria<sup>8</sup>. One study from Balochistan showed that main cause of pancytopenia was malaria (29.44%)<sup>9</sup>.

This study is not performed previously in Paediatrics department, Gomal medical college, Dera Ismail Khan. Malaria is endemic and epidemic in Dera Ismail Khan and surroundings of Punjab and Balochistan (Zhob, Bakkar). This research will support prompt identification and early treatment of reversible complication (pancytopenia) of malaria.

## MATERIALS AND METHODS

The descriptive cross-sectional study was conducted at the Pediatrics Department DHQ Teaching Hospital, Gomal Medical College, D. I Khan, over a period of 6 months.

### Inclusion Criteria:

- Patients from the age of 6 months to 18 years.
- Children having fever with rigors and chills showing positive test for malaria.

### Exclusion Criteria:

- Children with known hematological abnormalities.
- Children suffering from leukemia.
- Children with pancytopenia of other etiologies.

**Data Collection Procedure:** Before beginning of the research, approval was taken from ethical committee of hospital. Data was entered on questionnaire. Patients < 18 yrs with malaria were registered in research from OPD. Investigations like special smear & MP were done for patients presenting with fever. From parents Informed consent in written form was taken. In a pre-designed proforma all the above-mentioned information was entered. To control bias & confounders in the research's results, exclusion criteria was obeyed exactly. A single expert pathologist having experience  $\geq 5$  yrs carried out all investigations.

**Data Analysis:** Data was analyzed by using SPSS version 10. Quantitative variables were described in form of means  $\pm$  standard deviation. Data was explained in form of percentages & frequency. Pancytopenia was stratified among age gender to see effect modification. Post stratification was done through Chi Square test. Keeping P value less than 0.05 as significant. Data was presented as tables, diagrams and charts.

## RESULTS

This study included a total of 232 malarial patients. Females were 92 (39.66%) & males were 140 (60.34%). Female to Male proportion was 1:1.60.

8.51 yrs  $\pm$  4.23 SD was recorded as average patient's age with range 6 months- 18 yrs. Based on age, patients were classified in 4 groups, the common stone was 6-10 yrs. In the group of age  $\leq 5$  yrs, 64(27.6%) children were recorded, the group of 6-10 yrs contained 99(42.7%) children, 55(23.7%) children were 11-15 yrs old and 14(6%) children were of age more than 15 years. (Table 1)

**Table No. 1: Age wise distribution of the patients**

Age in Years	Frequency	Percent	Mean $\pm$ SD
$\leq 5$	64	27.6	8.51 Years $\pm$ 4.23 SD
6 – 10	99	42.7	
11 – 15	55	23.7	
16+	14	6.0	
Total	232	100.0	

**Table No. 2: Age wise distribution of pancytopenia**

		Pancytopenia		Total	p-value
		Yes	No		
age (in years)	$\leq 5$	22	42	64	0.008
		34.4%	65.6%	100.0%	
	6 - 10	47	52	99	
		47.5%	52.5%	100.0%	
	11 - 15	11	44	55	
		20.0%	80.0%	100.0%	
	16+	5	9	14	
		35.7%	64.3%	100.0%	
Total		85	147	232	
		36.6%	63.4%	100.0%	

**Table No. 3. Gender wise distribution of pancytopenia**

		Pancytopenia		Total	p-value
		Yes	No		
Gender	Male	53	87	140	0.369
		37.9%	62.1%	100.0%	
	Female	32	60	92	
		34.8%	65.2%	100.0%	
Total		85	147	232	
		36.6%	63.4%	100.0%	

Out of all the patients, 85(36.64%) children were having pancytopenia & in 147(63.36%) children there was no pancytopenia.

It is clear from this research that pancytopenia is common amongst younger children. Twenty-two (34.4%) patients have pancytopenia with age  $\leq 5$  years, age group 6-10 years contains 47.5% patients with pancytopenia and 35.7% patients having more than fifteen yrs of age have pancytopenia. Table 2

Gender wise aplastic anemia in children presenting with pancytopenia reveals that sex has no role over them. Pancytopenia was observed in 37.9% male and 34.8% female patients with malaria. Table 3

## DISCUSSION

In Tropics Malaria is one of the common health issues. In Pakistan Vivax & Falciparum malarias are the most important Public health issues. According to National Malaria Control Program Pakistan, falciparum malaria is more common & accounts 42% of all malaria patients which shows that there has been a 6-fold rise in falciparum malaria in the previous 10 yrs<sup>10</sup>.

Malaria caused by falciparum is the most fatal and severe disease if not treated properly. If remained undiagnosed or not diagnosed on time it will progress to severe malaria with complications. After diagnosis, maximum level of medical care with the provision of adequate, harmless doses of proper anti-malarial is required for treatment of severe F. Malaria with complications<sup>11</sup>.

Malaria caused by P.vivax is the commonest malaria & one of the major reason of illness in regions like South & Central America, Asia & Oceania.<sup>12</sup> However, P.Vivax malaria is not so severe & also have low blood parasite level. Parasitized RBCs have no knobs, so there is little chance of obstruction of microvasculature & as a result major organs like brain, lungs, kidney etc. develop complications infrequently<sup>13</sup>.

Pancytopenia is common hematological issue and whenever there is complaint of persistent fever or bleeding or pallor then pancytopenia should be suspected clinically. For the determination of the cause of the Pancytopenia bone marrow examination is advised. It comparatively harmless invasive technique with little chance of bleeding even in the existence of low platelet counts.<sup>11</sup>

This research included children of all ages, ranging from 2 month to 15 yrs. Comparable ranges of ages were observed in local<sup>3</sup> and foreign<sup>7, 13</sup> researches.

Since our study was not confined to gender so both female & male children were studied with pancytopenia. Female were 39.66%, Males were 60.34% and the female: male was 1:1.6. In other research work done locally in Peshawar<sup>3,4,14</sup> Jamshoro<sup>15</sup>, Abbottabad.<sup>1</sup> & abroad in Nepal<sup>7</sup>, India<sup>16</sup> and Yemen.<sup>17</sup> male dominance was noted

Rare causes of pancytopenia in our study are also uncommon in other studies including multiple myeloma and normal bone-marrow,<sup>7</sup> neuroblastoma,<sup>7, 15</sup> Myelodysplastic syndrome<sup>3,7</sup> malaria and abnormal mononuclear cell infiltrate.<sup>3</sup>

Malaria corresponded to the fourth and second most frequent cause in pancytopenic patients respectively.<sup>18-20</sup> Malaria due to Plasmodium falciparum has been implicated as a cause of pancytopenia. The high incidence of malaria is

observed in low income group with poor sanitation facilities. It is critical to eliminate places around home where mosquitoes breed / hide & spraying insecticides on home's premises to kill adult mosquitoes those come inside. Taking anti-malarial medications for malaria prophylaxis is good strategy to prevent malaria.<sup>21,22</sup>

The likely symptoms & signs of severe P. vivax malaria includes cerebral malaria, pancytopenia severe anaemia, jaundice, acute renal failure, splenic rupture & acute respiratory distress syndrome. acute pulmonary oedema & Severe anaemia are also common. It is notable that there are no distinct signs & symptoms/management of severe malaria caused by P. vivax, but, quick and efficient management should be like the complicated & severe malaria caused by P. falciparum according to the WHO.<sup>16</sup>

## CONCLUSION

Clinically and hematologically Pancytopenia is a very crucial health issue. Examination of Bone-marrow is a well-known investigation in assessment of pancytopenia. Greater prevalence of Pancytopenia has been noted in younger age group. In order to reduce morbidity and prolong survival due to pancytopenia it is crucial to understand various causes of pancytopenia, as some of the causes are completely curable while others can be treated symptomatically.

### Author's Contribution:

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

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# Hepatitis B Vaccination Coverage in Health Care Providers in Tertiary Care

## Hospitals: A Multicenter Study from Pakistan

Muhammad Asif<sup>1</sup>, Muhammad Zahid<sup>2</sup>, Murtaza Ali<sup>1</sup>, Shahid Ali<sup>4</sup> and Anwar Khan Wazir<sup>3</sup>

### ABSTRACT

**Objective:** To determine the frequency of vaccination coverage against hepatitis B virus (HBV) in Health Care Workers (HCWs) in tertiary care hospitals and to identify the common barriers to vaccination.

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

**Place and Duration of Study:** This study was conducted at the ten Tertiary Care Hospitals of Pakistan located in Rawalpindi, Islamabad and Peshawar from January 2018 to May 2018.

**Materials and Methods:** HCWs were evaluated through a self-administered questionnaire which included questions about demographics, HBV vaccination status and reasons for incomplete vaccination. Categorical variables were shown in percentages and Chi square test was used to determine the determinants of vaccination.

**Results:** Of the total 1130 participants, 693 (61.3%) were males and mean age of the study participants was 28.8±6.69 SD years. Of the total, 590 (52.2%) were fully vaccinated, 188 (16.6%) partially vaccinated, 307 (27.2%) non-vaccinated while 45 (4%) could not recall their vaccination history. Negligence followed by lack of knowledge were reported as common barriers to vaccination. Statistically significant association among age ( $p=0.025$ ), type of profession ( $p<0.001$ ), duration of employment ( $p=0.035$ ) and hepatitis B vaccine coverage was observed.

**Conclusion:** There was low hepatitis B vaccine coverage among HCWs. A free and mandatory immunization program should be offered to all HCWs to achieve 100% vaccination coverage and ensure their protection against HBV.

**Key Words:** Hepatitis B vaccination; Healthcare workers; Tertiary care hospitals, Pakistan.

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### INTRODUCTION

Hepatitis B virus (HBV) causes a potentially life-threatening infection associated with significant morbidity and mortality worldwide. According to World Health Organization (WHO) estimates, HBV infects approximately two billion people worldwide (30% of the world's population) as documented by serologic evidence of previous or current HBV infection.<sup>1</sup> The global prevalence of hepatitis B surface antigen positive population is 3.9%.<sup>2</sup> Course of chronic hepatitis B can be complicated by liver failure or hepatocellular carcinoma which causes at least 786,000 deaths annually worldwide.<sup>3</sup>

Being the 10<sup>th</sup> major deaths-causing disease, HBV has gained the status of global public health threat.<sup>4</sup>

HBV transmission can result from exposure to infected body fluids such as blood, serum, semen and vaginal secretions. Common routes of HBV transmission are sexual, vertical and parenteral like transfusion of blood and blood products, hemodialysis, intravenous drug abuse, unsafe injections and needle stick injuries. HCWs fall in the last category. Unvaccinated HCWs are four times more at risk of contracting HBV infection than general population.<sup>5</sup> HBV transmission from HCWs to patients has been documented.<sup>5</sup> The chances of contracting HBV infection after a single needle stick injury from HBsAg positive patient range from 6% to 40% depending on HBeAg-status.<sup>6</sup> In health care settings, risk of non-percutaneous exposure can contribute further to HBV transmission.<sup>6</sup>

Transmission of HBV can be prevented by adherence to universal infection control measures and vaccination against HBV. Vaccine against HBV is safe and effective with 95% seroconversion or immune response rates. Vaccination is the most effective method of preventing hepatitis B infection and its long term consequences.<sup>6</sup> Vaccination is recommended for high risk population including HCWs which significantly decreases the chances of getting HBV infection. In developing countries, 42.62% of HBV infection in HCWs was attributed to exposure in health care settings

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while in developed countries the attributed fraction was less than 10% due to better vaccination coverage in HCWs in developed countries.<sup>4,7</sup>

Internationally, HBV infection as a major occupational hazard of HCWs and vaccination coverage against HBV has received a good literature attention. In Pakistan, few small single center based studies have been conducted but the overall scarcity of data on this very important topic warrants more in-depth research to improve our level of understanding, help identify common barriers to vaccination and thus, highlight the subject. This study aimed to determine the frequency of vaccination coverage against HBV in HCWs in tertiary care hospitals and to identify the common barriers to vaccination.

## MATERIALS AND METHODS

This descriptive cross sectional study was conducted from January 2018 to May 2018, at ten tertiary care teaching hospitals of Pakistan. Fourteen hundred HCWs were selected through convenient sampling, invited to participate in the study; aims of the study explained and informed written consent taken. A self-administered, pre-tested questionnaire was used, which included questions about demographics, HBV vaccination status and reasons for non-vaccination or incomplete vaccination. Ethical approval was obtained from the Ethical Review Board of Military Hospital Rawalpindi Pakistan.

Participants who received  $\geq 3$  doses of vaccine were defined as vaccinated; those who did not receive any dose were defined as non-vaccinated. Those who received one or two doses but did not complete full course of three doses were defined as partially vaccinated. Collected data was coded, entered, and analyzed using SPSS version 22.0. Descriptive statistics were used for categorical variables and Chi square test to discover association between vaccination coverage and other variables. Variables with p-value of less than 0.05 were declared as statistically significant.

## RESULTS

Fourteen hundred HCWs were invited to participate in the study but only twelve hundred HCWs responded, giving response rate of 85.7%. Additional 70 participants were dropped from the study due to incomplete information and finally eleven hundred and thirty HCWs (1130) were enrolled in the study. Of the total, 693 (61.3%) were males and the mean age was 28.8 years ( $\pm 6.69$  SD years, range from 17-66). The mean duration of employment was 28.5 months (range 1-444 months). Doctors contributed maximally (60.9%) to the sample size followed by nurses. The demographic characteristic and profession-wise breakup of the participants is presented in Table 1.

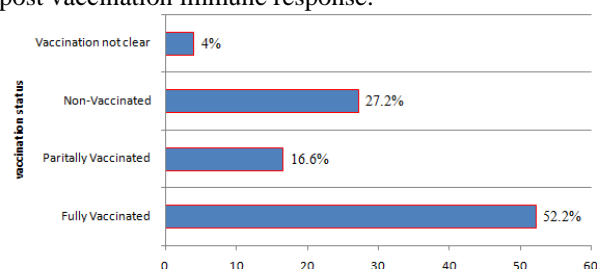
**Table No.1: General Characteristics of the Health Care Workers (n = 1130)**

Variable	Frequency(%)
<b>Gender</b>	
Male	693(61.3)
Female	437(38.7)
<b>Age group (years)</b> <b>Mean <math>\pm</math>SD (28.81 <math>\pm</math> 6.69)</b>	
< 20	15 (1.3)
21–30	840 (74.3)
31–40	207 (18.3)
> 40	68 (6.1)
<b>Profession</b>	
Doctor	688 (60.9)
Nurse	259 (22.9)
Technicians	78 (6.90)
Assistants	62(5.50)
Others	43(3.80)
<b>Duration of employment (years)</b> <b>Mean (5.04 <math>\pm</math> 6.32SD)</b>	
<1	209(18.50)
1-5	611(54.10)
6-10	170(15.00)
11-15	60(5.30)
>15	80(7.10)

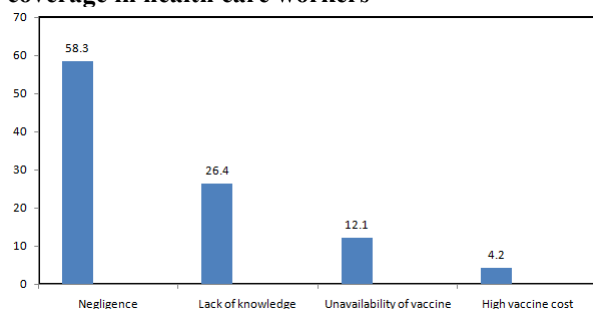
**Table 2: Cross tabulation of factors associated with complete Vaccination of the health care workers**

Variable	Complete vaccination (Number and Percentage)	Chi square value	p value
<b>Gender</b>			
Male	352 / 693 (50.79)	5.09	(0.165)
Female	238 / 437 (54.46)		
<b>Age group (years)</b>			
< 20	2 / 15 (13.33)	23.38	(0.025)
21–30	428 / 840 (50.95)		
31–40	114 / 207 (55.07)		
> 40	46 / 68 (67.65)		
<b>Profession</b>			
Doctor	422/688 (61.37)	113.10	(<0.001)
Nurse	114/259 (44.02)		
Technicians	23 / 78 (29.49)		
Others	18 / 62 (29.03)		
Assistants	13 / 43 (30.23)		
<b>Duration of employment (in years)</b>			
<1	103 / 209 (49.28)	26.32	(0.035)
1-5	321 / 611 (52.54)		
6-10	47 / 80 (58.75)		
11-15	28 / 60 (46.67)		
>15	91 / 170 (53.53)		

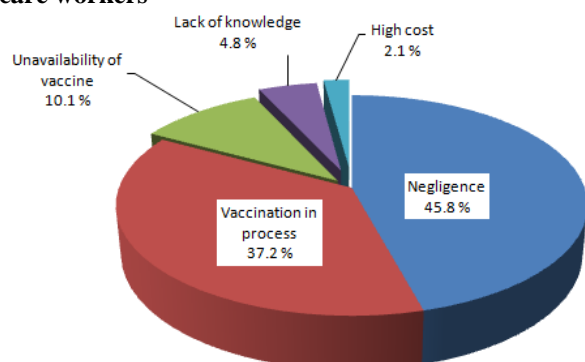
Of the total, 590 (52.2%) HCWs were fully vaccinated, 188 (16.6%) partially vaccinated, 307 (27.2%) non vaccinated and 45(4%) could not recall their vaccination history, as presented in figure 1. Complete vaccination coverage was higher in females compared to males (54.46% vs. 50.79%) but this difference was not statistically significant ( $p=0.165$ ). The vaccine uptake increased with increasing age and increased duration of employment ( $p < 0.05$ ). The vaccine uptake was higher in higher clinical profession (increased from 29.03% among assistants to 61.37% among doctors). The association of complete vaccination coverage with variables like age, gender, duration of employment and type of profession is presented in table 2. Of the fully vaccinated HCWs, only 122 (16.3%) had checked their post vaccination anti HBs antibodies titers to assess post vaccination immune response.



**Figure No.1: Graphical representation of vaccine coverage in health care workers**



**Figure No.2: Reasons for Non vaccination in health care workers**



**Figure No.3: Reasons for Incomplete vaccination in health care workers**

The most common reason reported for not being vaccinated was negligence (58.3%) followed by lack of knowledge (25.4%), unavailability of the vaccine

(12.1%) and high cost (4.2%) as represented in figure 2. Common reasons reported for incomplete vaccination were negligence (45.8%), vaccination in process (37.2%), unavailability of vaccine (10.1%), lack of awareness (4.8%) and high cost (2.1%).

## DISCUSSION

In the current study, we observed low hepatitis B vaccination coverage (52.2%) in HCWs. Previous studies from different regions of Pakistan have reported different vaccination rates ranging from 37.2% to 66.3%.<sup>7-12</sup> A vaccination rate of 52.2% is consistent with the findings of Abdul Rauf et al who reported a vaccination rate of 52% from Karachi and partially tallies with the findings of Shrestha et al who reported a vaccination rate of 48% among HCWs.<sup>13, 14</sup> A study by Ali NS et al from Agha Khan University (AKU) hospital Karachi in 2005 however; showed much higher rates of complete vaccination (86%) in HCWs.<sup>15</sup> Such a higher vaccination rate may be explained by the fact that AKU is private and largest hospital of the country where hospital provides free vaccine and follows standard rules and regulations. Nevertheless, this gap in vaccination coverage in institutional setting is disappointing as vaccination rate should have increased over a period of thirteen years in parallel with the increasing awareness about the problem over time. Similarly, Vaswani et al from Karachi reported higher complete vaccination rate of 62.8%.<sup>16</sup> This coincidence may be partially explained by higher public awareness about HBV in Karachi or perhaps better institutional standards in Karachi. Memon et al reported complete vaccination of 42.47% among HCWs. In the same study 21.34% were partially vaccinated and 36% not vaccinated at all.<sup>17</sup>

Globally, the statistics about HBV vaccination rate are highly variable and in part conflicting. Studies from Cameron, Uganda, Ethiopia, Tanzania and Iraq, reported rates of complete vaccination coverage, 5.5%, 6.2%, 28.7%, 33.6%, 45% which are lower in comparison with our results.<sup>18-22</sup> On the other hand, studies from Saudi Arabia and Libya have shown higher vaccination rates of 63.3% and 72% respectively.<sup>23-24</sup> Such a gross difference in vaccination rates across these countries may reflect different levels of economic and political stability in the countries.

The most frequent reason reported for not being vaccinated was negligence (58.3%) followed by lack of knowledge (25.4%), unavailability of the vaccine (12.1%) and high cost (4.2%). There is some uniformity and consistency in this connection with other local studies.<sup>15-17</sup> Khan et al reported work pressure, negligence and high cost of the vaccine as major hurdles to vaccination.<sup>4</sup> Negligence as a main barrier against vaccination was also reported by a study from Agha Khan University and two studies from Hyderabad medical universities.<sup>15,17</sup> Vaswani et al reported



unavailability of free vaccine followed by ignorance as the most frequent reasons for not receiving or discontinuing vaccination.<sup>16</sup> Some studies have reported high cost as the main reason cited for not receiving vaccination, followed by the non-availability of the vaccine.<sup>9, 15</sup> Few reported fear of injection and uncertainty about the efficacy and safety of the vaccine as additional causes for non-vaccination.<sup>9</sup>

In our study we observed higher vaccine uptake with increasing age and higher clinical profession. Increased vaccine uptake with advancing age and profession may indicate increasing awareness about the disease and in part, increasing self-care and economic stability with advancing age and professional grade. The highest vaccination rate was seen in doctors (61.37%) followed by nurses (44.02%), technicians (29.49%) and least in assistants (29.03%). Almost similar results of vaccination rates in different professions were reported in different studies.<sup>14, 16</sup> Current study showed increased vaccine uptake with increasing duration of employment which may reflect increased awareness regarding HBV and vaccination in hospital staff.

The centers for disease control and prevention (CDC) recommend post vaccination antibody (Anti-HBsAb) testing in HCWs, 1-2 months after completing 3 dose regimen of hepatitis B vaccination. If immune response is not adequate (defined by Anti-HBsAb < 10 IU/ml), the 3 dose series needs to be repeated and antibodies rechecked thereafter. If there is no immune response after second course, no further vaccination is recommended and they are considered vaccine non responders.<sup>23</sup> In this study we observed poor compliance with the recommendations of post vaccination serologic testing as only 16.3% had checked their post vaccination antibodies titers. Few local studies have reported comparable results of compliance with post vaccination serologic testing in HCWs, 18% reported by Vaswani et al<sup>16</sup> from Karachi, 11.5% reported by Younus et al<sup>25</sup> from Lahore and 19% in a study from Agha Khan University<sup>15</sup>. Again, one may safely speculate about such a poor trend in common to be attributable to the afore-mentioned reasons for non-vaccination like negligence, lack of awareness and perhaps economy reasons. A study from the Saudi Arabia reported that only 10% of the HCWs had checked their post vaccination antibodies.<sup>26</sup>

## CONCLUSION

A sizeable proportion of HCWs are not vaccinated. Such a low rate (52.2%) of vaccination in well informed, knowledgeable segment of general population may reflect an even worse situation in the general population. The most common reason reported for non-vaccination is negligence followed by lack of knowledge, perceived high vaccine cost and non-availability of the vaccine. Compliance with post vaccination antibodies testing is even worse. To achieve

100% vaccination coverage in HCWs, government should implement a mandatory and free immunization program for all the medical students and HCWs right at the time of admission in medical school and before employment. This program should also make sure post vaccination follow up with antibodies testing.

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

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# Incidental Papillary Thyroid Micro Carcinomas in Patients Undergone for Thyroidectomy

Incidental Papillary  
Thyroid Micro Carcinomas

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and Salman Hakim<sup>5</sup>

## ABSTRACT

**Objective:** The present study aims to ponder at incidence of incidental papillary thyroid microcarcinomas along with clinopathological features of the tumors.

**Study Design:** Cross sectional study

**Place and Duration of Study:** This study was conducted at the Department of Pathology and Surgery, Jinnah Medical College and Jinnah Teaching Hospital Peshawar from July 2016 to December 2017.

**Materials and Methods:** The research was performed on 1000 patients who were operated for thyroidectomy during one and a half year. For routine histopathological examination H&E stain was used while to stain tumor cells Immunohistochemical markers were used. All the slides were evaluated for papillary thyroid microcarcinomas.

**Results:** Out of 1000 patients, 186 (18.6%) were found with a malignancy. Among these, 6 (3.22%) were found with follicular carcinoma, 5 (2.68%) with lymphoma, 4 (2.15%) with anaplastic carcinoma, 4 (2.15%) with medullary carcinoma, 2(1.07%) with poorly differentiated carcinoma and 165 (88.70%) with papillary carcinoma. Incidental papillary thyroid microcarcinoma (IPTM) was present in 40 cases. In all the cases, total thyroidectomies were performed. Metastasis and relapse were not detected in any of the cases. Histopathological examination is necessary for thyroidectomy specimens as IPTM may escape fine needle aspiration cytology. As multifocality and bilaterality are quite high in IPTM, total thyroidectomies are best to be performed.

**Conclusion:** To diagnose papillary thyroid microcarcinoma, we could not depend FNAC alone rather detailed histopathological assessment is necessary.

**Key Words:** Papillary Thyroid Microcarcinoma , Immunohistochemical markers

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## INTRODUCTION

Thyroid carcinomas are considered as the commonest endocrine carcinoma and constitute about 90% of endocrine malfunctions. Recently, frequencies of incidental thyroid carcinomas are increasing (Askitis, 2013)<sup>1</sup>. Bilateral total excisions and histopathological examinations of thyroid tissue have boosted up thyroid surgery (Sipos,2010, Neuhold, 2011,Londero, 2013)<sup>2,3,4</sup>. Incidental papillary thyroid microcarcinomas have a prevalence of 7.1-16.3%. Incidental tumors are the ones

not suspected clinically but are diagnosed in histopathological examination of specimens during thyroidectomy operations (Vasileiadis,2014)<sup>5</sup>. The most common type of incidental thyroid carcinoma is papillary microcarcinoma (Sipos, 2010)<sup>2</sup>. If the tumor is 1cm or smaller, it is known as 'papillary thyroid microcarcinoma'(PTM). Most of the papillary thyroid carcinoma are diagnosed by chance during histopathological examinations. In multinodulargoiter cases (MNG), thyroid carcinoma has incidence of 7.5-13% (Slijepcevic,2015)<sup>6</sup>. The fine needle aspiration cytology has decrease in diagnostic value for malignancy as number of nodules increases in MNG cases, whereas, incidental thyroid carcinoma is quite common in MNG (Neuhold, 2011)<sup>3</sup>. Therefore, total thyroidectomy is recommended for nonmalignant thyroid diseases.

## MATERIALS AND METHODS

The present study comprises of 1000 patients who experiences thyroidectomies during January 2017 to January 2018. They were histopathologically examined at the clinic. The demographics and information of patient was gathered through phone calls and computer records. Gender, age, FNAC diagnoses, preoperative clinical diagnoses, histopathological findings and

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operative procedure for the patients were noted. The cases having tumor size more than 1cm and those with suspected or diagnosed malignancy were excluded. Evaluation for histopathological findings was conducted including multifocality, bilaterality, tumor type, tumor size, age, sex, preoperative diagnosis, lymphovascular invasion and thyroid capsule invasion. The follow up period lasts from diagnosis date to last follow up. The patients were given a follow up of 10 months. Postoperative prognostic indices were investigated including metastasis, relapse and survival. Serum thyroid-stimulating hormone (TSH) and Free thyroxine (FT4) levels were assessed to check LT4 dose in 1st and 3rd postoperative months. Thyroglobulin (Tg), Serum TSH, FT4, and anti-thyroglobulin antibody (anti-TgAb) were assessed in the 6th month. Ultrasonography helped in examination of cervical lymph nodes. Serum levels of TG, FT4, TSH and TgAb were examined through annual cervical USG.

## RESULTS

Within one year, 1000 thyroidectomies were conducted. Out of 1000 patients, 186 (18.6%) were found with a malignancy. Among these, 6 (3.22%) were found with follicular carcinoma, 5(2.68%) with lymphoma, 4(2.15%) with anaplastic carcinoma, 4(2.15%) with medullary carcinoma, 2(1.07%) with poorly differentiated carcinoma and 165 (88.70%) with papillary carcinoma. Among papillary carcinoma patients, 62 (37.57%) were found with classical papillary carcinoma and 103 (62.42%) were found with papillary microcarcinoma.

**Table No.1: Distribution of malignancy**

Type of malignancy (n=186)	Number	Percentage (%)
Follicular carcinoma	6	3.22%
Lymphoma	5	2.68%
Anaplastic carcinoma	4	2.15%
Medullary carcinoma	4	2.15%
Poorly differentiated carcinoma	2	1.07%
Papillary carcinoma	165	88.70%

Among 103 papillary microcarcinoma cases, 64 were regarded as benign by FNAC. Incidental papillary thyroid microcarcinoma (IPTM) was present in 40 cases.

**Table No.2: Distribution of papillary carcinoma patients**

Malignancy n=165	Number	Percentage (%)
Classical papillary carcinoma	62	37.5%

Papillary microcarcinoma	103	62.42%
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The patients with IPTM had average age of 42 years with range of 25 to 70 years. It comprised of 34 (85%) females and 6 (15%) male patients. Among 40 IPTM patients, 5 (12.5%) had a prediagnosis of toxic MNG, whereas, 35 (87.5%) had a prediagnosis of nontoxic MNG. In all the cases, total thyroidectomies were performed. The tumor size was found to be 1-10mm among cases with ITPM. Tumor had affiliation with left lobe in 21 (52.5%) cases, with right lobe in 9 (22.5%) cases, multifocal nature in 6 (15%) cases and bilateral nature in 4 (10%) cases. During histopathological examination, cells with nuclear clearing were settled near fibrovascular core.

Immunohistochemical markers were used to stain tumor cells. In all the cases, lymphovascular invasion was absent. Histopathological findings assessed in IPTM cases included follicular adenoma, lymphocytic thyroiditis and MNG. The suppression of TSH was brought about by LT4 in all patients. Radioactive iodine was rendered to patients with thyroid capsule invasion. In follow up, serum levels for TgAb, TG, FT4 and TSH were assessed along with cervical USG. In any of the cases, no relapse or metastasis were recorded.

## DISCUSSION

The most frequent kind of malignant thyroid carcinoma is papillary thyroid carcinoma. It is called papillary thyroid microcarcinoma if tumor is 1 cm or smaller (Mantinan, 2012, Gelmini, 2010)<sup>7,9</sup>. In literature the prevalence of IPTM is recorded to be 7.1% to 16.3% (Nanjappa, 2013 Ito, 2007)<sup>8,10</sup>. In the present study, it was found to be 9%. Incidental carcinomas has incidence of 49% to 75.5%. The present study has shown its incidence to be 63%. The ratio of IPTM has increased tremendously in the previous few years, due to increase in total thyroidectomies. Papillary thyroid microcarcinoma is asymptomatic in nature and found incidentally while examining histopathologically for thyroidectomy specimens (Yousuf, 2011, Tezelman, 2009)<sup>11,12</sup>. In the present study, only 64 cases out of 1000 were found to be benign. In accordance with IPTM cases, benign lesions were found to be 26 with MNG cases, 8 with thyroiditis cases and 6 with follicular adenoma cases. In the present study, 103 cases were diagnosed with papillary microcarcinoma, whereas 64 cases of papillary microcarcinoma were diagnosed by preoperative FNAC. The remaining 40 cases were diagnosed incidentally while examining thyroidectomy specimens histopathologically. Majority of the cases of papillary microcarcinoma were skipped by FNAC. This is due to low diagnostic value of FNAC. As many patients consist of MNG and tumors are minute, sampling of area with FNAC is difficult. The same findings were put forward by Senel, 2016 18.

For diagnosing papillary thyroid microcarcinoma, cautious histopathological examination is necessary (Abdelshaheed,2006)<sup>13</sup>. Macroscopic examinations are compulsory to be performed on thyroidectomy specimens due to probability of IPTM (Dunki-Jacobs, 2012).<sup>14</sup> The tumor may be diagnosed macroscopically as a broken white colored area, whereas, it may sometimes be detectable by a microscopic assessment. Multifocality and bilaterality are the most important characteristics of papillary thyroid microcarcinomas (Lombardi, 2010, John,2014).<sup>15,16</sup> The presence of tumor in both lobes or more than one focus in same thyroid lobe is called multifocality (Malandrino 2013)<sup>17</sup>. It is reported to occur at rate of 13-41% (Costamagna,2013)<sup>19</sup>. The present study reports multifocality of 26%. The chances of cancer were found to be 60% in opposite lobe in cases with multifocality. In the preoperative time, it is difficult to determine multifocality in papillary microcarcinoma (Sakorafas, 2007)<sup>20</sup>. The presence of tumor in both the lobes is called bilaterality. According to literature, bilaterality rate is found to be 20-27.5% (El-Foll, 2015)<sup>21</sup>. However, in present study it was found to be 1%, which is quite lower than the reported ones. This variation might have occurred due to use of different diagnostic criteria in various research works.

In papillary carcinoma cases, involvement of lymph node is quite common. Metastasis in regional lymph nodes was recorded to be 30-40%. In papillary thyroid microcarcinoma, low prevalence of nodal metastasis has been reported. The study conducted by Vlassopoulou et al; 2016<sup>24</sup> reported rate of 10.7%, whereas, Wang et al; 2013<sup>23</sup> showed 0% rate for metastasis. The present study was in accordance with the results of Wang et al., as it showed no lymph node involvement in any IPTM cases. Due to high rate of bilaterality and multifocality, total thyroidectomies are preferred for papillary thyroid microcarcinoma (Jagtap, 2018)<sup>22</sup>. The tumor size for IPTM previously reported is smaller than 5mm (Di Donna,2014)<sup>25</sup>. In the present study, mean tumor size was found to be 4.5mm, which is consistent with the previous literature. Primary adjuvant procedures are involved when treating patients with differentiated thyroid carcinoma. However, low rate of recurrence in IPTM cases nullifies need of adjuvant treatment. However, suppression of TSH levels with LT4 treatment is still applied (Shaha, 1998).<sup>26</sup> In case of cervical lymphadenopathy, modified neck dissection or central neck dissection is required (Ito, 2004).<sup>27</sup> As no cervical lymphadenopathy was diagnosed in present study, neck dissection was omitted. In all the cases, total thyroidectomies were performed. In case of tumormultifocality, vascular invasion or lymph node metastasis, adjuvant radioiodine therapy is required. RAI is avoided due to low risk of recurrence. In the present study, 6 cases of thyroid capsule invasion were given treatment of

RAI. The IPTM has recurrence rate of 0-5% (Hay,1992).<sup>28</sup> The present study had recurrence and metastasis rate of 0%. It can be concluded that IPTM has high incidence rate due to benign thyroid disease.

## CONCLUSION

In diagnosis of papillary thyroid microcarcinoma, FNAC cannot be relied. Thus, detailed histopathological assessment is required. Bilaterality and multifocality are important characteristics of papillary thyroid microcarcinoma. Total thyroidectomy is the preferred method of treatment.

### Author's Contribution:

Concept & Design of Study:	Muhammad Tariq
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**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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# Comparison of the Rate of Complications of Phacoemulsification in Patients with and without Pseudoexfoliation Syndrome

Zulfiqar Ali, Nadia Nazir, Soufia Farrukh, Imran Nazir and Zunaira Alvi.

## ABSTRACT

**Objective:** The objective of this study was to compare the rate of complications of Phacoemulsification in patients with and without pseudoexfoliation syndrome.

**Study Design:** Cohort study.

**Place and Duration of Study:** This study was conducted at the Department of Ophthalmology, Bahawal Victoria Hospital, Bahawalpur from July 2017 to December 2017.

**Materials and Methods:** This study included 50 eyes of the patient having cataract with pseudoexfoliation syndrome Group I, and another 50 eyes of patients having cataract without pseudoexfoliation syndrome Group II. All the patients underwent phacoemulsification. PMMA IOL 5.5 to 6mm was implanted in all patients after enlarging the incision. Per-operative and postoperative complications were assessed in both the groups and compared.

**Results:** In both the groups no per-operative complications were noted. On 1<sup>st</sup> postoperative day Group I, 38 (76%) patients had no complications, 12(24%) developed complications which are striate keratopathy 8 (16%), anterior chamber (AC) reaction 4 (8%).

Group II, 1<sup>st</sup> Postoperative day, 42(84%) patient had no complication, 8(16%) developed complications which are striate keratopathy, 6(12%) developed AC reaction 2(4%). In Group I, on first month 47(94%) had no complication and 3 (6%) developed complication which is AC reaction while in group II, 49(98%) had no complication, 1 (2%) developed complication which is AC reaction. on third month In Group I 47(94%) had no complications and 3(6%) developed complications which are AC reaction 1(2%) and pigment on the IOL surface 2(4%) while in Group II, 48(98%) had developed no complications and 2(4%) patients had developed complications which are AC reaction 1(2%) and pigment on the IOL surface 1(2%).

**Conclusion:** A planned approach to cataract surgery using the advanced techniques of phacoemulsification, significantly reduces the risk of complications during surgery. Therefore, phacoemulsification is a safe procedure in cataract without pseudoexfoliation syndrome and in selective cases of cataract with pseudoexfoliation syndrome.

**Key Words:** Pseudoexfoliation syndrome, cataract surgery, intraocular lens implant, complications

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## INTRODUCTION

Cataract still remains the world's leading cause of blindness and visual impairment in the elderly population, despite the decreasing number of people affected.<sup>1</sup> If age is the main risk factor for cataract progression, pseudoexfoliation syndrome (PXF) represents an independent additional hazard for the development of nuclear sclerosis and indication for cataract surgery.<sup>2,3</sup>

PXF syndrome is a multifactorial, genetically determined, age-related and environmentally influenced disorder of the elastic fiber structure, characterized by excessive production and accumulation of an elastic material within a multitude of intra and extraocular tissues.<sup>4-5</sup> For this reason, PXF is a diffuse disease with ocular and systemic manifestations.

Pseudoexfoliation syndrome is common among the people of various counties including India and Pakistan.<sup>6-7</sup> Pseudoexfoliation syndrome is rare before the age of 50 years but increases thereafter, nearly doubling in incidence every decade.<sup>8</sup>

PEX is diagnosed clinically by anterior segment examination, and is defined as the presence of grey-white fibrogranular pseudoexfoliation material on the anterior capsule of the lens and edges of the pupil.<sup>(9,10)</sup> The prevalence of PEX varies by population; however, PEX frequency increases with age and it is believed that an extremely significant relationship exists between age-related cataractous lens changes and PEX.<sup>(11)</sup>

Postoperative inflammation is higher in PEX versus routine cataracts.<sup>1</sup> This is due to a constitutively

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damaged blood-ocular barrier that leads to increased leakage of serum proteins into the aqueous humor after surgery (flare or Tyndall effect). The fragility of the blood-ocular barrier and intense postoperative inflammation may be responsible for a higher risk of pseudophakic macular edema in PEX eyes.<sup>12</sup>

Pseudophakic macular edema is due to the breakdown of the blood-retina barrier.<sup>13</sup> Eyes with PEX are at higher risk of developing pseudophakic macular edema.<sup>12</sup> The incidence and the effects of subclinical macular edema after phacoemulsification on vision are probably underestimated.<sup>13</sup>

Conventional wisdom holds that Pseudoexfoliation syndrome leads to increased risk of complications during cataract surgery with regard to zonular dehiscence rupture of posterior capsule and luxation of lens into the vitreous as a consequence of insufficient zonules.<sup>14</sup> Somehow, now many authorities believe that modern cataract surgery makes it possible to achieve good operative result even in these patients.<sup>15</sup>

Some studies believe that phacoemulsification is safe in most eyes with pseudoexfoliation syndrome even though significantly more complications occur intraoperatively in these eyes<sup>15</sup>, but other studies believe that intra operative performance with Pseudoexfoliation syndrome is comparable to that in normal eyes<sup>16</sup>.

## MATERIALS AND METHODS

This was a cohort study. The patients were selected from the outpatient department of Ophthalmology, BVH, Bahawalpur on non-probability consecutive sampling basis having 50 eyes of the patients having cataract with pseudoexfoliation syndrome Group I, age above 40 years, IOP range from 10-20mmHg and no history of ocular trauma and surgery were included and 50 eyes of patients having cataract without pseudoexfoliation syndrome Group II. Patients having age above 40 years, IOP range from 10-20mmHg and no history of ocular trauma and surgery were included. The patient having hard cataract with nuclear sclerosis Grade -3 or more and phacodonesis, iridoneiss, zonular dialysis, lens subluxation, Uveitis, corneal dystrophies and known pseudoexfoliative glaucoma were excluded. Complete history and examination including visual acuity, IOP, Slit lamp examination, detailed examination of iris and pupil, lens examination for pseudoexfoliation material, zonular dialysis, fundus examination and B-Scan for dense cataract, biometry for IOL Implant was done. Most patients were operated under topical anesthesia.

All the patients underwent phacoemulsification. PMMA IOL 5.5 to 6mm was implanted in all patients after enlarging the incision. Per-operative and postoperative complications were assessed in both the groups. Analyzing the rate of complications of both the groups were compared by chi-square test while qualitative data

was compared with student t-tests. Statistical analysis was performed using the computer assisted SPSS 10 software package. P Value less than 0.005 was taken as significant

The regimen followed was preoperative evaluation, surgical procedures, postoperative care and medication and follow-up.

Patients were examined on first postoperative day, one month and three months postoperatively. At each follow-up visit following were checked and recorded.

Slit lamp examination was done for anterior segment (Striate Keratopathy, Uveitis and Pigmentation on the anterior surface of the lens), wound condition and examination of posterior segment.

## RESULTS

In Group 1 the mean age of patients was  $63.64 \pm 6.42$  years with the range of 50-70 years. In Groups 2 mean age of patients was  $55.72 \pm 11.95$  year with a range of 27-71 years.

There were 32 males (64%) and 18 females (36%) in Group -I and 28 males (56%) and 22 females (44%) in Group-2.

In groups-1, 36(72%) eyes had pre-operative visual acuity (VA) counting finger (CF), 10(20%) were in the range of 6/60 to 6/36 and 4(8%) were 6/24. In Group-2 32(64%) had preop VA is CF 16(32) were in the range of 6/60 to 6/36 and 2 (4%) were of 6/24. The presence of complication of follow up are shown in Table-I while distribution of complications are shown in Table-2

**Table No. 1: Comparison of complications of two Groups I & II**

Time of Assessment	Group	No Complications	Complications	P Value
Day 1	Group 1	38(76%)	12 (24%)	P= 0.3173
	Group 2	42 (84%)	8 (16%)	
1 Month	Group 1	47 (94%)	3 (6%)	P=0.3075
	Group 2	49 (98%)	1 (2%)	
3 Months	Group 1	47 (94%)	3 (6%)	P=0.6464
	Group 2	48 (96%)	2 (4%)	

**Table No. 2: Distribution of Complications**

Time Of Assessment	Complications	Group I	Group II	P Value
Day 1	Striate Keratopathy	8(16%)	6 (12%)	P= 0.6903
	AC Reaction	4(8%)	2 (4%)	P= 0.6903
1 Month	AC Reaction	3 (6%)	1 (2%)	P=0.4936
3 Months	AC Reaction	1 (2%)	1 (2%)	P=0.7609
	Pigment on the IOL Surface	2(4%)	1 (2%)	P=0.7982

## DISCUSSION

The hospital based comparative interventional study was designed to estimate the rate of complication of



Phacoemulsification. The objective of this study was to compare the rate of complications of Phacoemulsification in patients with and without pseudoexfoliation syndrome. Cataract surgery is a leading intraocular surgery being performed throughout the world. Now a days phacoemulsification has revolutionized the surgical procedure with minimal post-operative complications swift visual rehabilitation and early mobility of the patients. Pseudoexfoliation syndrome leads to increased risk of complications during cataract surgery with regard to zonular dehiscence rupture of posterior capsule and luxation of lens into the vitreous as a consequence of insufficient zonules. Somehow, now many authorities believe that modern cataract surgery makes it possible to achieve good operative result even in these patients. Some studies believe that phacoemulsification is safe in most eyes with pseudoexfoliation syndrome even though significantly more complications occur intraoperatively in these eyes, but other studies believe that intraoperative performance with Pseudoexfoliation syndrome is comparable to that in normal eyes. This was a comparative interventional study. 100 patients were selected from the outpatient department of Ophthalmology, BVH, Bahawalpur. Patients were selected on convenient sampling basis into two groups. "Group I" contained 50 eyes of the patient having cataract with pseudoexfoliation syndrome, and "Group II" containing 50 eyes of patients having cataract without pseudoexfoliation syndrome. All the patients underwent phacoemulsification. PMMA IOL 5.5 to 6mm was implanted in all patients after enlarging the incision. Per-operative and postoperative complications were assessed in both the groups. Analyzing the rate of complications of both the groups were compared by chi-square test. Statistical analysis was performed using the computer assisted SPSS 10 software package. In both the groups no per-operative complications were noted. On 1<sup>st</sup> postoperative day Group I, 38 (76%) patients had no complications, 12 (24%) developed complications which are striate keratopathy, 8 (16%) developed anterior chamber (AC) reaction 4 (8%). Group II, 1<sup>st</sup> Postoperative day, 42 (84%) patient had no complication, 8 (16%) developed complications which are striate keratopathy 6 (12%), AC reaction 2 (4%). In Group I, on first month 47 (94%) had no complication and 3 (6%) developed complication which is AC reaction while in group II, 49 (98%) had no complication, 1 (2%) developed complication which is AC reaction. On third month In Group I 47 (94%) had no complications and 3 (6%) developed complications which are AC reaction 1 (2%) and pigment on the IOL surface 2 (4%) while in Group II, 48 (98%) had developed no complications and 2 (4%) patients had developed complications which are AC reaction 1 (2%) and pigment on the IOL surface 1 (2%). P values of all complications in Group I and Group II are insignificant.

Our results correlate well with those of Shastri L<sup>16</sup> which showed that intraoperative complications such as Zonular or capsular dehiscence were not seen in any eye. Postoperatively, IOP and aqueous cell response were comparable between group (P = .11 and P = 0.81, respectively). The visual outcome at 1 month was similar between groups.

Our results correlate with Menkhaus S<sup>15</sup> which has mentioned that intraoperative complications such as rupture of the posterior capsule zonular dialysis and displacement of the lens into the vitreous body were similar in the two groups. Modern cataract surgery makes it possible to achieve good operative results, even in risk patients. Preoperative presence of PEX had no influence on the complication rate of cataract surgery.

Our results also correlate with Dosso AA<sup>17</sup> in which it has been mentioned that intraoperatively, the incidence of zonular tears was the same in both groups (10%). In the 23 patients who had surgery one year later, no zonular tear occurred. The incidence of postoperative complications was similar in both groups. Phacoemulsification with posterior chamber IOL implantation appears to be safe in eyes with Pseudoexfoliation syndrome.

Our study showed that in selective cases of pseudoexfoliation with experienced hands, is quite a safe procedure. Both intra and post-operative complications are almost.

## CONCLUSION

A planned approach to cataract surgery using the advanced techniques of phacoemulsification, significantly reduces the risk of complications during surgery. Therefore, phacoemulsification is a safe procedure in cataract without pseudoexfoliation syndrome and in selective cases of cataract with pseudoexfoliation syndrome.

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# Outcome of Stapled Hemorrhoidectomy versus Traditional Hemorrhoidectomy in Patients with Advance Hemorrhoids

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## ABSTRACT

**Objective:** To evaluate the outcome of stapled hemorrhoidectomy versus traditional hemorrhoidectomy in patients presenting with advance hemorrhoids.

**Study Design:** Prospective study

**Place and Duration of Study:** This study was conducted at the Department of Surgery, University of Lahore Teaching Hospital Lahore from January 2018 to December 2018.

**Materials and Methods:** A total of 150 patients of both genders with ages 20 to 70 years who presented with advance hemorrhoids were included. Patient's demographical details including age, sex and residence were recorded. Patients were categorized in two groups; Group I consist of 75 patients and received stapled hemorrhoidectomy and Group II contains 75 patients and received traditional hemorrhoidectomy. Post-operative outcomes of both groups were recorded and findings compared between both groups. Follow-up was taken at 6 and 12 months after surgery to examine the recurrence rate.

**Results:** There were 45 (60%) male patients and 30 (40%) females in Group I and 48 (64%) patients were males and 27 (36%) were females in Group II. In Group I recurrence was found in 8 (10.66%) patients and in Group II 10 (13.33%) patients developed recurrence. Time duration of surgery was high in Group II patients 40.4±6.9 min. as compared to Group I 29±5.23 min. In Group I mean pain score was 6.23±2.24 and in Group II it was 7.2±1.45 according to the VAS. In group II 7 (9.33%) patients had postoperative pain and in Group I, 3 (4%) patients had postoperative pain. Post operative bleeding found in 8 (10.67%) patients in Group II and 2 (2.67%) in Group I.

**Conclusion:** Stapled hemorrhoidectomy is a safer and effective technique with low rate complications as compared to traditional hemorrhoidectomy.

**Key Words:** Hemorrhoids, Stapled hemorrhoidectomy, Traditional hemorrhoidectomy, Outcome

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## INTRODUCTION

Hemorrhoids are normal component of the anal canal and are composed predominantly of vascular tissue supported by smooth muscle and connective tissue. It functions as a compressible lining allows the anus to close completely.

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They become symptomatic through bleeding or prolapse. Gollinger classified haemorrhoids into four grades.<sup>1</sup> At least 50% of the people over the age of fifty have some degree of haemorrhoids formation. Generally 1<sup>st</sup> grade hemorrhoids are treated by changing diet, life pattern and using stool softeners. First and second degree haemorrhoids are generally treated by changing bowel habits, diet and lifestyles and by using stool softeners or laxatives. Sclerotherapy, infrared coagulation and rubber band ligation are the useful modalities for the treatment of 2<sup>nd</sup> degree hemorrhoids. Surgical management is a preferred treatment for 2<sup>nd</sup> and third grade hemorrhoids. Surgical hemorrhoidectomy is very useful and effective procedure for the treatment of advance hemorrhoids. Hemorrhoidectomy is generally performed by open and close technique. The Milligan-Morgan technique is basically used to dissect the hemorrhoid but the Ferguson technique is the advanced method of open surgical hemorrhoidectomy that involves wound closure with continuous suture to promote healing.<sup>2</sup> Surgical hemorrhoidectomy may cause postoperative pain, bleeding and wound infection as short term

postoperative complications while anal fissure, stenosis and recurrence are the long term complications. Globally hemorrhoidectomy is the most performed surgical treatment for hemorrhoids.<sup>2</sup> Milligan-Morgan method is the most performed technique among all the surgical methods.<sup>3</sup> Surgical treatment (hemorrhoidectomy) is considered a painful method for benign disorder with average hospital stay of 2 to 3 days.<sup>4,5</sup> Stapled hemorrhoidectomy is an advance technique for the treatment of hemorrhoids with very low rate of complications such as pain, bleeding and less hospital stay and shorter time duration of surgery.<sup>6-10</sup>

The present study was conducted aimed to examine the short term outcome and recurrence rate between stapled hemorrhoidectomy and traditional hemorrhoidectomy technique in patients with advance hemorrhoids.

## MATERIALS AND METHODS

This prospective study was conducted at Department of Surgery, University of Lahore Teaching Hospital Lahore from 1<sup>st</sup> January 2018 to 31<sup>st</sup> December 2018. One hundred and fifty patients of both genders with ages 20 to 70 years presented with advance hemorrhoids were included. Patient's demographical details including age, sex and residence were recorded. Patient's previous history of hemorrhoidectomy, history of recurrence, patients with acute hemorrhoidal episodes, patients with anal stenosis and those who were not interested were excluded from the study. Patients were categorized into two groups i.e. Group I consisted of 75 patients who received stapled hemorrhoidectomy, Group II also had 75 patients who received traditional hemorrhoidectomy. Post-operative outcomes such as hospital stay, surgery duration, postoperative bleeding and pain were recorded and the findings compared between both groups. Data was analyzed by SPSS 21.0. P value < 0.05 was set as significant. Mean±SD were applied.

## RESULTS

45 (60%) patients were males and 30 (40%) were females in Group I and 48 (64%) patients were males and 27(36%) were females in Group II. In Group I (Stapled) 15 (20%) patients were ages 20 to 30 years, 25 (33.33%) patients were ages 31 to 40 years, 28 (37.33%) patients were ages 41 to 50 years, 7 (9.33%) patients were ages above 50 years. In Group II, 13 (17.33%) patients had ages 20 to 30 years, 24 (32%) patients were ages 31 to 40 years, 29 (38.67%) patients were ages 41 to 50 years and 9 (12%) patients had ages above 50 years (Table 1)

According to the outcomes between both techniques we found time duration of surgery was high in Group II patients was 40.4±6.9 min as compared to Group I 29±5.23 min. In Group I mean Hospital stay was 2.65±1.24 days and in Group II it was 5.45±3.62 days

respectively. In Group I mean pain score was 6.23±2.24 and in Group II it was 7.2±1.45 according to the VAS. Post-operative bleeding was found in 8 (10.67%) patients in Group II and 2 (2.67%) in Group I (Table 2). At follow-up, in Group I recurrence developed in 8 (10.66%) patients and in Group II 10 (13.33%) patients developed recurrence (Table 3).

**Table No.1: Frequency of age and gender**

Variable	Group I (n=75)	Group II (n=75)
<b>Gender</b>		
Male	45 (60%)	48 (64%)
Female	30 (40%)	27 (36%)
<b>Age (years)</b>		
20 – 30	15 (20%)	13 (17.33%)
31 – 40	25 (33.33%)	24 (32%)
41 – 50	28 (37.33%)	29 (38.67%)
> 40	7 (9.33%)	9 (12%)

**Table No.2: Outcomes findings between both groups**

Variable	Group I	Group II	P value
Time Duration Surgery min	29±5.23	40.4±6.9	<0.05
Hospital stay (days)	2.65±1.24	5.45±3.62	<0.05
PO Pain VAS	6.23±2.24	7.2±1.45	N.S
PO Bleeding	2 (2.67%)	8 (10.67%)	<0.05

**Table No.3: At final follow-up rate of recurrence between both groups**

Recurrence	Group I	Group II	P value
Yes	8 (10.66%)	10 (13.33%)	N.S
No	67 (89.34%)	65 (86.67%)	

## DISCUSSION

Many studies have been conducted to examine the outcomes of stapled hemorrhoidectomy as compared with traditional hemorrhoidectomy and different outcomes values were demonstrated.<sup>11,12</sup> The present study was also conducted to examine the outcomes of stapled hemorrhoidectomy versus traditional hemorrhoidectomy in patients with advance hemorrhoids. We found that 45 (60%) patients were males and 30 (40%) were females in Group I (Stapled) and 48 (64%) patients were males and 27(36%) were females in Group II (Traditional). These results showed similarity to some other studies in which male patients population was high 50 to 65% as compared to females.<sup>13,14</sup> In Group I (stapled) 15 (20%) patients were ages 20 to 30 years, 25 (33.33%) patients were ages 31 to 40 years, 28 (37.33%) patients were ages 41 to 50 years, 7 (9.33%) patients were ages above 50 years. In Group II, 13 (17.33%) patients had ages 20 to 30 years, 24 (32%) patients were ages 31 to 40 years, 29 (38.67%) patients were ages 41 to 50 years and 9

(12%) patients had ages above 50 years. A study conducted by Sachin et al<sup>15</sup> reported mean age of patients in stapled hemorrhoidectomy group was  $39.50 \pm 9.82$  years and in traditional hemorrhoidectomy the mean age of patients was  $40.05 \pm 10.88$  years.

In the present study, we found that time duration of surgery was high in traditional management  $40.4 \pm 6.9$  min as compared to stapled hemorrhoidectomy  $29 \pm 5.23$  min. These results were similar to some other studies in which patients who received stapled hemorrhoidectomy had a shorter time duration of surgery as compared to traditional hemorrhoidectomy.<sup>16,17</sup>

This study showed that patients who were treated with stapled hemorrhoidectomy had a shorter hospital stay  $2.65 \pm 1.24$  days than the traditional hemorrhoidectomy treated patients  $5.45 \pm 3.62$  days. These results were similar to the study conducted by Shukla et al<sup>18</sup> in which they reported that patients treated with stapled hemorrhoidectomy had a less hospital stay than the traditional hemorrhoidectomy treated patients P-value  $< 0.05$ .

In the current study we found that in Group I mean pain score was  $6.23 \pm 2.24$  and in Group II it was  $7.2 \pm 1.45$  according to the VAS. Post operative bleeding was found in 8 (10.67%) patients in Group II and 2 (2.67%) in Group I. These results were similar to some previous studies.<sup>19,20</sup> In our study at final follow-up we found that in Group I (stapled) recurrence developed in 8 (10.66%) patients and in Group II (traditional) 10 (13.33%) patients developed recurrence. Arslani et al<sup>21</sup> reported that the recurrence rate was high in patients treated with stapled hemorrhoidectomy as compared to traditional hemorrhoidectomy Lee et al<sup>22</sup> showed similarity to our results regarding recurrence rate and reported no significant difference between both techniques.

## CONCLUSION

The stapled hemorrhoidectomy technique is safer and effective with low rate of complications as compared to traditional hemorrhoidectomy and there was no significant difference observed regarding recurrence rate between both techniques.

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

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# Possible Routes of Transmission/Risk Factors of Hepatitis-C Virus in Urban and Rural Areas

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## ABSTRACT

**Objective:** The objective of this study was to determine the possible routes of transmission of hepatitis C virus and to compare routes of transmission of hepatitis C between urban and rural areas.

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

**Place and Duration of Study:** This was conducted at the Jinnah Teaching Hospital attached to Jinnah Medical College, Peshawar from October, 2017 to December 2018

**Materials and Methods:** This study was conducted on 100 consecutive patients. Participants were diagnosed for hepatitis C by suggesting Anti-HCV antibody through immune chromatographic technique (ICT) followed by ELISA and PCR (qualitative) to confirm and abdominal ultrasound to detect ascites or any hepatic parenchymal change or focal hepatic mass. Patient's names, age, sex, marital status, address (rural and urban) and possible routes of transmission/risk factors were recorded. Descriptive statistics were calculated in SPSS 20.0. Comparison was made for possible routes of transmission/risk factors of Hepatitis C between rural and urban using chi-square test. P-value  $\leq 0.05$  was considered significant.

**Results:** Males were 40(40%) and female were 60(60%). The mean age was  $41.78 \pm 14.19$  years. The most common routes of transmission of Hepatitis C were surgical procedures and skin piercing  $n=32(32\%)$  followed by surgical procedures  $n=31(31\%)$ . Only skin piercing, surgical procedures for orodental and gynecological reasons, surgical procedures and blood transfusions were found in 11%, 7% and 8% cases respectively. Skin piercing as a possible route of transmission of Hepatitis C was more in rural areas (30%) than urban (13%). Similarly orodental/gynecological procedures were more in rural (4%) than urban (3%). On other hand surgical procedures as a risk factor for Hepatitis C was more in urban (18%) than rural (13%). Invasive medical procedures were also common in urban (3%) than rural (1%). All these results were statistically significant ( $P=0.008$ ).

**Conclusion:** The major risk factors/possible routes of transmission of hepatitis C were surgical procedures followed by skin piercing by injection needles and least risk factors were invasive medical procedures. Skin piercing and orodental/gynecological procedures to be a possible routes of transmission of Hepatitis C were more in rural areas than urban areas. On other hand surgical procedures and invasive medical procedures were more in urban than rural areas.

**Key Words:** Hepatitis C, route of transmission, risk factor, rural, urban

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## INTRODUCTION

Hepatitis C virus (HCV) is a pathogenic organism that transmit mainly through blood and remains a significant global health concern.<sup>1</sup> After the acquirement of the virus, acute hepatitis C virus infection can lead to chronic stage.<sup>2</sup>

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The chronic HCV infection is associated with numerous complications like liver cirrhosis and hepato cellular carcinoma(HCC).<sup>3</sup> Morbidity related to HCV tensed healthcare systems throughout world, with around 71 million individuals chronically infected worldwide.<sup>4</sup> Direct-acting antiviral drugs, an extremely efficient HCV therapy, can clear HCV infection and may significantly decrease HCV disease burden and its further transmission.<sup>5</sup> Now the global targets have been set by the World Health Organization (WHO) is to eliminate HCV by 2030.<sup>6</sup> In developed countries like USA, the fast improvement in health-care systems and the anti-HCV screening introduction especially for blood donors results in sharp decrease in the incidence of iatrogenic transmission of hepatitis C in developed countries, on the other hand the epidemic of HCV is spreading in developing countries. In developing countries the unscreened blood transfusions and non-

sterile injections are still the main sources of transmission.<sup>7</sup>

Numerous routes of transmission of HCV have been documented and generally accepted while some are less well defined and need further investigations. The most common route of transmission of Hepatitis-C virus is through direct percutaneous exposure to infected blood. Socioeconomic differences may be responsible for geographic variability of HCV.<sup>8</sup> Illegal injection drug use and iatrogenic exposures have been the main risk factors for HCV transmission throughout the world. Incidence of HCV remains high among injection users, injectable drug users, and tattoo users. Continuing monitoring of the epidemiology of HCV infection is vital for prevention of future infections.<sup>9</sup>

Conry-Cantilena et al.<sup>10</sup> reported that strongly associated risk factors for HCV infection in the HCV affected individuals were blood transfusion in 66 (27%), intra-nasal cocaine use in 169 (68%), intravenous drug use 103 (42%), sexual contact 132 (53%), and ear piercing. Another study reported that overall perinatal HCV transmission rate was 2.4%.<sup>11</sup> Terrault et al.<sup>12</sup> reported that overall HCV prevalence among sexual partners was 4%.

## MATERIALS AND METHODS

This cross sectional descriptive study was conducted at Jinnah Teaching Hospital attached to Jinnah Medical College, Peshawar from October, 2017 to December 2018 on 100 consecutive patients. Sampling was done using convenient sampling technique. Approval was taken from ethical review committee of the hospital. After detailed explanation to the participants regarding the purpose of the study a verbal informed consent was taken.

A detail history was taken followed by relevant examination. All participants were diagnosed for hepatitis C by history, examination and appropriate laboratory investigations. The participants were diagnosed for hepatitis C by suggesting anti-HCV antibody through immune chromatographic technique (ICT) followed by confirmation with Enzyme-linked immune sorbent assay (ELISA) and qualitative Polymerase chain reaction (PCR). Abdominal ultrasound was also advised for each patient to look for the presence of Ascites and any parenchymal liver disease or focal mass lesion e.g. hepato cellular carcinoma. Patient's name, age, sex, marital status, address (rural and urban) and possible routes of transmission/risk factors were recorded in pre-structured proforma. Pakistani nationals, both genders, age above 15 years and cooperative patients were included in this study.

The collected data were analyzed using SPSS version 20.0. Mean and standard deviation were calculated for quantitative variables like age. Frequency and percentages were computed for qualitative variables

like sex, marital status, address (rural and urban) and possible routes of transmission/risk factors of Hepatitis C. Comparison was made for possible routes of transmission/risk factors of Hepatitis C between rural and urban area using chi-square test. P-value less or equal to 0.05 ( $\leq 0.05$ ) was considered significant.

## RESULTS

The total participants were hundred (100), in which male were n=40(40%) and female were n=60(60%). The mean age was  $41.78 \pm 14.19$  years. The age ranged from 17 to 75 years. Most of the participants were married n=95(95%). Half of the sample belong to urban n=50(50%) and half to rural areas n=50(50%). The details of frequency of gender, marital status and rural/urban are given in table 1.

The most common age group was 31-45 years n=31(31%) followed by 46-60 years n=29(29%) and 15-30 years n=28(28%). The least number of participants were in age group 61-75 years n=12(12%). (Fig 1)

The major risk factor/possible route of transmission of hepatitis C was surgical procedure for various purposes like gynecological, finger pathology, laparotomy n=85(85%) followed by skin piercing by injection needle n=11(11%) and least risk factor were invasive medical procedures n=4(4%). (Fig 2)

However most (54%) participants had more than one risk factor which is shown in table 2. The most common routes of transmission/risk factors of Hepatitis C was surgical procedures and skin piercing due to needle injection n=32(32%) followed by only surgical procedure n=31(31%). Skin piercing as a risk factor for Hepatitis C was found in 11(11%) cases. Surgical procedures for orodental and gynecological reasons were found in 7(7%) participants. Surgical procedures and blood transfusion were found in 8% cases. Rests of details are given in table 2.

**Table No.1: Frequency of gender, marital status and rural/urban area**

Variable		Frequency	Percent
Gender	Male	40	40
	Female	60	60
	Total	100	100
Marital status	Married	95	95.0
	Unmarried	5	5.0
	Total	100	100.0
Urban/ Rural	Urban	50	50.0
	Rural	50	50.0
	Total	100	100.0

Comparison of possible routes of transmission/risk factors of Hepatitis C between rural and urban showed that skin piercing as possible route of transmission of Hepatitis C was more in rural areas n=30(24+6%) than Urban n=13(8+5%). Similarly orodental/gynecological



procedure was more in rural n=4(4%) than urban n=3(3%). On other hand only surgical procedure was more in urban n=18(18%) than rural n=13(13%). Invasive medical procedure was also common in urban n=3(3%) than rural n=1(1%). All these results were statistically significant (P=0.008). (Table 3)

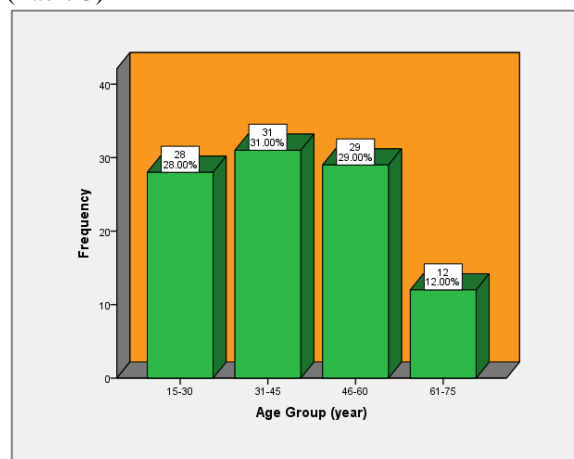


Figure No.1: Age distribution of the study

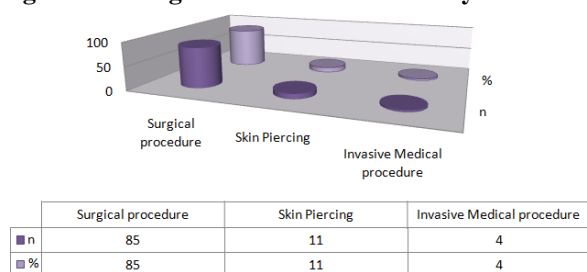


Figure No. 2: Pattern of routes of transmission of Hepatitis C

Table No.2: Frequency of routes of transmission/ risk factors of Hepatitis-C

Routes of transmission/risk factors	Freq- uency	Percent
Surgical procedures, Skin piercing (Inj)	32	32
Skin Piercing	11	11
Surgical procedures	31	31
Surgical procedures(Orodenal/Gynae)	7	7
Surgical procedures(Gyn), Blood transfusions, Skin piercing (Inj)	6	6
Surgical procedures , Invasive medical procedures	1	1
Surgical procedures, Blood transfusions	8	8
Invasive medical procedures	4	4
<b>Total</b>	<b>100</b>	<b>100</b>

Table No.3: Comparison of Routes of transmission/ risk factors of Hepatitis C between rural and urban

Routes of transmission/ risk factors	Address				P-value*
	Urban		Rural		
	n	%	n	%	
Surgical procedures, Skin piercing (Inj)	8	8.0	24	24.0	0.008
Skin Piercing	5	5.0	6	6.0	
Surgical procedures	18	18.0	13	13.0	
Surg procedures (Orodenal/Gynae)	3	3.0	4	4.0	
Surgical procedures(Gyn), Blood transfusions , Skin piercing (Inj)	6	6.0	0	0.0	
Surgical procedures , Invasive medical procedures	1	1.0	0	0.0	
Surgical procedures, Blood transfusion	6	6.0	2	2.0	
Invasive medical procedures	3	3.0	1	1.0	

\*Pearson Chi-Square Test;  $P \leq 0.05$  significant

## DISCUSSION

The most efficient transmission of HCV is by the parenteral route. This transmission is possible even at low levels of viral contamination. From 2008 to 2012 CDC got notice of 15 outbreaks of health-care about HCV transmission in non-dental treatment.<sup>13</sup> Generally, infectious agents transmission in healthcare systems can occur from patient to patient (e.g. due to inappropriate injection use), patient to clinician (like from needle sticks), or doctor to patient (like during surgery). The factors affecting the risk of transmission are related to the agent, the host, and the environment. Hepatitis C virus can stay alive in the environment for 16 hours on a dry surface,<sup>14</sup> at low temperatures in water for up to 5 months, and in saliva.<sup>15</sup>

This study was aimed to determine the possible routes of transmission/risk factors for hepatitis C and to see whether there is a difference between rural and urban areas in its transmission. We selected age above 15 years for our study. This was because most invasive procedures involving blood contact are required in above 15 years age. In our study the least number of participants were in age group 61-75 n=12(12%). This shows lack of prompt diagnosis and treatment of hepatitis in Pakistan which lead to early deaths.<sup>16</sup> In the current study the major risk factor/possible route of transmission of hepatitis C was surgical procedure followed by skin piercing by injection needles and least risk factor was invasive medical procedure. A study conducted by Chlabicz et al.<sup>17</sup> on known and probable risk factors for hepatitis C infection in north-eastern Poland. They reported that potential sources of exposure to HCV among 103 persons without known or probable risk factor was dental n=91(88.3%), hospitalizations more than 5 times n=22(21.4%) and major surgical procedure n=49(47.6%). The differences

in results may due to lack of proper sterilization in our surgical procedures, treatment by non-qualified persons, low quality autoclaves.

Our findings showed that skin piercing and orodental/gynecological procedure as possible route of transmission of Hepatitis-C was more in rural areas than urban areas. On other hand surgical procedure and invasive medical procedure was more in urban than rural ( $P=0.008$ ). This may be due lack of health regulations in Pakistan which results in quackery and non-professional treatment including dental extraction by quacks, delivery by leady health visitors, and re-use of syringes in rural area. Most of the surgeries and invasive medical procedure are performed in cities so this may be responsible for more risk factors for hepatitis C in urban. No study was traced in literature on comparison of risk factors/possible route of transmission of Hepatitis between urban and rural areas. Our study had some limitations. It focused only on treatment seeking population; hence the results may not be a true representation of prevalence and profile in the community.

## CONCLUSION

Our findings showed that:

- The major risk factor/possible route of transmission of hepatitis C was surgical procedure followed by skin piercing by needle injection and least risk factor was invasive medical procedure.
- More than one risk factors/possible route of transmission of hepatitis were found in most patients
- Skin piercing and orodental/gynecological procedure as possible route of transmission of Hepatitis C was more in rural areas than urban area. On other hand surgical procedure and invasive medical procedure was more in urban than rural. All these were statistically significant ( $P=0.008$ ).

### Author's Contribution:

Concept & Design of Study: Marifat Shah.  
 Drafting: Marifat Shah.  
 Data Analysis: Marifat Shah.  
 Revisiting Critically: Marifat Shah.  
 Final Approval of version: Marifat Shah.

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

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## Diabetes Mellitus With Good Glycemic Control

Syeda Nosheen Zehra, Hamid Ali, Shahid Karim and Farheen Fatima Zaidi

## ABSTRACT

**Objective:** To determine the frequency of microalbuminuria in Type II Diabetes Mellitus with good glycemic control in a tertiary care hospital of Karachi

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

**Place and Duration of Study:** This study was conducted at the Department of Internal Medicine, Liaquat National Hospital Karachi from Feb 2018 to July 2018.

**Materials and Methods:** A total of 140 patients of type II diabetes mellitus with good glycemic control were selected. Urine for micro albumin level was sent to the institutional laboratory to assess microalbuminuria. All the collected information was entered in the prescribed Proforma.

**Results:** A total of 140 type II DM patients with good glycemic control were included in our study. Out of 140 patients 63 (45%) were female and 77 (55%) were male with mean age of  $44.47 \pm 4.99$  years. Mean duration of DM was  $4.21 \pm 0.94$  years. Mean HbA1c level was  $6.897 \pm 0.1779$ . Twelve patients (8.6%) were found to have microalbuminuria

**Conclusion:** Type II diabetic patients are at increased risk of developing microalbuminuria even when they have a good or moderately good glycemic control. This complication invariably leads to the development of overt nephropathy over a period of time. In order to prevent this complication, intense Screening protocols should be employed to check for microalbuminuria and HbA1c in both the newly and already diagnosed type II diabetic, so that the progression of micro and macro vascular complications can be halted by timely intervention.

**Key Words:** Microalbuminuria (MA) Type II Diabetes Mellitus, Good Glycemic control (6.7-7)

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## INTRODUCTION

Diabetes mellitus was reported to be the sixth leading cause of death listed on US death certificates in 2010.<sup>1</sup> Ramachandran and Colleagues in 2012 documented that Prevalence of diabetes mellitus in Pakistan is 7.7% in rural and 10.6% in urban population with more than 7.2 million people suffering from this illness.<sup>2,3</sup> The prevalence of diabetes and prediabetes increased with age and were more frequent among men.

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both.<sup>4</sup>

Microalbuminuria is defined as a urinary albumin excretion ranging from 30 to 299 mg/24 h, and is a marker for renal damage and a risk factor for the progression of chronic kidney disease, cardiovascular disease, cerebrovascular disease and mortality.<sup>5</sup>

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Hyperglycemia and duration of diabetes are known risk factors for diabetic nephropathy, and the presence of microalbuminuria is a strong indicator of impending nephropathy.<sup>6</sup> Diabetic nephropathy is the leading cause of end stage renal disease in United States<sup>7</sup> and a leading cause of diabetes mellitus related morbidity and mortality. The laboratory test for early detection of diabetic nephropathy is the measurement of micro albumin in urine. Microalbuminuria may not be associated with abnormal serum creatinine, but can be an important warning signal which if ignored can result in irreversible renal damage.<sup>8</sup> moreover it is a worldwide public health problem and puts a substantial burden on health care resources. In Pakistan the burden of diabetes Mellitus is increasing with passing years, diabetic patients usually present to us with overt nephropathy when it's already late to halt the impending complications. Here because of low per capita income of average population patients mostly fall in the lower income bracket and the resources are constraint, thus prevention of diabetic complications are the need of the hour. Checking for microalbuminuria in our local patients suffering from diabetes mellitus type II seemed to be a very logical rationale for our study, which was expected to give us an idea about the magnitude of problem in our patients and would help us make stringier protocols for routinely checking for micro albuminuria in every diabetic patient on first visit

so that diabetic nephropathy is caught earlier and renal complications are prevented.

## MATERIALS AND METHODS

After approval from hospital ethical committee, 140 patients fulfilling selection criteria were included in the study from Medical OPD of department of Internal Medicine Liaquat National hospital and Medical College Karachi Pakistan. Informed consent, demographic data and history regarding name, age, duration of DM was taken. Venous blood was collected in a test tube with ethylene diamine tetra acetic acid (EDTA) anticoagulant for HbA1c. Twenty four hours urine was collected for estimation of MA. HbA1c is estimated by boronate affinity chromatography (HPLC) which separately totals glycated hemoglobin by binding to solid-phase dehydroxylation using Nycocard immunoassay kit (USA). In order to measure urinary albumin concentration accurately, patients were trained regarding the collection of urine samples by researcher himself. When no evidence of infection and / or hematuria is found in the urinalysis, urine samples were examined for microalbuminuria. Urinary albumin was measured with an autoanalyzer (analyzer medical system, Italy) using Randox kits (urinary albumin measured with immunoturbidimetry method, UK). A second 24-hours urine sample was obtained and examined for microalbuminuria, if the first measurement exceeded 30mg of albumin. The diagnosis of microalbuminuria was confirmed when > 30mg/dl albumin was found in the second sample. 24-hours urinary albumin concentration of < 30mg were considered as normal (Normoalbuminuria), 30 - 300mg as microalbuminuria and > 300mg as macroalbuminuria (Overt proteinuria). Exclusion criteria were followed to control bias in the study results. Patient comfort was taken care of during clinical examination. All the information from the patients was recorded on proforma which is attached at the end.

Data was analyzed by using SPSS version 22. Mean and standard deviation was computed for quantitative variables like age, duration of type II DM, HbA1c level. Frequency and percentages were calculated for qualitative variables like gender, microalbuminuria. Effect modifier like age, gender and duration of diabetes was controlled through stratifications. Post stratification Chi-square test was applied to see the effect of these on outcomes (i.e. microalbuminuria) by taking P-Value  $\leq 0.05$  was considered significant.

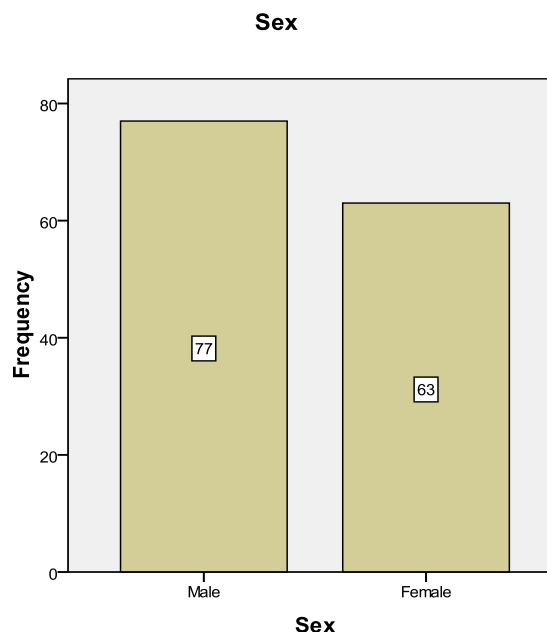
## RESULTS

A total 140 patients having Type 2 Diabetes Mellitus with good glycemic control were included in our study. The mean age of  $44.47 \pm 4.99$  years. The descriptive statistics of age is presented in Table-1. 63 (45%) were female and 77 (55%) were male, as mentioned in graph-1.

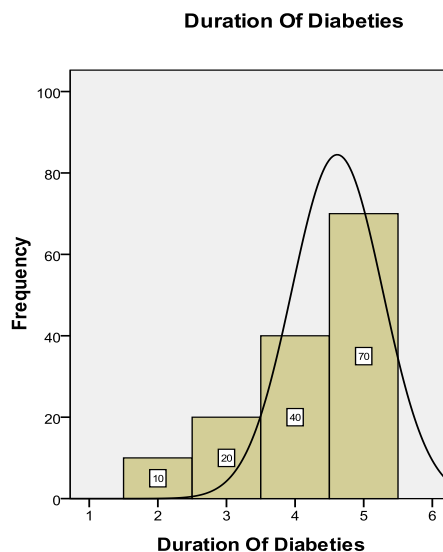
Mean duration of Diabetes Mellitus (DM) was found to be  $4.21 \pm 0.94$  years. The descriptive statistics of duration of DM is presented in Table-I. The frequency and percentages are presented in Graph-II.

Mean HbA1c level was found to be  $6.897 \pm 0.1779$ . The descriptive statistics of HbA1c is presented in Table-I. Twelve patients (8.6%) type 2 DM patients with good glycemic control were found to have microalbuminuria. The frequency distribution of microalbuminuria is presented in Table-II.

Microalbuminuria was predominant in female gender and was more common in age group of 45 to 50 years, as shown in Table-III & table-IV.



**Graph No.1: Frequency distribution of Gender**



**Graph No.2: Frequency distribution of Duration of Diabetes mellitus**

**Table No.1: Frequency distribution of Age, Duration of Diabetes mellitus & HbA1c level. (n=140)**

Variables	Statistics		
	Minimum	Maximum	Mean & standard deviation
Age (Years)	30	50	44.47±4.99
Duration of Diabetes mellitus (years)	2	5	4.21±0.94
Serum HbA1c level (%)	6.7	7.5	6.897±0.1779

**Table No.2: Frequency distribution of Microalbuminuria(n=140)**

Microalbuminuria	Frequency n=(140)	Percentage (%)
No	128	91.4%
Yes	12	8.6%
Total	140	100%

**Table No.3: Microalbuminuria according to Age. (n=140)**

Age	Microalbuminuria			P-value
	No (n=128)	Yes (n=12)	Total	
30-40 years	24	2	26	0.005
44-50 Years	104	10	114	
Total	128	12	140	

**Table No.4: Microalbuminuria according to gender (n=140)**

Gender	Microalbuminuria			P-value
	No (n=128)	Yes (n=12)	Total	
Male	73	4	77	0.120
Female	55	8	63	
Total	128	12	140	

## DISCUSSION

Diabetes mellitus is a global health problem. Majority of patients diagnosed are in the young and middle age group<sup>9</sup>. It is a major health problem in Pakistan where, its prevalence range from 3-14%, this prevalence rate varies in the urban and rural areas<sup>10</sup>. Microalbuminuria is an early marker of diabetic nephropathy; it may be present at the point of initial diagnosis of type 2 diabetes. It progresses to overt nephropathy and eventually leads to decline in glomerular filtration rate and end stage renal disease or premature cardiovascular mortality.<sup>11</sup> The exact cause of diabetic nephropathy is unknown but various postulated mechanisms are hyperglycemia, and advanced glycation products and activation of cytokines.<sup>28</sup> Diabetic nephropathy rarely develops before 10 years after the onset of disease, but striking epidemiological variations exist even in the

European countries about the incidence of diabetic nephropathy. A study from Neitherland shows that diabetic nephropathy is under diagnosed<sup>29</sup> other studies have shown that early signs of impending nephropathy appear much earlier in the shape of microalbuminuria in not only patients with poor glycaemic control but also in patients who had good glycaemic control<sup>20</sup>. Therefore screening of type 2 diabetics for microalbuminuria should begin at the time of diagnosis to retard the progression and perhaps reversion to normoalbuminuria at an early stage of disease. Once sustained microalbuminuria develops then urinary albumin excretion rate increases by 10-20% per year to overt nephropathy over a period of 10-15 years. The rate of fall of glomerular filtration rate in patients of diabetes with overt nephropathy in type 2 diabetes is variable ranging from 2–20ml/min/yr.<sup>23</sup> Therapeutic and non-therapeutic intervention can reverse the process at this stage but if untreated then will lead to end stage renal disease and cardiovascular mortality

Good evidence suggests that early treatment delays or prevents the onset of diabetic kidney disease<sup>30</sup>. The frequency of microalbuminuria in our study in type 2 DM with good glycaemic control was 8.57% as compared to 29.5% in one study and 24-34% in others<sup>12-16,20</sup>. Presence of micro albuminuria in subjects who had a comparatively good glycaemic control that is a hemoglobin A1C in the range of 6.7-7 is an alarming finding which underlines the fact that renal damage may start appearing when HbA1c crosses the line anywhere above 6.5, the latest cut off for diagnosing diabetes mellitus<sup>10</sup>. The other reasons for this finding might be that although we excluded the patients with hypertension from our study by taking blood pressure measurements initially at the time of induction as well as taking thorough history of hypertension but may be these patients had silent hypertension not yet clinically diagnosed, secondly it is found in some studies that the cause of microalbuminuria might be some non-diabetic renal diseases (NDRD)<sup>31</sup>. This calls for dealing with newly diagnosed diabetic patients with intensive and focused screening for microalbuminuria so that steps are taken to treat that in time by keeping a blood pressure in the safe range of less than or equal to 120/85, life style modifications, weight monitoring and introducing antihypertensive drugs especially ACE inhibitors or ARBs to avert proteinuria and by maintaining lipid profiles in the optimum range so that macro and microvascular complication could be averted.

Our study showed that females were major sufferers of microalbuminuria as compared to males out of the total 140 cases 04 cases were male while females were 08. Similar female dominance has been noted by other studies.<sup>20,17,18</sup> This could be because of the fact that females in our study had higher BMI than males owing to increased central obesity, this could be explained by

the fact that the purdah observing women in our society have less opportunities of exercising due to social norms of restraining to homes and repeated child birth result in increased central obesity which can lead to greater insulin resistance, many studies have linked insulin resistance and microalbuminuria<sup>27</sup>

Our study showed higher frequency of micro albuminuria in patients between 40–50 years of age. Similar results were also reported by another study<sup>19</sup> this is in keeping with the fact that, diabetic nephropathy rarely develops before 10 years. The peak incidence (3%/y) is usually found in persons who have had diabetes for 10–20 years, after which the rate progressively declines. However some studies showed diabetic patients had micro albuminuria even when the duration of diabetes was less than 11 years<sup>20,24</sup>. Which again stresses the fact that early detection of diabetic nephropathy is important so that pharmacological and non-pharmacological interventions could be done to stop the progression to end stage renal disease.

Haemoglobin A1c is a measure of erythrocyte hemoglobin glycation and reflects mean glycemic value for the previous 03 months.<sup>25</sup> This variable was also been measured in this study. Our study since was done in patients with good glycaemic control was expected to find very low incidence of microalbuminuria, but contrary to our expectations we found significant number of patients with this complications despite being with good controls of blood sugar levels over the past three months. Such results were seen in another study also which showed presence of 10% of microalbuminuria in good glycemic control (HbA1c <7) group<sup>11</sup>. This finding can be explained on the basis that either some people are more predisposed to microalbuminuria the moment HbA1c crosses the threshold of 6.5 which calls for tighter control of blood sugar levels in order to halt future nephropathy or the patients studied might be suffering from some non-diabetic cause of albuminuria as has already been found in literature search<sup>31</sup>, these causes might be genetic predisposition, socioeconomic factors, dietary patterns, covert hypertension, subclinical urinary tract infections etc for which we have to undertake further studies.

**Acknowledgement:** We thank our colleagues of Liaquat national hospital who supported us during the course of our study period

## CONCLUSION

Microalbuminuria the first sign of diabetic nephropathy can be found in DM type II patients with good glycaemic control hence Screening for microalbuminuria and HbA1c test should be done both in newly and already diagnosed type II diabetic patients to detect an early marker of renal dysfunction.

## Author's Contribution:

Concept & Design of Study: Syeda Nosheen Zehra  
 Drafting: Hamid Ali  
 Data Analysis: Shahid Karim, Farheen Fatima Zaidi.  
 Revisiting Critically: Syeda Nosheen Zehra, Hamid Ali  
 Final Approval of version: Syeda Nosheen Zehra

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

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# To Compare the Efficacy of Single Dose Oral Dexamethasone versus Multi-Dose Prednisolone in the Treatment of Acute Asthma Exacerbation

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## ABSTRACT

**Objective:** To compare the efficacy of single dose oral dexamethasone versus multi-dose prednisolone in the treatment of acute asthma exacerbation.

**Study Design:** Randomized controlled trial Study.

**Place and Duration of Study:** This study was conducted at the Department of pediatrics, Gomal Medical College D.I Khan from Sep 2015 to March 2016.

**Materials and Methods:** A total of 160 children under 12 years of age were divided in 2 groups at random, dexamethasone was given to children in A group and in group B prednisolone was given. All children were followed until 10th day after discharge to determine the efficacy of treatment in terms of relapse.

**Results:** Group A contained children having mean age  $7.53 \pm 2.23$  years & group B had children with mean age  $8.1 \pm 2.3$  years (p value 0.107). Of the whole sample, we had 65% males in group A and 55% in group B, female gender was found in 25% in group A while 45% in group B. (p 0.197). Efficacy in terms of relapse for group A was 85% while that of group B was 70%, (p value of 0.023).

**Conclusion:** The oral dexamethasone is more effective than oral prednisolone in the treatment of acute exacerbation of bronchial asthma in children below 12 years, however, we recommend more randomized controlled trials specially in various combinations with bronchodilators for the generation of solid evidence in the treatment of acute asthma.

**Key Words:** Acute Asthma, dexamethasone, prednisolone, glucocorticoid, steroid, relapse

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## INTRODUCTION

Asthma is a chronic & recurrent ailment, having significant morbidity. In 2007, 96 lac(13.1%) patients were identified as asthmatic. In which, 70% had at least one asthmatic attack in the previous 12 months.<sup>1</sup>

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The goal of treatment is to achieve control of clinical manifestation of the disease and maintain this control for prolonged period, with appropriate regard to safety and cost of treatment.<sup>2</sup> Broncho constriction is best targeted with beta-2 agonists, the airway edema and secretion that accompany an acute exacerbation respond to systemic corticosteroid therapy.<sup>3</sup>

The British thoracic society guidelines on management of asthma, recommend commencing oral prednisolone early for children presenting with exacerbations of asthma and if discharged, continuing treatment for up to three to five days.<sup>4</sup>

Oral prednisolone and dexamethasone are the currently recommended systemic steroids for acute asthma exacerbations. Dexamethasone is a long acting glucocorticoid with half-life of 36 to 72 hours and is 6 times more potent than prednisolone. Prednisolone is a short acting glucocorticoid with half-life of 18 to 36 hours.<sup>5</sup>

Studies regarding comparison of oral dexamethasone and prednisolone show that short course dexamethasone has a parental preference with better compliance,<sup>6</sup> and also more cost effective and cost saving.<sup>7</sup> In one study, 4.1% of prednisolone patients were admitted before the 2-week follow-up<sup>8</sup> and another study shows 16% in



Dexagroup needed un-planned visits on follow up ( $P = .27$ ).<sup>9</sup>

Aim of this study is to compare the efficacy of dexamethasone and prednisolone in acute asthma in terms of relapse within 10 days. This study will also help to improve drug administration, compliance, leading to decrease hospital visits, with better asthma control and parental preference for single dose steroid.

## MATERIALS AND METHODS

### Inclusion Criteria:

- Age: 2-12 years and both gender
- Diagnosed patients of asthma presenting with acute asthma exacerbation.

### Exclusion Criteria:

- Subjects with severe or life-threatening asthma (Severe respiratory distress ( $RR > 40/\text{min}$  and use of accessory muscles, agitated or drowsy, unable to speak in sentences, having loud wheeze or silent chest, not responding to usual treatment of asthma i.e. Bronchodilators and Steroids).
- Fever  $> 39.5^\circ\text{C}$
- Other medical illness (Congenital heart disease, cystic fibrosis, T.B)
- Corticosteroids use Orally in the last month

**Data Collection Procedure:** The study has been approved from hospital ethical committee of Gomal Medical College, D.I Khan. Eligible patients were enrolled in trial after taking informed consent from parents. Patients presenting to the emergency department fulfilling the inclusion criteria was randomized to either Prednisolone one tablet (2 mg/kg/day not exceeding 60 mg / day in 2 divided doses) for five days or single-dose Dexamet has one tablet (0.6 mg/kg not exceeding eighteen mg). All patients with an acute asthma exacerbation were treated according to the institution's asthma clinical care guideline. Patients were discharged after stabilization. After discharge, subjects were followed after ten days. The major conclusion is the relation between both groups for relapse. All the information was collected on a specially designed proforma (attached).

By using software SPSS the data was recorded & evaluated in the computer. For variables like age the mean and  $\pm SD$  was computed. Frequency & % was computed for the variable like relapse. The proportion of patients with relapse was compared among two study groups using chi square test. A P-value of  $< 0.05$  was considered statistically significant. The results were entered in table form.

## RESULTS

Patients of age 2-12 yrs were enrolled in the study. The sample was selected according to operational definition of acute exacerbation of Asthma and was divided in 2 groups at random. In A group 80 children was given a Dexamet has one single-dose orally (0.6 mg/kg not exceeding 18 mg) while 80 children in group B were subjected to Oral Prednisolone (1 mg/kg per dose to a maximum of 30 mg) twice daily for 5 days.

The mean age of the whole study sample was  $7.82 \pm 2.27$  years. Mean age of children in group A was  $7.53 \pm 2.23$  years while in group B it was  $8.1 \pm 2.3$  yrs. By applying T-test (p value of 0.107) the difference was insignificant statistically. (Table 1)

Children were divided in various age groups categorically. The groups made included children up to 6.00 yrs of age, from 6.01 to 9.00 yrs and from 9.01 to 12.00 yrs. The percentages of various categories are elaborated in Table 2.

After gender wise distribution of the sample, we observed that we had 65% males in group A and 55% in group B, female gender was found in 25% in group A while 45% in B group. While applying chi square test (p value of 0.197) the difference was not significant statistically. (Table 3)

**Table No. 1: Comparison of mean age of both groups (n = 80 each)**

Treatment Groups	N	Mean Age	Std. Deviation	Std. Error Mean	p-value
Oral Dexamethasone	80	7.5300	2.23598	.24999	0.107
Oral Prednisolone	80	8.1100	2.29516	.25661	

**Table No. 2: Age categories of both groups (n = 80 each)**

Age Groups in Years		Treatment Groups	
		Oral Dexamethasone Group	Oral Prednisolone Group
Up to 6.00	Count	36	20
	% within Treatment Groups	45.0%	25.0%
6.01 to 9.00	Count	24	32
	% within Treatment Groups	30.0%	40.0%
9.01 to 12.00	Count	20	28
	% within Treatment Groups	25.0%	35.0%
Total	Count	80	80
	% within Treatment Groups	100.0%	100.0%

All the children were given standard doses of the dexamethasone and prednisolone according to their treatment arms. Patients once stabilized were discharged and a follow up visit was done till the 10th day of discharge to determine the relapse. On follow up, we observed that in group A 15% of patients represented with relapse (Table 4) while in group B 30% of patients presented with relapse within 10 days after the discharge (Table 5). In this connection, efficacy of group A was 85% while that of group B was 70%. The difference was significant statistically (p value of 0.023) after using chi square test, (Table 6)

**Table No. 3: Comparison of gender between both groups (n = 80 each)**

Gender of Child		Treatment Groups		Total	p-value
		Oral Dexamethasone Group	Oral Prednisolone Group		
Male	Count	52	44	96	
	% within Treatment Groups	65.0%	55.0%	60.0%	
Female	Count	28	36	64	
	% within Treatment Groups	35.0%	45.0%	40.0%	0.197
Total	Count	80	80	160	
	% within Treatment Groups	100.0%	100.0%	100.0 %	

**Table No. 4: Frequency of relapse in group A (n = 80)**

	Frequency	Percent
Yes	12	15.0
No	68	85.0
Total	80	100.0

**Table No. 5: Frequency of relapse in group B (n = 80)**

	Frequency	Percent
Yes	24	30.0
No	56	70.0
Total	80	100.0

**Table No. 6: Comparison of efficacy between both groups (n = 80 each)**

Efficacy of Treatment		Treatment Groups		Total	p-value
		Oral Dexamethasone Group	Oral Prednisolone Group		
Yes	Count	68	56	124	
	% within Treatment Groups	85.0%	70.0%	77.5%	
No	Count	12	24	36	
	% within Treatment Groups	15.0%	30.0%	22.5%	0.023
Total	Count	80	80	160	
	% within Treatment Groups	100.0%	100.0 %	100.0%	

## DISCUSSION

Comparatively Prednisolone has short half-life (12 - 36 hours), so it needs daily intake.<sup>10</sup> After compliance steroid treatment is valuable on outpatient basis. One research has cleared that at least 7% of patients examined in a pediatric emergency department (ED) showed non-compliance in prescriptions filling.<sup>11</sup> From other study it is clear that, patients had taken the corticosteroids orally up to 64 % of the prescribed time length of treatment.<sup>12</sup> Factors for Prednisolone non-compliance includes bitter taste, Nausea /vomiting & Lengthy course of treatment.<sup>13</sup>

Dexamethasone has prolonged half-life (36 - 72 hours).<sup>10</sup> It has good oral and parenteral absorption.<sup>10</sup> In a comparative research, 2-day treatment with hydrocortisone, a dexamethasone single dose of 0.6 mg/kg caused a decreased stay at hospital in patients with asthma exacerbations.<sup>14</sup> Taste wise dexamethasone is more acceptable as compared to prednisolone inpatients with asthma exacerbations.<sup>15</sup>

The present study evaluated the efficacy of oral dexamethasone vs oral prednisolone in the treatment of pediatric acute asthma in terms of relapse rate.

Several studies relating prednisolone with dexamethasone in the management of acute exacerbations of asthma in pediatric patients are available.<sup>16-22</sup>

Three studies relating prednisolone with dexamethasone (oral) have been noted.<sup>18,19,21</sup> It is clear from these research trials that prednisolone & dexamethasone were alike in managing acute asthma exacerbations.<sup>16-21</sup>

In another study, 96 prednisone and 104 dexamethasone subjects completed the study regimen and follow-up. More patients in the dexamethasone group reported a return to normal activities within 3 days compared with the prednisolone group.<sup>23</sup>

The pharmacological properties of dexamethasone give it preference over other steroids due a shorter course of treatment, which increases compliance. Research shows that compliance to therapy causes effective asthma management outcomes.<sup>24,25</sup>

In comparison to preceding two trials, in our study greater relapse rate for dexamethasone (16%) was noted.<sup>18,19</sup> 30% relapse rate for prednisone was noted which is greater than the preceding trials. However, major difference in efficacy between the prednisone & dexamethasone was noted in our research. However, due to less number of children, we cannot ignore that there may be a slight difference in anti-inflammatory roles of prednisone & dexamethasone for the treatment of acute pediatric asthma exacerbations.

In another review by Redman et al, there are six other studies relating to dexamethasone with prednisolone, none of which provides any major difference in effectiveness for clinical feature rates, relapse rates, or Hospital admission rates.<sup>26</sup>

## CONCLUSION

In conclusion, for the management of acute asthma, the relapse rates were better between children who received Single dose oral Dexamethasone compared to multiple doses of oral Prednisolone. Advantages of Dexamethasone as reported in literature include fewer doses, reduced emesis, and a decrease in the number of school/workdays missed. Further studies locally on patient compliance may be required for developing practical recommendations for the treatment of acute asthma among children.

### Author's Contribution:

Concept & Design of Study: Ikram Ullah  
 Drafting: Sami ul Haq, Raza  
 Muhammad Khan  
 Data Analysis: Sadaqat Ali, Zahoor ul

Revisiting Critically: Haq, Mulazim Hussain  
Ikram Ullah, Raza  
Muhammad Khan  
Final Approval of version: Sami ul Haq

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

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# Post Partum Hemorrhage; Risk Factors and Management among Women Presenting to a THQ Hospital

Sara Gulbaz<sup>1</sup>, Shahnilah Zafar<sup>2</sup> and Sheeba Rehman<sup>3</sup>

## ABSTRACT

**Objective:** To evaluate risk factors of post partum hemorrhage and its management among women presenting to a tertiary care hospital.

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

**Place and Duration of Study:** This study was conducted at the THQ hospital, Indus Hospital (Manawan Campus) Lahore from January to July 2018.

**Materials and Methods:** Women presenting to the study hospital with post partum hemorrhage or developed it after admission during study period were included in this study. Retrospective data was collected regarding mode of delivery, causes of hemorrhage, treatment modalities and maternal mortality rate. Blood loss during post partum hemorrhage was estimated on the basis of visual parameters, history and signs of anemia in patients. Proper consent was taken from all patients included in this study and also from the ethical committee. All relevant data was properly documented and analyzed using Microsoft office and SPSS.

**Results:** Total 900 cases were admitted in the ward for obstetrical emergency. Out of them 2.2% cases developed post partum hemorrhage. Ages of these cases were 15 to 37 years with mean age of 25 years. Out of 20 cases having PPH, 85% were severe anemic and blood transfusion was done in them, 30% cases were critical and admitted in HDU for intensive care. One patient died despite all measures, so mortality rate was 5%. Out of 20 cases 15% were delivered in other private hospitals, 25% delivered at home and 60% delivered in the study hospital. 35% mothers underwent spontaneous vaginal delivery, in 45% cases cesarean section done and in 20% cases instrumental delivery performed.

**Conclusion:** Although post partum hemorrhage has low prevalence but it can lead to lethal complications and can be fatal. Early diagnosis and prompt management is mainstay of treatment. It can be prevented if risk factors are evaluated during pregnancy such as high parity, uterine atony, previous history of PPH or bleeding disorders, multiple pregnancies or large fetus etc.

**Key Words:** Post partum hemorrhage, Risk factors, complicated labour.

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## INTRODUCTION

Post partum hemorrhage is defined as excessive bleeding more than 500-1000ml within first 24 hours following childbirth. This is a major cause of maternal mortality worldwide. Prolonged pregnancy of more than 20 weeks is its risk factor.<sup>1</sup> According to a WHO study conducted in 28 countries; rate of post partum hemorrhage was reported as 1.2%.<sup>2</sup>

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Maternal mortality rate is high in underdeveloped and developing countries due to inadequate health facilities and skilled health professionals. In developed countries this rate is low. PPH is a major cause of morbidity and mortality in Africa and Asian countries.<sup>3</sup> It can be defined as loss of more than 500ml blood from genital tract after delivery of baby in first 24 hours is called post partum hemorrhage.<sup>4</sup> Incidence of PPH reported in various studies was around 6%, which can be different in different geographical areas depending on health facilities.<sup>5</sup> PPH causes much disturbed life for women and disease burden. Complications associated with PPH include anemia, DIC, liver or renal failure and ARDS.<sup>6,7</sup> Uterine atony is a major cause of post partum excessive bleeding. Use of uterotonic medications before child birth can reduce chances of PPH.<sup>8</sup> In this regard use of oxytocin is best to control bleeding by increasing tone of uterus as proved by a WHO report.<sup>9</sup> Causes of post partum hemorrhage are uterine tony, tissue trauma, retained tissue or thrombosis. In emergency cesarean section chances of PPH are more as compared to

elective cesarean. According to a study 76% deliveries in Pakistan take place at home.

Maternal mortality rate can be reduced 80% by improving medical care. Proper active management of third phase of labour can reduce maternal mortality rate by avoiding tissue trauma and prevention of blood loss anemia. Blood transfusion is life saving in critical situation.

In some cases having PPH, there are no risk factors. Prompt management with saving lives of mother and child is the best result of treatment moreover life of mother is superior to that of child. When bleeding is not stoppable by conservative management then surgical option can be used to stop hemorrhage to save life of the patient.

## MATERIALS AND METHODS

This is a retrospective type of study started in January 2018 and completed after 7 months duration in July 2018. This study was conducted in Indus Hospital Lahore (Manawan campus). Permission was taken from ethical committee of the hospital for conducting study. An inclusion and exclusion criteria were defined for patients.

According to inclusion criteria all patients presenting with postpartum hemorrhage to the study institution within duration of study were selected for the study. Blood loss was estimated from number of soaked gauzes, clothes and blood in drainage bag.

According to exclusion criteria those cases with secondary PPH, referred from other hospitals after 24 hours of the event and those without complete previous record were not included in this study.

All data relevant to the study was documented properly such as age of the patients, mode of delivery either at home or in hospital, SVD or via cesarean section, estimated blood loss, cause of PPH, mode of admission either through out-patient doors or COD in general ward or ICU, any history of previous abortion or PPH, parity, multiple pregnancies, oligohydromnias or polyhydromnias, induction of labor, prolonged labor and maternal outcome after management either recovered or died.

Such patients admitted to the study institution were categorized on the basis of blood loss and their condition. Those with massive blood loss and severe anemic were kept in medical ICU and others with stable condition and less severe hemorrhage were kept in general ward.

Management given to them included either single or multiple blood transfusions depending on severity of anemia, uterine massage, use of drugs to enhance uterine contraction such as oxytocin and prostaglandins and surgical exploration of uterus. All collected data was analyzed using Microsoft office and SPSS version 2017. Frequencies, percentages and P-value were

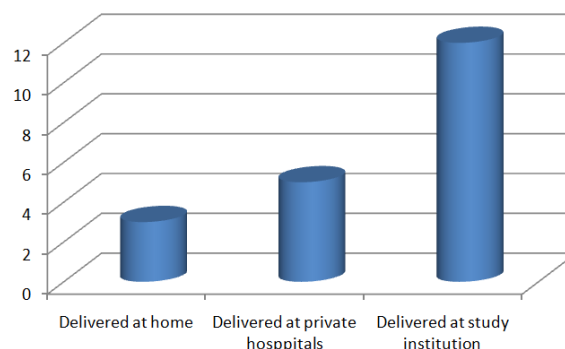
determined and results were expressed via tables and graphs.

## RESULTS

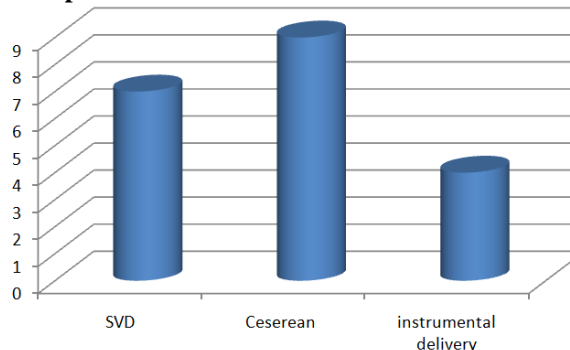
Patients admitted to gynecology and obstetrics ward of study institution during study period of one year were included in this study. There were total 900 obstetrical admissions in the ward during seven months. These cases were in reproductive age group. Out of 900 cases only 20(2.2%) cases developed post partum hemorrhage.

**Table No.1: Risk factors of Post partum hemorrhage in 20 study cases.**

Risk factors of PPH	N	% (N/20)
Parity	14	70
Age (25-40 years)	12	60
Anti partum hemorrhage	02	10
More than 3 hours delay in delivery	09	45
Unqualified birth attendants	01	05
Delivery outside of hospital	05	25
Pre-eclampsia	01	05



**Figure No.1: Place of delivery in 20 study cases who developed PPH**



**Figure No.2: Mode of delivery among 20 cases in study group which developed PPH**

Risk factors of PPH evaluated in these 20 cases were, age between 25-40 years in 18(90%) cases, high parity in 14(70%) cases, 5(25%) cases delivered outside of study hospital, 3(15%) cases delivered at private

hospitals somewhere and 2(10%) delivered at home by birth attendants, more than 3 hours delay in delivery in 9(45%) cases, history of antipartum hemorrhage in 2(10%) cases and pre-eclampsia was risk factor in 1(5%) case out of 20 cases (Table-1). Out of 20 cases 17(85%) were severe anemic and 6(30%) were admitted in medical ICU. Mean blood loss in patients with PPH was 1900ml. SVD was done in 7(35%) cases, cesarean done in 9() cases and instrumental delivery done in 4(20%) cases (Figure-2). Out of these 20 cases 5(25%) were booked and 15(75%) were non booked cases. P-value less than 0.05 were considered significant.

## DISCUSSION

Obstetric causes of maternal mortality are very common worldwide. According to a report about 0.5 million women die each year due to complications of pregnancy especially hemorrhagic cause.<sup>10</sup> Post partum hemorrhage is defined as blood loss more than 500ml in vaginal delivery and more than 1500ml in C-section, another definition says that as much blood loss which causes hypovolemia or may decrease hematocrit by 10% or blood transfusion is indicated.<sup>11</sup> According to a study conducted in Abotabad a city of Pakistan, prevalence of PPH was 35%.<sup>12</sup> Post partum hemorrhage is of two types, primary and secondary PPH. Primary PPH occurs in first 24 hours after delivery while in secondary PPH blood loss occurs after 24 hours of delivery.<sup>13</sup> According to many studies main cause of PPH is decreased tone of uterus causing hematoma in vaginal wall, tears in vagina or cervix, adherence and retention of placenta. Other causes include inversion of uterus, in this condition placenta does not detach from uterus after child birth and turns uterus inside out which can be fatal for mother. Post partum hemorrhage may lead to acute renal shut down, liver failure, DIC and acute respiratory distress syndrome. According to another study PPH is 5<sup>th</sup> most common cause of maternal mortality and according to an estimation, one women die due to PPH in every 4 minutes.<sup>13</sup> Massive blood loss leads to tachycardia, sweating and hypovolemic shock which indicates immediately blood transfusion to save life of the mother. In some cases even prior recognition of condition and despite proper management, PPH cannot be prevented and maternal mortality may occur. Medications used to enhance tone of uterus are life saving by controlling bleeding. Such medications are called uterotonic. Misoprostol is very effective in this regard but very few studies support its use and still it is controversial. According to three studies in which misoprostol was administered in home delivered and hospital delivered patients and outcome was reported satisfactory.<sup>15-17</sup> In our study risk factors of PPH and management of it was discussed. Out of 20 cases with PPH mostly needed blood transfusion due to hypovolemic shock and few of them were so critical

that they required admission in ICU. Few doctors prefer to give oxytocin as a uterotonic drug which is also effective to some extent but it is controversial as well. Blood loss in patients presenting to the hospital can be estimated by counting of number of soaked gauzes or clothes or weighing them and by fall of hematocrit and signs of anemia.<sup>18-20</sup> History of blood loss and physical examination to evaluate severity of anemia is very important in planning management.

## CONCLUSION

Post partum hemorrhage is much prevalent in Pakistan with high morbidity and mortality rate which can be prevented if risk factors are evaluated early and delivery of mothers having risk of PPH is conducted in tertiary care hospital having proper ICU care and all necessary management facilities. Major cause of PPH is decreased tone of uterus, increased parity, pre-eclampsia, large size of fetus or multiple pregnancies and previous history of PPH.

### Author's Contribution:

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Data Analysis:	Sheeba Rehman
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# Diurnal Variation of Leukocytosis and its Prognostic Significance in Head Trauma in Local Population

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## ABSTRACT

**Objective:** To study the Predictive value of leukocytosis in minor, moderate and severe head trauma.

**Study Design:** Prospective and analytical study.

**Place and Duration of Study:** This study was conducted at the Department of Physiology, B.M.S.I in Accident and Emergency, ICU of Neurosurgery Department (ward -16) JMPC Karachi Pakistan from January 2009 to January 2011.

**Materials and Methods:** 90 patients of head trauma were included, after taking complete history from the conscious patients and from the attendants of unconscious patients. Glass Coma Score were observed immediately with Glass Coma Score and blood sample was taken for white cell count with hemocytometer (Neubaur chamber), peripheral smear were prepared at the spot for differential leukocyte count within the time.

**Results:** 90 patients of head trauma of age 16 to 70 years were included of either sex. Statistically the mean leukocyte count revealed that significantly higher as compared to minor and moderate ( $p < 0.001$ )

**Conclusion:** On admission, white blood cells (WBC) count exceeding 19000/ mm<sup>3</sup> has a predictive as well as value for poor Glasgow coma scale (GCS) and serves as a significant parameter of severity of injury and predictor neurological out coma in patients with moderate and severe head injury in local population.

**Key Words:** White Blood Corpuscles, Glasgow coma score, Head trauma

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## INTRODUCTION

In multisystem trauma, the head is the most frequently injured part of the body. The incidence of closed head injury is estimated to be 200 per 100,000, totaling more than half a million patients annually. About 80% of head injured patients are classified as mild, approximately 10% have moderate to severe, head injury that requires significant resources for management. Traumatic brain injury (TBI) is a major public health problem both in the United States and abroad, with over one and half million American sustaining a TBI annually (Valadka, 2000)<sup>1</sup>, with a lethal

outcome in 56,000 cases (McArthur et al., 2005; Schmidt et al., 2005)<sup>2</sup> and is the most frequent cause of deaths in young adults (Shlosberg et al., 2011)<sup>3</sup>. As developing countries become increasingly motorized, this is only set to increase (Kossmann et al., 2007)<sup>4</sup>.

The majority of traumatic brain injuries are considered mild and primarily the result of motor vehicle crashes and falls (Jager et al., 2000; Finfer and Cohen 2001; Bazarian et al., 2005; Myburgh et al., 2008; Wu et al., 2008)<sup>5,6,7,8</sup>. The World Health Organization (2004)<sup>9</sup> reports on road traffic injury prevention, found that by 2020, road traffic accidents would be within the top three leading causes of the global burden of disease, ahead of HIV and tuberculosis. The aims of current research are to apply scientific discoveries in basic science into the clinical level hoping to provide measures that predict outcome and to decrease the mortality rate in human (Keramiris et al., 2008)<sup>10</sup>. TBI (Traumatic brain injury) can now be considered a neuro inflammatory condition of CNS. Trauma to the brain results in rupture of the blood brain barrier (BBB), effect on vascular permeability leading to accumulation of leukocytes from the systemic circulation, which themselves release pro-inflammatory cytokines, cytotoxic proteases and reactive oxygen species, edema is limited by the cranium, but have devastating effects. Brain swelling occurring in turn initiating the immune functions of native glia (Lucas et al., 2006<sup>11</sup>; Juurlink,

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2000; Lenzlinger et al., 2001; Morganti-Kossmann et al., 2001 & 2002; Morganti et al., 2002; Hurley et al., 2002; Fee et al., 2003; Dietrich et al., 2004<sup>12</sup>; Morganti-Kossmann et al., 2005; Streit, 2005)<sup>13,14</sup>. The acute phase response is also characterized by a leukocytosis upon admission. Therefore, it is possible that an increase in the white blood cell (WBC) count might serve as an additional diagnostic and prognostic indicator in head injury. (Rovalis and Kotsou ;2001)<sup>15</sup> Chemokines represent a class of cytokine-like Immunomodulators that are gaining attention as potential therapeutic targets for various inflammatory diseases (Jin et al., 2008; Viola and Luster, 2008)<sup>16</sup>. The severity of head injury is most commonly classified by the initial postresuscitation GCS Score, which generates a numerical summed score for eye, motor and verbal abilities. Traditionally, a score of 13 -15 indicates mild injury, a score of 9-12 indicates moderate injury and score of 8 or less indicates severe injury. (Ghajar 2000; Stein, 2001; Finfer and Cohen 2001)<sup>17,18</sup>. The present study was designed to assess the predictive value of leukocytosis in minor, moderate and severe head trauma.

## MATERIALS AND METHODS

It was prospective and analytical study in Accident & Emergency, ICU of Neurosurgery Department (Ward-16), JPMC, Karachi from August 2009 to August 2010. 90 patients of Head trauma, of Age 16 to 70 years of either sex were included after taking complete history, from the conscious patients and from the attendants of unconscious patients. Glasgow Coma Score were observed immediately with the Glasgow coma scale, and blood sample was taken for laboratory analysis especially for white blood cells count with hemocytometer (Neubaur Chamber).

Lastly all the findings were recorded in the proforma specially designed for this purpose.

Glasgow Coma Scale (GCS) is a neurological scale which aims to give a reliable, objective way of recording the conscious state of a person, for initial as well as subsequent assessment. A patient is assessed against the criteria of the scale, and the resulting points give a patient score between 3 (indicating deep unconsciousness) and either 14 (original scale) or 15 (the more widely used modified or revised scale).

The patients were grouped according to Glasgow coma score. Each group includes 30 patients.

Group I 14 to 15 GCS	Group II 9 to 13 GCS	Group III 3 to 8 GCS
Minor Head Trauma Patients	Moderate Head Trauma Patients	Severe Head Trauma Patients
n=30	n=30	n=30

Total Leukocyte Count (TLC) was done blood was sucked up into WBC pipette up to 0.5 mark from collected sample. This blood was diluted with Turk's solution up to mark of 11 (dilution 1:20). The pipette

was allowed to stand for 5-10 minutes to hemolyze erythrocytes. First 3 to 4 drops were discarded and then the Neubaur's counting chamber was charged. Under the high power lens 1 x 40, 16 large squares at each corner of chamber were counted (total of 64 squares).

### Formula for total leukocyte count:

$$\text{TLC} = \frac{\text{Number of cells counted} \times 160 \times \text{dilution}^2}{\text{No. of squares counted (64)}}$$

## RESULTS

The results of this study showed the significant difference ( $p < 0.001$ ) in the mean value of total leukocyte count in severe head trauma immediately as compared to moderate and minor head trauma.

A significantly higher mean immediate soon after trauma total leukocyte count was observed in severe head trauma patients as compared to moderate and minor head trauma ( $p < 0.001$ ) results were observed.

Statistically, the mean total leukocyte count was significantly higher in moderate as compared to minor head trauma cases ( $p < 0.001$ )

The mean total leukocyte count was also significant when comparing severe head trauma patient to minor head trauma patient ( $p < 0.001$ ).

**Table No.1: Comparison of Mean Total Leukocytes Count in Patients of Severe and Moderate Head Trauma :**

According to GCS score	Severe head trauma (3-8)	Moderate head trauma (9-13)
No. of patients	30	30
Mean TLC count	19030.70*	13230.00
S.D	2006.60	738.10
SEM	365.350	134.750

**Table No.2: Comparison of Mean Total Leukocytes Count in Patients of Moderate and Minor Head Trauma:**

According to GCS score	Moderate head trauma (9-13)	Minor head trauma (14-15)
No. of patients	30	30
Mean TLC count	13230.00	12388.00
S.D	738.10	508.83
SEM	134.750	93.00

**Table No.3: Comparison of Mean Total Leukocytes Count in Patients of Severe and Minor Head Trauma:**

According to GCS score	Severe head trauma (3-8)	Minor head trauma (14-15)
No. of patients	30	30
Mean TLC count	19030.70*	12388.00
S.D	2006.60	508.83
SEM	365.350	93.00

\*Significantly higher as compared to minor and moderate ( $p < 0.001$ ) \*\*Significant Correlation ( $P < 0.001$ )

## DISCUSSION

Akkose et al (2003)<sup>19</sup> performed a retrospective study evaluating 713 blunt trauma patients and found a positive correlation between WBC count and severity of injury. The present study correlates with the above study in terms of severity of head trauma.

Chang et al (2003)<sup>22</sup> prospectively studied 882 patients admitted to a Level 1 trauma center evaluating admission on the basis of race, injury mechanism, blood pressure, GCS, WBC and patients requiring early transfusion versus no early transfusion. He found that only ISS greater than 15, GCS  $\leq 8$ , and white race were associated with an increase in white blood cell count. The results of the present study are in agreement with the results of above said study. However, the main difference is of the population.

Rovlias and Kotsou (2004)<sup>23</sup> has used a Classification and Regression Tree (CART) Technique and employed it in the analysis of data from 345 patients with isolated severe brain injury and a total of 16 prognostic indicators were examined to predict neurological outcome. The results indicated that the GCS was the best predictor of the outcome with regard to the other data, not only most widely examined variables such as, pupillary reactivity or computer tomographic findings proved to be strong predictors, but less commonly applied parameters, indirectly associated with brain damage, such as leukocytosis were also found to correlate significantly.

The results of above study also supported the results of present study. Gurkanlar et al. (2009)<sup>24</sup> conducted a retrospective study of WBC count in

59 patients with severe, moderate and minor craniocerebral injury in emergency department. They compared WBC count with GCS scores, in which GCS scores highly correlated with WBC count. There were also statistically significant differences between severe and moderate, severe and minor and moderate and minor patients ( $P < 0.01$ ). The results of present study are in agreement with the above said findings.

The results of present study are also in agreement with the study conducted by Bhatia et al. (2004), who in their prospective study observed 116 patients (77 male and 39 female) of stroke (within 72 hours of onset). After clinical evaluation, neuroimaging and blood investigation, high total leukocyte count and ESR at admission correlated significantly with an undesirable outcome during the initial 30 days and logistic regression analysis demonstrated that a low GCS score and total leukocyte count correlated with death. Matis and Birbilis (2009)<sup>25</sup> observed in their retrospective study, 60 patients with head trauma who had been admitted to a ICU of tertiary care hospital and undertaken to explore the possible correlation between the GCS and outcome. Their results suggested that GCS is limited to predict the outcome in

head injured patients particularly when it is used as sole predictor in mild or moderately severe head injury. The results of present study in terms of GCS are totally in accordance with the results of above study.

Santucci et al. (2007)<sup>26</sup> studied two groups of head injured patients by comparing the initial WBC in significant injury and without significant injury in Emergency Department, they correlate the findings with the degree of injury using 'Injury Severity Score' (ISS) in both groups and found that WBC count could be used as a predictor of serious injury. Further, they reported difference in mean WBC count between the two groups and found that the difference was statistically significant ( $P < 0.001$ ). A positive relationship between ISS and WBC also was found, although, the association was weak, while the WBC had moderate discriminatory capability for serious injury. However WBC count could not in isolation, rule in or rule out serious injury, but remarking the WBC on presentation to the Emergency Department could be used as an adjunct for making disposition decisions. The results of present study are partially in agreement with the above said study.

Asadollahi et al. (2010)<sup>27</sup> evaluated the significance of leukocytosis, as a best predictor of mortality and morbidity not only in head trauma patients, but also in various other diseases. White Cell Count (WCC) exceeding  $11 \times 10^9/l$  is widely considered to be an indicator of infection or inflammation and other clinical situations such as, trauma and exercise. The above findings also collaborates the results of present study.

## CONCLUSION

It is therefore, concluded that on admission, white blood cell (WBC) count exceeding  $19000/mm^3$  has a predictive value for poor Glasgow Coma Scale (GCS) score and could serve as a significant parameter of severity of injury, and as an additional predictor of neurological outcome in patients with severe head injury. WBC count could be used in patients with moderate and severe head injury to predict outcome in our local population.

### Author's Contribution:

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# Conventional Cavity Preparation Versus Atraumatic Restorative Treatment (ART) Technique: A Clinical Evaluation Revealing the Success of Glass Ionomer Cement (GIC) in Mandibular Molars Having Class 1 Carious Lesions

Conventional Cavity Preparation Versus Atraumatic Restorative Treatment

Dilawar Sultan, Zuhair Arif, Kashif Nayyar, Anas Muhammad, Syed Moiz Ali and Saad Zafar Rana

## ABSTRACT

**Objective:** To assess and evaluate how successful is glass ionomer cement restorations while tooth being restored either by the conventional cavity preparation using air turbine or the atraumatic restorative treatment (ART) technique.

**Study Design:** Descriptive study.

**Place and Duration of Study:** This study was conducted at the Department of Operative Dentistry, Akhtar Saeed Medical College Lahore from October 2018 to March 2019.

**Materials and Methods:** A total of 161 patients was selected who received the high viscosity glass ionomer restorations in mandibular molars having Black's class 1 carious lesion in mandibular molars. 71 patients received the restorations with the conventional cavity preparation while 90 patients were treated using the ART technique. All the patients were having the age between the 25-40 years. Success ratio of the restorations was scored according to the WHO criteria having 0-8 score. The data was analyzed using the chi square tool in order to test the hypothesis.

**Results:** The Chi square statistic value obtained with degree of freedom 1 (df) is 1.1949. The result is not significant at  $p < 0.05$ . So the null hypothesis is not rejected.

**Conclusion:** There is no difference in terms of restoration success in mandibular molars having class 1 carious lesions prepared either by atraumatic restorative treatment technique or using air turbine and restored by high viscosity glass ionomer cement.

**Key Words:** Atraumatic restorative treatment, Air turbine Class 1 cavity, Tooth preparation, Chemical bond, Remineralization

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## INTRODUCTION

The word caries in dentistry refers to the disintegration of the tooth tissue due to bacterial action leading to cavitations or defect in the teeth. This caries can be prevented by a number of prophylactic measures including the improvement of oral hygiene, and uptake of certain remineralization agents like Casein Phospho-

peptide-Amorphous Calcium Phosphate (CPP-ACP), combination of CPP-ACP and fluoride, tri calcium phosphate etc. these agents arrest the caries since its inception. But when there is an actual loss of tooth structure leading to cavitation. It might be troublesome for the patient and needed to be restored at earliest. However whatsoever the cause of the defect is present, it needs special protocol to restore. It involves removal of all the diseased portion of the tooth making it bacteria free and then restoration of that very lost portion. As far as the removal of the diseased portion is concerned, currently a number of techniques are available like air turbine rotary system, air abrasion, lasers, ultra sonic instrumentations and fusty atraumatic restorative treatment (ART) techniques.

The method of cavity preparation devised by G V Black long ago is still in practice and followed widely. It briefs all the steps of cavity preparation. Extension for prevention is an important step of this cavity preparation method. However, due to current research in dentistry and with the innovation of certain modern

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restorative materials, the main focus is primarily given to preserve what is present as much as possible. Here the difference lies between the older and the newer concept. When we want to conserve the tooth, only the diseased portion is removed. In addition this minimally invasive technique of ART can equally be employed to get the desired outcome. In this technique a hand instrument is used manually to remove the carious part and then filled with the appropriate restorative material. All the movements are well controlled even in the deep lesions. While in case of conventional cavity preparation with the air turbine, skating on thin ice sometimes may lead to unnecessary tooth removal. All the preparation guidelines are followed in addition to the caries removal. Some portion of the sound tooth structure can be removed if needed to have a comprehensive design. The development of the high viscosity glass ionomer cement (GIC) has made it possible to restore the teeth in this way. Clinicians could see the handwriting on the wall when going to start the procedure. An exemious key factor of these cements is their ability to make the chemical bond to the tooth structure and release the fluoride ions over prolonged time.<sup>1</sup> These are very biocompatible and having good coefficient of thermal expansion which is close to the teeth.<sup>2</sup> There is an ionic exchange that happens between the tooth and material.<sup>3</sup> The release of the fluoride ions not only makes the teeth stronger but also prevents the recurrent caries.<sup>4,5</sup> Moreover it has anti bacterial properties having the potential to remineralize the tooth.<sup>6,7</sup>

## MATERIALS AND METHODS

This descriptive study was conducted at Department of Operative Dentistry, Akhtar Saeed Medical College Lahore from 1<sup>st</sup> October 2018 to 31<sup>st</sup> March 2019.. A total number of 161 patients were selected. These were divided into two groups randomly. All the patients had good oral hygiene having all the mandibular molars including the third molar. The patients had class 1 carious lesion in any of the mandibular molars. The radiograph was taken before initiating the operative procedures and complete dental and medical history was recorded. 71 patients were treated by the conventional cavity preparation with air turbine while 90 patients got the ART treatment approach. In this technique only the dental excavator was used to remove the caries. After the cavity preparation the material was mixed according to manufacturers' instructions and was placed in the cavity following the isolation. We used the high viscosity glass ionomer cement for permanent restorations. All the cavities were evaluated at three and six months interval and were evaluated using the WHO criteria having 0-8 score for the restoration success.<sup>8</sup> The restorations having the 0-2 scores were declared as successful while 3-6 were dropped in the failures. Score 7 and 8 were given to the exclusion of the cases. We assumed a null hypothesis (Ho) which says that there is no difference between the methods of cavity preparation on the success for the restoration. The

alternative hypothesis (Ha) says that there is difference between the modes of cavity preparation and the success of the restoration. Chi square test was applied to judge the outcome and to test the hypothesis. The level of significance is 0.05.

## RESULTS

There were 95 male patients and 66 were female patients (Table 1). The Chi square statistic value we got with degree of freedom 1 (df) is 1.1949. The p-value is 0.27434. The result is not significant at  $p < 0.05$  (Table 2).

**Table No.1: Frequency of genders in both groups**

Gender	Conventional Method		ART Method	
	No.	%	No.	%
Male	55	34.2	40	24.9
Female	35	21.7	31	19.2

**Table No.2: Frequency of successful and failure of patients in both groups**

Method	Successful		Failure	
	No.	%	No.	%
Conventional Method	57	35.5	14	8.6
ART Method	78	48.5	12	7.4

## DISCUSSION

A unique feature of the glass ionomer cement is its capability to bond with the tooth structure. There is no other cement available that makes bond with the tooth structure. The historic back ground reveals that zinc polycarboxylic cement was initially formulated in which the poly acrylic acid was used. It was invented by Dennis Smith in 1963.<sup>9</sup>

The recently used glass ionomer is a later invention with some modifications. Since amalgam is more popular restorative material yet it always remained a hub of controversy among the clinicians having different school of thoughts regarding the mercury toxicity. The currently available glass ionomer cements (GICs) have the two components i.e. powder and liquid. On mixing these together an acid base reaction occurs that leads into precipitation in the form of gel that hardens within a few minutes. The chemical bond type that is formed is the covalent bond which is stronger than other types of bonds. There is also a preparation named resin modified that has been marketed exclusively these days. This modification has an improved strength and bonding. Our objective revolves around the basic theme of chemically bonding to the tooth structure and the mode of tooth preparation. In our study total 71 teeth were prepared with conventional air turbine preparation while 90 teeth were prepared with the help of atraumatic method using the hand excavator only. 57 teeth were declared as successful in the conventional preparation while 78 teeth were successful in the atraumatic restorative preparation. The high viscosity glass ionomer cement

has even the same failure rate as compared to the amalgam in the posterior permanent teeth that gained ART approach for the glass ionomer restoration, according to work of Mickenautsch.<sup>10</sup> This result corresponds to our research work that the success ratio between the two modes of preparation is almost same. Not only in the glass ionomer, these minimally invasive technique has also proved to be beneficial for the increased micro tensile bond strength for the single bottle self etch adhesive bonding on the dentine according to work of Naik.<sup>11</sup> This is also in accordance to our work in terms of success rate. It has also been recommended that the older patients should be provided with the minimally invasive technique to preserve the naturally present tooth in order to maintain the maximum permanent teeth.<sup>12</sup> This is in fact responsible for the longer longevity as well.

Whenever we take the clinical aspect of the diseased tooth, it is also important to consider that the portion of the tooth that is healthy and caries free is more important as compared to the diseased one which is to be removed. Currently invented materials have more potential towards the micro and macro mechanical retentions for the restorations. The all new modern concepts incline towards the preservation of what is available instead the extension for prevention. This atraumatic restorative technique has also been vital in the dental treatments of children. There is less chance of fear, non cooperation by the child, less anxiety and preservation of maximum bulk of tooth tissue.<sup>13</sup> There is handsome clinical evidence that the ART approach using the high viscosity glass ionomer cement has the equal acceptable effectiveness even in comparison to the bulk filled resin composites in the posterior teeth. According to Cruz Gonzalez the conventional tooth preparation has a more successful rate and is highly significant, however the ART approach has also been found to be equally effective having the 81% of survival rate during the whole study period. Although a number of restorative materials are present in the market for the ART approach yet the low priced materials may have certain shortcomings. Also the other materials have a distinct physical and mechanical properties.<sup>14</sup>

## CONCLUSION

The ART technique of cavity preparation being a steal in the mandibular molars with class 1 cavity is no longer has a significant difference in terms of success rate as compared to successful restorations prepared by conventional cavity preparation method. In our work both methods went smooth sailing producing a fructified successful ratio.

### Author's Contribution:

Concept & Design of Study: Dilawar Sultan  
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# Utilization of Keystone Flaps in High Voltage Electrical Burns

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## ABSTRACT

**Objective:** This study aims to describe the use of Keystone flaps in patients with high voltage electrical injuries where local flaps were a possibility.

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

**Place and Duration of Study:** This study was conducted at the Bolan Medical Complex Hospital and Jilani Hospital Quetta, Pakistan from April 2013 to August 2015

**Materials and Methods:** A total of ten patients with eleven high voltage electrical injury wounds reconstructed with keystone flaps were identified. Variables noted were patient demographics, comorbid conditions, size and location of defect, type of keystone flap used, and complications noted. SPSS 14 was used to note the variables. No statistical test applies to this study.

**Results:** Eleven defects in ten patients were reconstructed with Keystone flaps. Eight of the defects were on lower extremity, two on upper extremity and one on abdomen. The most commonly employed flap was Type IV keystone flap in six patients, Type II A in two patients, Type III in one and Type II B in one patient. No total flap failures were noted. One flap suffered distal one cm flap loss but after debridement, direct closure was obtained. Two patients had wound dehiscence requiring resuturing.

**Conclusion:** This case series demonstrated the safety, reliability and applicability of Keystone flaps in selected defects secondary to high voltage electrical injury.

**Key Words:** Keystone Flap, High voltage electrical burn, local flaps

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## INTRODUCTION

High voltage electrical injury is a devastating injury as it affects not only the skin but also the muscle, nerves and vessels and thus is a major cause of morbidity and mortality<sup>1</sup>. Usually, it is work related injury in young individuals. It also happens as a result of negligence in third world countries, when common people try to gain illegal access to the cities' electrical grid work<sup>2</sup>. Electrical burns are either flash, flame or contact burns or their combination<sup>3</sup>. The severity of burn is dependent on source contact area entry and exit points. 80% of entry wounds occur in upper extremity while 70% of exit wounds occur in lower extremity. Amputation rates vary between 10% to 68%<sup>4,5</sup>.

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To preserve important structures and function of limb, early debridement and coverage with vascularized tissue is rule<sup>6,7</sup>.

Flap coverage is the best method as electrical injuries are full thickness burns and wounds need coverage of vital structures and exposed bone. As a rule, if local tissue is available, local flaps are preferred<sup>8</sup>. However, certain wounds like around the wrist are so large and extensively damaged that they demand distant or free tissue transfer as a coverage option<sup>9,10</sup>.

Keystone perforator flaps were first described in 2003 by Behan<sup>11</sup> and has now been used in reconstruction of wounds from head to toe<sup>12,13</sup>. Their easy elevation requiring minimal training, short operative time, minimal postoperative care and like with like replacement characteristics have made them a useful tool in the armamentarium of constructive surgeon. The purpose of this retrospective case series is to document its use and safety in selected defect secondary to high voltage electrical injuries. This is the first documented series in patients with high voltage electrical injuries.

## MATERIALS AND METHODS

All case records of patients presenting with electrical injury and where keystone perforator flap was used as primary mode of reconstruction were reviewed using a data collection protocol. The patients were operated at Bolan medical complex hospital and Jilani hospital



Quetta, Pakistan from April 2013 to August 2015. Variables noted were patient demographics, comorbid conditions, size and location of defect, type of keystone flap used, and complications noted. SPSS 14 was used to note the variables. No statistical test applies to this study.

## RESULTS

A total of ten patients with eleven high voltage electrical injury wounds reconstructed with keystone flaps were identified (Table 1). All of them were males. Average age was 15 to 45 years with mean of 26 years. Only one patient was smoker and had hypertension too. None of other patients had any comorbidities. All patients had other injuries as well and this was not the only procedure done in those patients. Most of the defects were on lower extremities (n=8), followed by upper extremity (n=2) and abdomen (n=1). In case of lower extremity, five defects were around knee, two on anterior middle part of leg and one on dorsum of foot. In upper extremity wounds, one wound was in axilla and one was a cubital fossa wound. The trunk wound was in the right lower quadrant. Type IV was the most common keystone flap used (n=6) followed by type II A (n=3), type III in one and type II B in one patient. All the knee defects were reconstructed by type IV flaps, anterior leg and axillary defects by type II, abdominal defect by type II and elbow defect by type III flaps. Complications were observed in 27% of patients. Partial flap necrosis was observed in one patient that was managed by skin grafting and wound dehiscence in two patients, which required secondary suturing. No total necrosis of flap was observed.

### Case examples:

**Case 1: (Patient # 2)** is a 45 years old patient with High voltage electrical injury of right forearm leading to amputation and contact full thickness burn of right axilla. After debridement, Type II A flap designed and incised till the fascia. Deep fascia was also divided to get enough movement of the flap. Flap survived completely with good range of motion of shoulder joint afterwards.

**Case 2: (Patient # 4)** is a 28 years old patient with high voltage electrical injuries of scalp and two wounds on knee joint. Scalp wound was managed by scalp rotation flaps with skin grafting of donor site while larger wound (9.5cm x 8cm) around knee with exposed patella was covered by type IV keystone flap with proximal portion undermined. Knee was kept in splint for two and half weeks and sutures removed after three weeks. Knee joint had full range of motion, but sutures marks left ugly scarring.

**Case 3: (Patient # 7)** is 30 years old male with late presented contact full thickness burn secondary to high voltage electrical injury to his Right knee. Size of wound was 8 cm x 7.5 cm. Wound was marked as elliptical to design keystone flap and proximal portion

of flap elevated. Donor site of flap was primarily closed.



**Figure No.1: (Case 1: Patient # 2; Pre op, Per op and one month post op)**



**Figure No.2: (Case 2: Patient # 4; Pre op, per op, one month post op)**



**Figure No.3: (Case 3: Patient # 7; Pre Op and Post Op)**

**Case 4: (Patient # 9)** is 24 years old male with high voltage contact burn resulting in (7 cm x 5 cm) wound on tibia and a small wound proximally. Although wound could be skin grafted we designed a keystone flap and incised a type II-A flap dividing the fascia and were able to close the donor site. Flap on third day showing complete survival.



**Case 5: (Patient # 10)** is a 6 cm x 4 cm wound on dorsum of foot. Type IV flap elevated but we were unable to approximate donor site primarily, so it was skin grafted. Distal portion underwent necrosis that was managed by debridement and primary closure.



**Figure No.4: (Case 4: Patient # 9; Pre Op, Per Op and Post Op)**



**Figure No.5: (Case: 5: Patient # 10; Pre op, Per op and one month post op)**

**Table No.1: Electrical injury wounds reconstructed with keystone flaps in patients**

Patient #	Age	Gender	Defect			Type of flap used	Complications		
			Location	Nature	Size in cm		Total flap loss	Partial flap loss	others
1A	28	Male	Right middle leg	Tibia visible	7*3.5	2A	None	None	
1B	28	Male	Right lower abdomen	Full thickness	5.5*5	2B	None	None	Wound dehiscence
2	45	Male	Right axilla	Full thickness	7*3.5	2A	None	None	
3	21	Male	Left knee	Patella visible	7*5	4	None	None	
4	21	Male	Left knee	Patella visible	8*8.5	4	None	None	Poor scarring
5	15	Male	Left elbow	Full thickness	8*5.5	3	None	None	
6	20	Male	Left distal thigh	Full thickness	7.5*5	4 with skin graft	None	None	
7	24	Male	Right knee	Full thickness	6*5	4	None	None	
8	27	Male	Right knee	Exposed knee	15*9	4 with skin graft	None	None	Delayed healing
9	25	Male	Left distal leg	Tibia visible	6*3.5	2A	None	None	
10	30	Male	Right dorsum of foot	Visible tendon	5*3.5	4 with skin graft	None	Distal one cm	

## DISCUSSION

It is obvious from our study that keystone flap is useful for selected wounds that have resulted from high voltage electrical injury. Although keystone flap usage in full thickness burns has been reported<sup>14</sup> but this is

first case series documenting its usage in high voltage electrical burns. High voltage electrical burns are usually full thickness burns mainly around joints with a high amputation rate. When extremity is salvageable, these wounds require complex reconstructions, so keystone flap is useful only when local tissue is

available. It is useful only for small exit wounds in lower extremity or around the joints. Smaller defects on legs can be reconstructed by type I or II flaps<sup>15,16</sup> but knee defects are difficult to approximate by type I or II flaps<sup>17</sup>. Type IV flaps are best suited for this purpose, but their design is technically demanding and require a bit of thought process<sup>15</sup>. Whenever possible, proximal portion of flap should be elevated as distal portion is known to be supplied by perforators from around the knee anastomosis. It is essential to keep the leg extended by a splint as there is significant tension during closure. We have also found use of horizontal mattress sutures better for skin closure as advocated by Behan<sup>17</sup> than skin staples, but they leave ugly suture marks when removed after three weeks. We have used type IV keystone flap for very large defect around knee but with skin grafting of donor site. These wounds would have otherwise required bilateral gastrocnemius flaps or free flaps. However, it has the obvious advantage of not sacrificing a functional muscle for knee coverage, shorter operative time and less technicality when compared to a free flap.

When reconstructing leg defects, keystone flaps are superior to bipedicle flaps because of its vascularity<sup>18</sup>, possibility of future usage, variability of usage as different types<sup>16</sup>. However, it is not useful for large defects and its arc of rotation is limited<sup>19</sup>. These two limitations must be kept in mind before embarking in usage of this flap. Perforator flaps are another option in leg defects, but they are tedious, technically demanding, and more time consuming when compared to keystone flaps<sup>13</sup>. We have observed as mentioned in literature<sup>13</sup> the designing and planning more difficult and artistic than elevation of flap that is straight forward and most complication arise because of the poor designing.

Partial flap necrosis was seen when type IV flap was attempted to cover dorsum of ankle defect with flap from dorsum of foot. We were not able to close the donor site primarily and skin grafted it. However, after debridement, wound approximation could be achieved. This shows that keystone flaps are not a good option for reconstruction of medium sized defects of anterior ankle and distant flap like distally based sural flap may be a better option for these defects.

As most of our patients were young and all of them were Asians, no effect of skin type on vascularity of flap was observed. This has also been documented previously<sup>13</sup>. However, age and location of defect were the two precluding factors in getting the skin laxity required for usage of type I or type II flaps. It is not achievable; Type III or Type IV flaps will be needed. We elevated initial flaps as mentioned by Behan using blunt dissection to preserve lateral vessels and nerves entering flap, however later, we used diathermy to dissect down to fascia sacrificing these vessels and found no detrimental effect on vascularity of flap. This has been observed by others as well<sup>12</sup>. We have not

used drains in any of our patients and think if hemostasis is secured intraoperatively, no drains are necessary.

This is a retrospective, small case series documenting reconstruction of high voltage contact burns with keystone flaps. We know these limitations and purpose of presenting this is to show that keystone flap is a possibility in high voltage burns in selected patients. This should be interpreted in this context.

## CONCLUSION

This case series documents the use of keystone flaps in full thickness wounds of high voltage electrical injury in selected patients. It is the availability of local tissue that allows usage of this flap while location and laxity of tissues determine the type of flap used for coverage. This study confirms that keystone is highly versatile and technically straight forward reconstructive option for wounds from head to toe.

### Author's Contribution:

Concept & Design of Study:	Faisal Ashfaq
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# Frequency of Infertility, Hirsutism and Acne in Patients with Polycystic Ovarian Syndrome and their Association with Body Mass index: A Cross Sectional Study

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## ABSTRACT

**Objective:** To determine the frequency of infertility, hirsutism and acne in patients of PCOS and compare it with the body mass index(BMI) of the subjects.

**Study Design:** Cross-sectional, descriptive study.

**Place and Duration of Study:** This study was conducted at the Outpatient Department of Obstetrics and gynecology, Mardan medical Complex Teaching Hospital from January 2017 to October 2017.

**Materials and Methods:** This study was conducted on 250 patients of Polycystic Ovarian Syndrome. Frequency of infertility, hirsutism and acne was compared with the body mass index(BMI). Diagnosis of Polycystic Ovarian Syndrome was done on the basis of 2003 Rotterdam diagnostic criteria. FerrimanGallwey score was used for assessment of hirsutism and WHO cut-offs of Body Mass Index modified for Asian population was used for assessment of Body mass index.

**Results:** Of the total 250 patients with Polycystic Ovarian Syndrome, the mean age was  $25.63 \pm 4.44$  years and the mean BMI was  $30.12 \pm 6.63$  Kg/m<sup>2</sup>. The frequency of infertility, hirsutism and acne was 64 % (n=151), 72.8 % (n=182) and 32 % (n=80) respectively and all had a statistically significant association with obesity. The frequency of obesity in those with infertility, hirsutism and acne was 80.6 %, 89.02 % and 90 % respectively.

**Conclusion:** Hirsutism, infertility and acne were significantly common in patients with Polycystic Ovarian Syndrome and most of the patients were pre-obese as per WHO cut-offs of Body Mass Index for Asian population.

**Key Words:** Infertility, hirsutism, Acne, Body Mass Index, Polycystic Ovarian Syndrome

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## INTRODUCTION

Polycystic ovary syndrome (PCOS) is a common endocrinopathy of reproductive age women<sup>1, 2</sup>. The prevalence of PCOS in women of reproductive age varies with the criteria used for its diagnosis. The reported prevalence ranges from as low as 5-7%<sup>3</sup>, based on the original 1990 US National Institutes of Health (NIH) diagnostic criteria.

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Using the broader 2003 Rotterdam diagnostic criteria now endorsed by the NIH and accepted internationally, the prevalence of PCOS ranges from 5.5% to 19.9%<sup>5</sup>.

The commonly reported associated problems include amenorrhea or oligomenorrhea, hirsutism, obesity, acne, androgenic alopecia and reproductive disorders<sup>6</sup>. PCOS however; is not a disease exclusive to fertility and adolescence period; rather it can be associated with varying effects on a person's life.

Women with PCOS commonly suffer from menstrual disturbances including amenorrhea and oligomenorrhea. Whereas 31% women with PCOS have regular menstrual cycle, 86%--91% have oligomenorrhea and 31%--40% have amenorrhea<sup>7</sup>. The menstrual abnormalities mainly contribute to infertility in the affected women, including both primary and secondary infertility. In large number of women with polycystic ovary syndrome, 50% present as cases of primary infertility and 26% present as secondary infertility<sup>8</sup>.

Over 80 % of women with PCOS exhibit androgen excess. Hyperandrogenism commonly presents in the form of hirsutism that affects up to 71% of women with PCOS. In general population, the frequency of

hirsutism ranges from 6%-15% with appropriate differences according to geographic location and ethnicity<sup>9</sup>. Hirsutism is particularly more severe in patients with abdominal obesity<sup>10</sup>. Ferriman-Gallwey scoring system<sup>11</sup> is usually used for the evaluation of hirsutism. It assesses hair growth at the seven sites of the body: chin/face, upperlip, back, chest, arms, abdomen and thighs. A zero score indicates absence of terminal hair growth and a score of 4 indicates extensive hair growth. A total score of less than 8 indicates normal hair growth, a score of 8-15 indicates mild hirsutism and a score greater than 15 indicates moderate or severe hirsutism<sup>12,13</sup>. Besides, the androgen excess in PCOS also contributes to the pathogenesis of acne in the affected patients. Acne affects 15-25 % of patients with PCOS and varies significantly with ethnicity<sup>14</sup>.

Owing to its high frequency and the allied worrisome complications and healthcare cost, Polycystic Ovary Syndrome is a subject of considerable research in Pakistan like the rest of the world. But there is relative scarcity of data in population of Khyber Pakhtunkhwa.

## MATERIALS AND METHODS

It was a cross sectional study. Sample size was 250 cases. Women with Polycystic Ovary Syndrome were recruited from the outpatient department of gynecology and obstetrics unit of Mardan Medical Complex Teaching Hospital, Mardan.

**Inclusion criteria:** Cases aged 20 - 40 years with menstrual cycle irregularities (anovulation or oligo-ovulation), Raised serum testosterone level, hirsutism and ultrasonic features suggestive of Polycystic Ovarian Syndrome as per American Society of Reproductive Medicine and European Society of Human Reproduction and Embryo (ESHRE/ASRM) criteria, 2003 i.e. increased ovarian volume of 10 cm in maximal diameter or 10 or more follicular cysts ranging in size from 2-9 mm were included in the study.

**Exclusion criteria:** Women with previous history of Cushing syndrome, hyperprolactinemia, pregnancy or those taking medicines that changes the hormonal or biochemical profile were excluded by appropriate clinical and medical examination.

Written informed consent was taken from the head of concerned Gynecology and Obstetrics unit. Written informed consents were also taken from the subjects included in the study. A comprehensive questionnaire form was filled for all the participants, including socio-demographic data, menstrual, marital and reproductive history.

Clinical assessment included measurement of height, weight, body mass index (BMI), pulse, blood pressure, assessment of hirsutism, history of infertility and skin acne. BMI was calculated by Quelet's Formula i.e. dividing weight (kg) by height in meter squared (m<sup>2</sup>).

Modified WHO criteria of BMI for Asian population, was applied as under:

1. Normal weight (18.5-24.9 kg/m<sup>2</sup>)
2. Pre-obese (25-29.9 kg/m<sup>2</sup>)
3. Obesity class-I (30-34.9 kg/m<sup>2</sup>)
4. Obesity class-II (35-39.9 kg/m<sup>2</sup>) and
5. Obesity class-III (> 40 kg/m<sup>2</sup>).

Hirsutism was assessed by Ferriman-Gallwey (F-G) scoring according to which a score of 1 to 4 was given for seven areas of body. A total score less than 8 was classified as normal, a score of 8-15 was mild hirsutism and a score greater than 15 was moderate or severe hirsutism.

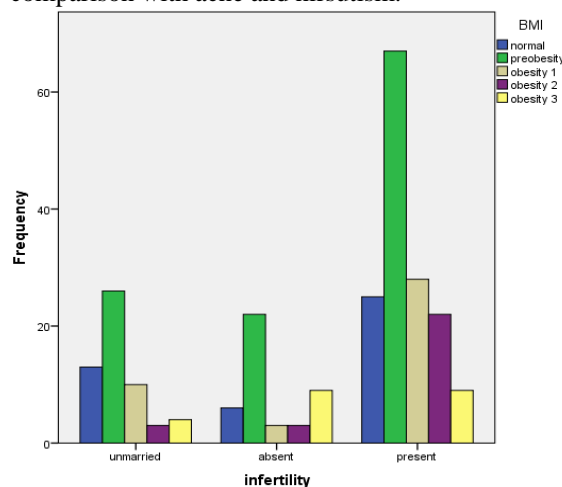
**Statistical Analysis:** Data was compiled and analyzed using SPSS version 20. The frequencies and percentages were calculated. The frequency of infertility, hirsutism and acne was compared with BMI individually, using Pearson Chi-Square test.

## RESULTS

A total of 250 females with PCOS were included in this study. Mean age of the cases was  $25.63 \pm 4.44$  years and the mean BMI was  $30.12 \pm 6.63$  Kg/m<sup>2</sup>. Table.1 shows the frequency of infertility, hirsutism and acne in the study population with comparison of Body mass index as per WHO cut-offs of BMI for Asian population.

The frequency of infertility, hirsutism and acne was 64% (n=151), 72.8% (n=182) and 32 % (n=80) respectively and all had a statistically significant association with obesity. The frequency of obesity in those with infertility, hirsutism and acne was 80.6 %, 89.02 % and 90 % respectively. Most of the obese patients however; were in the pre-obese group. Moreover, most of the hirsute patients exhibited mild severity of hirsutism.

Comparison of infertility with BMI was found to be statistically significant ( $p=0.028$ ), so was the comparison with acne and hirsutism.



**Figure No.1 Comparison of the frequency of patients with and without infertility with their BMI respectively**

**Table No.1: Stratification of patients with infertility, hirsutism and acne on the basis of Body Mass Index (BMI)**

	Categories	BMI					P value
		Normal	Pre-obesity N (%)	Obesity I N (%)	Obesity II N (%)	Obesity III N (%)	
<b>Infertility</b>	Unmarried	13 (23.21)	26 (46.42)	10 (1.78)	3 (5.35)	4 (7.14)	0.028
	Nil	6 (13.95)	22 (51.16)	3 (6.97)	3 (6.97)	9 (20.93)	
	Yes	25 (19.37)	67 (51.93)	28 (21.70)	22 (17.05)	9 (6.97)	
<b>Hirsutism</b>	Normal	24 (35.29)	28 (41.17)	10 (14.7)	5 (7.35)	1 (1.47)	0.001
	mild	20 (10.98)	87 (47.80)	31 (17.00)	23 (12.64)	21 (11.53)	
<b>Acne</b>	Yes	8 (10.00)	33 (41.25)	13 (16.25)	15 (18.75)	11 (13.75)	0.008
	Nil	36 (21.17)	82 (48.2)	28 (16.47)	13 (7.64)	11 (6.47)	

## DISCUSSION

Polycystic Ovary Syndrome is the most common hormonal abnormality affecting females during their reproductive age<sup>1,2,15</sup>. This syndrome cause reproductive as well as metabolic abnormalities. The reproductive disturbances in Polycystic Ovary Syndrome occur due to abnormality in gonadotropin secretions and increased androgen production causing irregular menstrual cycles, infertility, and hirsutism<sup>15</sup>. The metabolic disturbances include abnormal function of the beta cells of pancreas thereby increasing the risk for Diabetes Mellitus<sup>16</sup>. Obesity is the most common feature of patients with Polycystic Ovary Syndrome. In fact it occurs so frequently in these patients that it becomes difficult to conclude that whether obesity is a manifestation or cause of Polycystic Ovary Syndrome. The frequency of infertility, hirsutism and acne in patients with Polycystic Ovary Syndrome turned out to be 64 % (n=151), 72.8 % (n=182) and 32 % (n=80) respectively. All these clinical parameters/complications had a striking and statistically significant association with obesity.

The prevalence of infertility (64 %) is comparable with results of study conducted by Munir SS et al.<sup>17</sup> from Lahore, Pakistan who reported a 67.6 % combined prevalence of primary and secondary infertility in patients with Polycystic Ovarian Syndrome and increasing frequency of infertility, hirsutism and acne with increasing Body Mass Index. The frequency of infertility however; is significantly higher than the reported frequency of 46.42 % by Riaz M et al. in Polycystic Ovarian Syndrome patients from Karachi, Pakistan<sup>18</sup>. This discrepancy in frequency of infertility may be possibly due to population-based differences. The same study however; reported almost the same frequency of 80% of obesity in Polycystic Ovarian Syndrome patients<sup>18</sup>. The difference in frequency of infertility due to a population difference is supported by the finding of significantly lower frequency of infertility (6.4 %) in Chinese population as reported by Li R. et al.<sup>19</sup>. Similarly, meta-analysis of PCOS-related studies reported a very low frequency of infertility (8%) in Irani population<sup>25</sup>. Our findings partially tally with

results concluded by Al-azemi et al. who reported that 76.3 % of infertile women exceeded the normal BMI range<sup>23</sup>.

Overall, 72.8 % (n=182) of the subjects were found to have hirsutism. Majority of those affected, had mild hirsutism. A strong correlation with obesity was observed with about 89 % of the hirsute subjects being obese. A study from Lahore, Pakistan by Munir SS. et al.<sup>17</sup> reported a slightly lower frequency of hirsutism (67.64 %) in Polycystic Ovarian Syndrome patients with positive concordance in terms of mild severity. The frequency of hirsutism however; clearly exceeds that reported by Riaz M et al.<sup>18</sup> (51.61 %) and Haq F. et al.<sup>20</sup> (58.9 %) in population of Karachi, Pakistan.

Acne was observed in 64 % (n=151) of patients with Polycystic Ovarian Syndrome. Among those, 90 % had a Body Mass Index above normal with most being pre-obese. The frequency of obesity was significantly higher than that reported by Munir SS et al.<sup>17</sup> (25.9 %) from Lahore, Pakistan and Hussain R. et al.<sup>21</sup> (33.33 %) from Karachi, Pakistan.

Irrespective of population-based differences in the prevalence of clinical features of Polycystic Ovarian Syndrome, the striking association of these features with obesity reinforces the findings of MehruNisa et al.<sup>22</sup>, Al-azemi et al.<sup>23</sup>, Norman et al.<sup>24</sup> reporting an increase in the frequency and severity of all features of Polycystic Ovarian Syndrome with increasing Body Mass Index. These consistencies in results lend to the idea of focusing more on obesity for both prevention and management of Polycystic Ovarian Syndrome.

## CONCLUSION

This study concluded that in patients with Polycystic Ovarian Syndrome, the prevalence of infertility, hirsutism, and acne is higher in patients with high Body Mass Index. All of these strongly correlate with obesity. Thus, weight reduction must be mandatory for patients who are being treated for Polycystic Ovarian Syndrome. Restoration of normal reproductive health requires achieving a normal Body Mass Index.

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# Role of Topical Vancomycin in Reduction of Sternal Wound Infection in Patients Undergoing Cardiac Surgery

Role of  
Vancomycin  
Reduction of  
Sternal Wound  
Infection

Iqbal Alam Khan<sup>1</sup>, Jalal-ud-Din<sup>2</sup> and Syed Ehsanullah<sup>3</sup>

## ABSTRACT

**Objective:** To examine the effectiveness of topical vancomycin to reduce the rate of wound infection in patients undergoing open heart surgery.

**Study Design:** Randomized controlled trial.

**Place and Duration of Study:** This study was conducted at the Department of Cardiac Surgery, Sandeman Provincial Hospital Quetta from June 2018 to December 2018.

**Materials and Methods:** One hundred and eighty patients of both genders undergoing open heart surgery were included in this study. Patient ages ranged from 40 to 70 years. All the patients were divided into two groups. Group I consisted of 90 patients and received topical vancomycin paste on the sternal wound, Group II also consisted of 90 patients who received topical normal saline before sternal wound closure. The rate of sternal wound infection was examined.

**Results:** There were 133 (73.89%) males and 26.11% females. Patients who received vancomycin had less superficial and deep sternal wound infections than the patients who didn't received vancomycin (2.22% vs 6.67%) and (1.11% vs 4.4%).

**Conclusion:** The use of vancomycin paste to the sternal edges with perioperative antibiotics helps to reduce the sternal wound infection rate.

**Key Words:** Heart surgery, Vancomycin, Sternal Wound infection

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## INTRODUCTION

Worldwide, heart surgeries perform in very clean atmosphere to prevent the infectious complications. The rate of sternal wound infection is ranging from 0.5 to 8%. Sternal wound infection causes morbidity, mortality and increase cost of treatment. After cardiac surgery use of only antibiotics may not helps to prevent infectious complications.<sup>1-3</sup> Many of factors involved in developing surgical site infection such as diabetes mellitus, COPD, obesity and time taken emergency surgery.<sup>4,5</sup>

Cardiac surgeries with these comorbidities may increase the incidence of sternal wound infection. Many of studies and researches conducted to reduce the rate of infectious complication using different antibiotics

and treatment protocols but still there is no improvement demonstrated regarding infectious complication.<sup>6,7</sup>

The use of topical antibiotics at the time of cardiac surgery may helps to reduce the surgical site infection. In these topical antibiotics, topical vancomycin and cefazolin and gentamycin use on the sternal edges resulted better outcomes.<sup>8</sup> Many of studies regarding sternal wound infection resulted that the use of topical antibiotics at the time of cardiac surgery helps to reduce the sternal wound infection.<sup>9</sup> For antibiotic prophylaxis, vancomycin used IV after cardiac surgery and use vancomycin topically on the sternal edges.<sup>10</sup>

The present study was conducted aimed to examine the effectiveness of topical vancomycin along with antibiotic prophylaxis after cardiac surgery.

## MATERIALS AND METHODS

This randomized controlled trial was conducted at Department of Cardiac Surgery Sandeman Provincial Hospital Quetta from 1<sup>st</sup> June 2017 to 31<sup>st</sup> December 2017. A total of 180 patients of both genders who underwent open heart surgery were included. Patient's ages ranged from 40 to 70 years. Patients detailed medical history including age, sex, history of previous cardiac surgery, diabetes mellitus, smoking history, hypertension, were examined after taking informed consent from all the patients. All patients received peri-

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operative antibiotics, comprising of ceftriaxone (1g IV every 12 hours) and gentamicin (80mg IV every 8 hours) on induction of anesthesia and early postoperatively. After surgery antibiotics IV were used for 48 hours. Insulin IV was used to maintain the glucose level after surgery. All the patients were equally divided into two groups; Group I consist of 90 patients and received topical vancomycin solution (2gms in 5ml of normal saline) and Group II consist of 90 patients received spray of 50ml normal saline on the sternal wound before closure. Effectiveness of topical vancomycin regarding SWI was examined. Risk factors such as diabetes mellitus, smoking history, hypertension was also examined. Mean operative time and cross clamp time was recorded.

All the statistical data was analyzed by SPSS 20. Frequencies and percentages were obtained. P-value <0.05 was considered as significant.

## RESULTS

There were 70 (77.78%) males and 20 (22.22%) females in group I while in group II, 63 (70%) males and 27 (30%) females. Thirty four patients belonged to age group <50, 42 were between 50-60 years and 14 patients were >60 in group I. Whereas in group II, 30 patients were <50 years, 44 patients were between 50-60 and 16 patients were >60 years of age. In group I, 26 (28.89%) were hypertensive while in group II, 29 (32.22%) patients had this comorbidity. The incidence of diabetes was higher in group I, 18 (20%) vs 10 (11.1%). There were 20 (22.22%) and 14 (15.55%) smokers in Group I and Group II respectively. We found no significant difference according to age, sex, BMI except diabetes mellitus and smoking (Table 1).

**Table No.1: Baseline characteristics of all the patients**

patients			
Characteristics	Group I	Group II	P-value
Gender			
Male	70 (77.78%)	63 (70%)	0.53
Female	20 (22.22%)	27 (30%)	
Age (years)			
< 50	34 (37.78%)	30 (33.33%)	0.41
50 – 60	42 (46.67%)	44 (48.89%)	
> 60	14 (15.55%)	16 (17.78%)	
Body mass index	25.6±5.9	26.2±5.7	0.68
Hypertension	26 (28.89%)	29 (32.22%)	0.6
Diabetes mellitus	18(20%)	10(11.11)	0.05
Smokers	20 (22.22%)	14 (15.55%)	0.32

Patients who received topical vancomycin had less superficial and deep sternal wound infections than the patients who didn't received vancomycin (1.11% vs 8.89%), (1.11% vs 6.67%) and this showed that significant difference between both groups regarding the rate of sternal wound infection (P<0.05). The mean

bypass time in Group I and Group II was 114.7±48.5 and 122.6±40.2 minutes, statistically no significant difference was recorded (P>0.05). Cross clamp time in Group I and Group II was 64.4±31.5 and 74.7±30.2 (Table 2).

**Table No.2: Post-operative incidence of sternal wound infections**

Characteristics	Group I	Group II	P-value
<b>Infections</b>			
Superficial	1 (1.11%)	8 (8.89%)	0.001
Deep Sternal	1 (1.11%)	6 (6.67%)	0.000
Total incidence	2 (2.22%)	14 (15.56%)	0.000
<b>Diabetic Patients</b>			
All sternal infections	0 (0.0%)	3 (3.33%)	0.000
Mean bypass time (min)	114.7±48.5	122.6±40.2	0.000
Cross clamp time (min)	64.4±31.5	74.7±30.2	0.000

## DISCUSSION

Sternal wound infection is a major concern after cardiac surgery. Many of studies were conducted to prevent the infectious complications with antibiotics prophylaxis after cardiac surgical procedures. The present study was conducted to examine the effectiveness of topical vancomycin along with perioperative antibiotics to reduce the sternal wound infection rate. In our study most the patients were male 77.78% as compared to females 22.22%. These results shows similarity to some of the studies in which males patients population rate was high 65 to 80%.<sup>11,12</sup> We found that most of the patients were ages above 50 years. These results were similar to other studies in which mostly patients were ages above 45 years.<sup>13</sup>

In present study, we found that the use of topical vancomycin along with perioperative antibiotics with tight glycemic control reduced deep sternal and superficial wound infection in patients undergoing coronary artery bypass surgery. A study conducted by Fowler et al<sup>14</sup> reported that the use of topical vancomycin on the sternal edges reduced the sternal wound infection in patients undergoing cardiac surgery. In present study we found on 1.11% patients developed deep wound infection and 1.11% patients had superficial infection in vancomycin group and 14.56% patients developed both superficial and deep wound infection in without vancomycin group. These results showed that use of topical vancomycin along with perioperative antibiotics had very low rate of sternal wound infection as compared to other antibiotics prophylaxis. Many of studies were comparable to our study in which use of topical vancomycin with perioperative antibiotics reduces the sternal wound infection.<sup>15-17</sup> Arruda et al<sup>18</sup> reported that the rate of

sternal wound infection after topical vancomycin in cardiac surgery was 0.49% out of 1020 patients.

In the present study, we found sternal wound infection in diabetic patients was 0% with topical vancomycin and 3.33% patients developed SWI without vancomycin. We found that use of topical vancomycin with tight glycemic control reduces the rate of SWI. These results was similar to another study.<sup>19</sup> In our study, the mean bypass time in Group I and Group II was  $114.7 \pm 48.5$  and  $122.6 \pm 40.2$  minutes, statistically no significant difference was recorded ( $P > 0.05$ ) Cross clamp time in Group I and Group II was  $64.4 \pm 31.5$  and  $74.7 \pm 30.2$ . These results were comparable to some other studies in which patients received vancomycin topically had less operative time as compared to those who didn't received vancomycin.<sup>20-22</sup>

Thus, we observed that the use of topical vancomycin with combination of perioperative antibiotics and tight glycemic control reduces the SWI rate in patients undergoing cardiac surgery.

## CONCLUSION

Sternal wound infection after cardiac surgery involving median sternotomy is a significant cause of morbidity and mortality. Our study was designed to reduce the rate of sternal wound infection in open heart surgery patients and the results have shown that the use of vancomycin to the sternal edges with perioperative antibiotics helps to reduce the incidence of sternal wound infection.

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# Protective Role of Vitamins E in Doxorubicin Induced Toxicity in Rat Testes: A Histomorphometric Study

Farooq Khan, Nighat Ara, Shamila Hafizi, Nomanullah Wazir, Fahadullah and Ambareen Hamayun

## ABSTRACT

**Objective:** To observe the antioxidant effect of vitamin E on the toxicity of doxorubicin of rat testes.

**Study Design:** Analytical experimental randomized control study

**Place and Duration of Study:** This study was conducted at the Department of Anatomy, Peshawar Medical College Peshawar from February 2013 to July 2013.

**Materials and Methods:** Thirty two rats were randomly divided into two main groups; normal and the experimental groups. Experimental group was further divided into the toxic and vitamin E groups. The toxic group (B-I) was given doxorubicin at the dose of 2 mg/kg body weight, i.e. weekly for four weeks. While the vitamin E group (B-II) was introduced with the oral administration of vitamin E at the dose of 150 mg/kg daily for four weeks along with the doxorubicin i.e. weekly for four weeks. After scarifying the animal according to the protocol the testis were sectioned and then preparatory slides were used to apply the basic stains i.e. H and E stain, PAS stain and Massan Trichrome stains.

**Results:** Group B-I treated with Doxorubicin only showed marked decreased in body weight, testicular weight, decreased height of epithelium and germ cells count as compared to B-II.

**Conclusion:** The simultaneous use of vitamin E as an antioxidant, can protect the toxic effects of Doxorubicin and thus damage to the testes.

**Key Words:** Doxorubicin, Testicular toxicity, vitamin E

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## INTRODUCTION

Cancer continues to represent the largest cause of mortality in the world. It takes almost six million lives every year.<sup>1</sup> Chemotherapy involves the use of chemical agents to stop the growth and eliminate cancer cells even at distant sites from the origin of primary tumor.<sup>2</sup>

Among these chemotherapeutic agents, Doxorubicin has long been widely used for its potent efficiency.<sup>3</sup> Doxorubicin belongs to a class of medications called anthracyclines. It works by slowing or stopping the growth of cancer cells in the body. It is derived from the algae, *Streptomyces peucetius* Sp. Caesius.<sup>4</sup> Doxorubicin can impair the motility of sperms<sup>5</sup>, induce germ cell apoptosis<sup>6</sup>, and result in testicular damage

ultimately.<sup>7</sup> The exact mechanism of doxorubicin testicular toxicity is still completely not known, but doxorubicin induced cardiomyopathy implicates the breakage of DNA continuity, overload of oxidative stress, and apoptosis of cells.<sup>8</sup>

An antioxidant is a molecule that inhibits the oxidation of other molecules. The most popular and abundant antioxidant vitamin is vitamin E, which is used worldwide nowadays. Supplementation of vitamins E has protected the testicular tissues and sperms.<sup>9,10</sup>

Vitamin E is an essential fat-soluble nutrient that serves as an antioxidant and is also used in cell signaling, regulation of gene expression and immune functions. It was discovered by Evans and Bishop in 1922, as a necessary dietary factor for reproduction of rats<sup>11</sup>.

As a fat soluble antioxidant, it stops the production of reactive oxygen species formed when fat undergoes oxidation<sup>12,13,14</sup>. Vitamin E has many biological functions. As an antioxidant, vitamin E acts as a peroxyl radical scavenger, preventing the propagation of free radicals in tissue, by reacting with them to form a tocopheryl radical by the help of a hydrogen donor i.e.: vitamin C, and thus return to reduced state<sup>15</sup>.

Vitamin E also plays a role in neurological functions<sup>16</sup>, and inhibition of platelet aggregation.<sup>17,18</sup> Vitamin E also protects lipids and prevents the oxidation of polyunsaturated fatty acids.<sup>19</sup>

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## MATERIALS AND METHODS

Thirty two male albino rats of Sprague Dawley strain, 8 weeks of age, weighing 200-220 gm were procured from the animal house of Peshawar Medical College animal house. These animals were kept in solid bottom polypropylene cages. Group 1 (control group): animals of this group received intraperitoneal normal saline injection once a week for a period of four weeks. Group 2 (experimental group): Sub-group I. Animals of this group received intraperitoneal doxorubicin at 2mg/kg body weight, on weekly basis for a period of four weeks. Sub-group II. Animals of this group received intraperitoneal doxorubicin at 2mg/kg body weight, on weekly basis for a period of four weeks and Vitamin E, at a dose of 150mg/ kg body weight daily for four weeks. On 28<sup>th</sup> day, animals were euthanized and organs were collected in 10 % neutral buffered formalin to be processed for paraffin embedding, 0.5  $\mu$ m thick sections were cut on rotary microtome and were stained with Haematoxylin and Eosin for routine microscopy. Sections were also stained with Masson's Trichrome to see the changes in the connective tissue elements of the stroma. PAS stain was also applied to see the integrity of the basement membrane and the carbohydrates contents of the cellular and non-cellular elements of the testis. Following observations were made under the microscope; thickness of seminiferous epithelium, number of spermatogenic cells/cross section of seminiferous tubule, integrity of Basement membrane by PAS stain, demonstration of the connective tissue by Masson's Trichrome and demonstration of Muscular tissue By H and E stain. Data was analyzed by using the SPSS version 15, and the P value was considerably significant statistically.

## RESULTS

At the beginning of the study, average weight of animals in group A was  $193.5 \pm 4.7$  in group B-I was  $192.0 \pm 4.60$ , group B-II was  $195.5 \pm 4.27$ . The difference in the weights of control group and antioxidant group showed insignificant ( $P > 0.009$ ). At the end of the study, average weights of animals in control group was  $246 \pm 4.6$ , in group B-I was  $228.5 \pm 6.2$ , in group B-II was  $238 \pm 4.8$  respectively. The body weight was increased in group A and became significantly higher as compared to experimental group B-I as shown table 1.

The weights of testes of all the groups were measured and compared. The average weight in control group was  $1.54 \pm 0.044$ , in group B-I the weight was  $1.46 \pm 0.030$  in group B-II was  $1.52 \pm 0.038$  grams. There was a significant difference in body weight of control group and group B-I with p value of ( $< 0.0052$ ). So far the weights of testes is concerned, the result of present study indicate that the most affected group was B-I which was only given doxorubicin as compared to the groups B-II, which was treated with antioxidants in

addition to doxorubicin during the experiment. This confirms the protective role of antioxidants when given in combination with doxorubicin as shown in table 2.

In control group the testes were pink, firm in consistency and ovoid in shape. The H and E stain showed tunica albuginea with dark pink fibers running in bundles showing compact arrangement. These fibers are identified as collagen fibers. There were marked changes in the experimental group B-I. There is decreased in the germ cells count in group B-I, also there is decreased is epithelial height of the seminiferous epithelium as compared to the experimental group B-II as seen in Figs. 1-6.

The height of the seminiferous epithelium in all the groups was measured and compared. The average height in control group was  $9.8 \pm 0.044 \mu$ m in group B-I was  $9.3 \pm 0.035 \mu$ m in group B-II was  $9.7 \pm 0.038 \mu$ m. There was significant difference in epithelial height among the control group and the group B-I with a p value of ( $< 0.0051$ ). So far the height of epithelia is concerned; the results of present study indicate that the most affected group was the B-I which was given doxorubicin only as compared to the groups B-II, which received both doxorubicin and antioxidant as shown in table 3.

The average germ cells count of all the groups were measured and compared. The average germ cells count in control group was  $293.35 \pm 0.044$  cells/HPF, in group B-I was  $217.625 \pm 0.030$  cells/HPF, in group B-II was  $253.87 \pm 0.038$  cells/HPF. The difference in amount of germ cells count among the control group and the antioxidant treated groups was insignificant ( $P < 0.001$ ) as shown in Table 4.

**Table No.1: Body weight of animals in control group**

Animal number	Initial weights of animals (gm)	Final weights of animals (gm)	Difference in weights (gm)
A1-A4	193.5	246	52.5
BI-1— BI-8	192	213.13	21.13
BII-1--- BII-8	195.5	233	37.5

**Table No.2: Weight of testis in all groups**

Animal number	Initial weights of right testis (gm)	Mean weights of left testis (gm)	Mean average weight of testis (gm)
A1-A4	1.54	1.53	1.54
BI-1— BI-8	1.46	1.47	1.46
BII-1--- BII-8	1.51	1.53	1.52

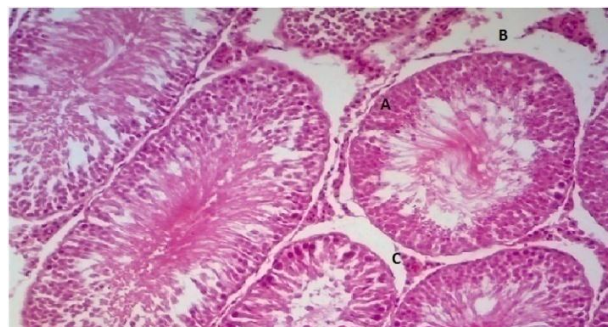
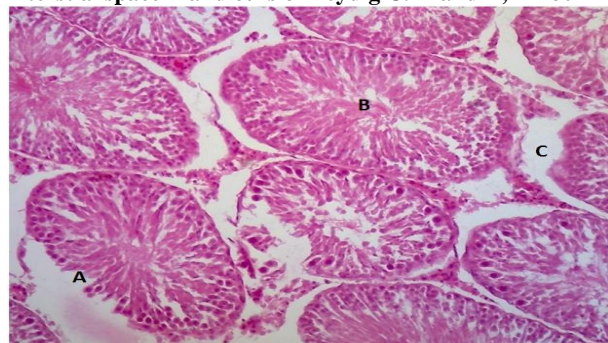
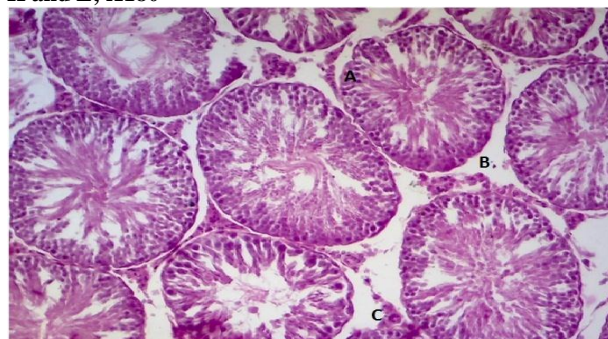
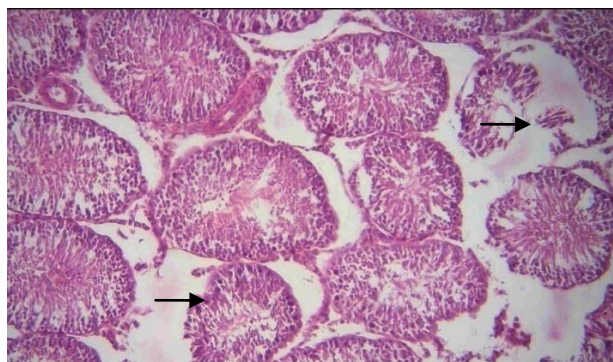
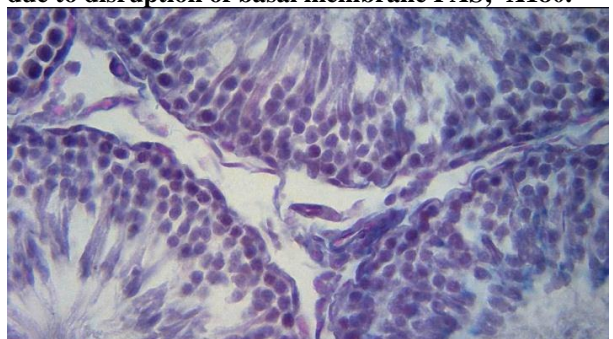
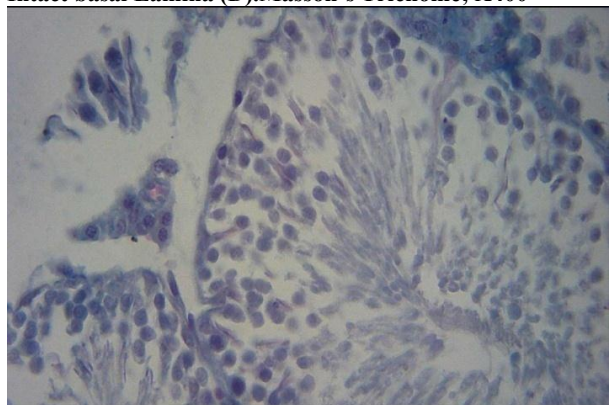


**Table No.3: Epithelial height (thickness) of all groups**

Animal number	Mean Thickness ( $\mu\text{m}$ )
A1-A4	9.9
BI-1---BI-8	8.52
BII-1---BII-8	9.3

**Table No.4: Mean germ cells count in all group**

Animal number	Mean germ cell count (cell/HPF)
A1-A4	293.5
BI-1---BI-8	217.63
BII-1---BII-8	253.87

**Figure No. 1: Photomicrograph of 5 $\mu\text{m}$  thick section of testis of a control group showing normal histology of the seminiferous tubules A, interstitial space B and cells of Leydig C. H and E; X 180****Figure No.2: Photomicrograph of 5 $\mu\text{m}$  thick section of a group B-I showing histopathological changes in the seminiferous tubules i.e. Disrupted Basement membrane (A), congested Lumen (B) and wide interstitial space (C). H and E; X 180****Figure No.3: Photomicrograph of 5 $\mu\text{m}$  thick section of control group showing normal seminiferous tubules (A), interstitial space (C), cells of Leydig (D).PAS; X180****Figure No.4: Photomicrograph of 5 $\mu\text{m}$  thick section of a group B-I Showing sloughing of the germ cells due to disruption of basal membrane PAS; X180.****Figure No.5: Photomicrograph of 5 $\mu\text{m}$  thick section of control group showing normal histology of the seminiferous tubules (A), Lumen (B), interstitial space (C), Intact basal Lamina (D).Masson's Trichome; X400****Figure No.6: Photomicrograph of 5 $\mu\text{m}$  thick Masson Trichome stained section of a group B-I showing normal histology of the seminiferous tubules. Masson's Trichome; X 400.**

## DISCUSSION

Cancer is considered as a major health problem that has become the most common leading cause of death throughout the world. To fight against this *deleterious* disease a number of anti cancer medicines have been introduced in the field of medicine. Doxorubicin is one of the commonest medicines used for this purpose. It is worth mentioning that doxorubicin like any other drug is also having adverse effects on the body of the individuals being treated. To reduce the adverse effects

of doxorubicin during chemotherapy co-administration of antioxidants have been proved to be beneficial.

After administration of the doxorubicin for a period of 4 weeks, we observed 20% weight loss in the animals that were treated with doxorubicin only (group B-I), however none of the remaining experimental groups showed any statistically significant weight loss. Loss of appetite due to adverse effects of doxorubicin on GIT is an obvious reason for the weight loss in this particular group. Therefore, our finding is in accord with the result of a study conducted by Harvey (1987), who found that there was a significant weight loss in those albino rats that were treated with doxorubicin. Harvey attributed this weight loss to appetite loss and gastrointestinal disturbances.<sup>20</sup> The current study is also in close agreement with the study of Der R, Fahim et al. (1974), where they found that the animals of the experimental groups had 16% loss of the body weight as an adverse effect of doxorubicin which had led to ulcerative lesions at the sites of the injections.<sup>21</sup>

We found that there was a significant loss in the weight of testes of group B-I animals as compared to animals of the control group. Groups B-II animals protected with vitamin E did not show remarkable loss of testicular weight during the experiment. Our study is in agreement with a study conducted by Evenson and Jost, (1993) who recorded loss in weights of testes of animals treated with doxorubicin.<sup>22</sup> Our study is also in conformity with the study done by Patil and Balaraman (2009) who reported testicular weight loss of animals treated with doxorubicin for a period of 5 weeks.<sup>23</sup>

This finding of the present study correlates with the results of a similar study conducted by Lu and Meistrich (1979), where it was found that even a low dose of doxorubicin (1 mg/kg.b.w.) could target the germ cells and spermatogonia, leading to a decrease in the height of seminiferous epithelium.<sup>24</sup>

So far the germ cells count is concerned, we found that group B-I showed marked decrease in germ cells count as compared to the groups B-II which were given antioxidant along with doxorubicin during experiments. In this aspect our study stands in complete harmony with the study conducted by Ward et al. (1988), who reported doxorubicin induced reductions in germ cells count.<sup>25</sup> The present study also strongly supports the findings of a study conducted by Biswas NM (1996) and Ghosh (2002), in which vitamin C was given to rats being treated with doxorubicin<sup>26</sup>. Their results showed a significant elevation in the activities of the testes, and an increase in germ cells count, which may be due to the direct stimulatory effect of the vitamin on the enzyme i.e. 3 $\beta$ -HSD (hydroxysteroid dehydrogenase deficiency) and 17  $\beta$ -HSD.<sup>27,28</sup> It may also be due to antioxidant effect of vitamin C against oxidative stress induced by doxorubicin.<sup>29-31</sup>

## CONCLUSION

Simultaneous use of antioxidant vitamin C can prevent the testicular damage which can be caused by doxorubicin toxicity.

## Author's Contribution:

Concept & Design of Study:	Farooq Khan
Drafting:	Nighat Ara, Shamila Hafizi
Data Analysis:	Nomanullah Wazir, Fahadullah, Ambareen Hamayun
Revisiting Critically:	Farooq Khan, Nighat Ara
Final Approval of version:	Farooq Khan

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

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# Types of Gynecological Cancers Detect in Females at Tertiary Care Tertiary Centre

Sadia Zahoor, Sonia Zulfiqar and Iffat Yasmeen

## ABSTRACT

**Objective:** To determine the frequency of various gynecological cancers at a tertiary care hospital.

**Study Design:** Cross sectional study.

**Place and Duration of Study:** This study was conducted at the Department of Obstet and Gynae, Sheikh Zayed Hospital, Rahim Yar Khan from January 2018 to December 2018.

**Materials and Methods:** In this study, the females with age more than 30 years irrespective of their gravida and parity presenting with per vaginal bleeding were included. All these cases underwent biopsy under direct vision and assessed for its results on histopathology for various malignancies.

**Results:** In this study, 50 cases with positive malignancy outcome were selected. The mean age of the participants was  $55.67 \pm 13.31$  years and mean duration of symptoms was  $7.45 \pm 1.61$  months. Out of 50 cases, only 32% were educated, 84% were from rural population and 10% were smokers. Out of 50 cases cervical malignancy was seen in 26 (52%), ovarian in 15 (30%) and endometrial or uterine in 9 (18%) of the cases.

**Conclusion:** Gynecological malignancies are not that rare and the cervical cancer is the commonest CA detected followed by ovarian carcinoma.

**Key Words:** CA, Biopsy, Smoker, cervical

**Citation of articles:** Zahoor S, Zulfiqar S, Yasmeen I. Types of Gynecological Cancers Detect in Females at Tertiary Care Tertiary Centre. Med Forum 2019;30(7):92-94.

## INTRODUCTION

Gynecological cancers are considered as one of the salient health care problems as they add to a great degree of cost and as well as morbidity and mortality in females all across the globe. They are observed worldwide with variable degree of prevalence.<sup>1</sup> The malignancies originating from the genital tract origin range from 31.6% to 35% of the cases in underdeveloped countries and 12 to 13% in cases of North America<sup>2</sup> and other developed countries.<sup>3</sup>

These malignancies include cervical carcinoma (CA), ovarian carcinoma, uterine and or endometrial carcinoma, vaginal carcinoma and vulvar carcinoma.<sup>4,5</sup> There are different risk factors that can predispose to this and include age of the patient, parity status, smoking, family history of gynecological malignancies, exposure to radiations etc.<sup>6-8</sup>

There are number of investigations to guide for further management. Radiological investigations are to guide only & tissue diagnosis is always needed for definitive

diagnosis and to direct for further curative or palliative management, which is another challenge in the under developed countries. The data has shown that the most common malignancy observed is cervical cell carcinoma and it is followed by ovarian carcinoma. Rapid detection and early management can reduce the degree of morbidity and mortality significantly.<sup>9-10</sup> The local data is very scarce regarding the overall prevalence as well as for its spectrum of types.

## MATERIALS AND METHODS

This cross-sectional study was carried out at Sheikh Zayed Hospital, Rahim Yar Khan during 01-01-2018 to 31-12-2018. In this study, the females with age more than 30 years irrespective of their gravida and parity presenting with per vaginal bleeding of at least 3 months are more were included via non probability, consecutive sampling. The cases with any bleeding disorder, or taking treatment with antiplatelet therapy or those with platelet count less than 50 thousand per ml or with end stage renal or liver failure were excluded from this study. Then these cases underwent USG. The suspected lesion assessed on USG was noted and the biopsy was taken and sent for histopathology of the same institute and the various gynecological malignancies were labelled by the presence of malignant cells with or without small areas of necrotizing tissue, surrounded by anaplastic as well as the presence of hyperplastic blood vessels and were labelled as cervical, ovarian or endometrial depending upon the site of biopsy.

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**Statistical analysis;** SPSS version 23.0 was used for data analysis. Frequency and percentages were calculated for qualitative and mean and SD for quantitative data.

## RESULTS

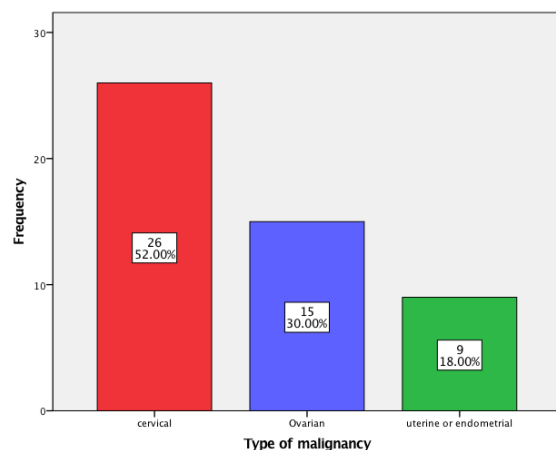
In this study, 50 cases with positive malignancy outcome were selected. The mean age of the participants was  $55.67 \pm 13.31$  years and mean duration of symptoms was  $7.45 \pm 1.61$  months as shown in table I. Out of 50 cases, only 32% were educated, 84% were from rural population and 10% were smokers as in table 2. Out of 50 cases cervical malignancy was seen in 26 (52%), ovarian in 15 (30%) and endometrial or uterine in 9 (18%) of the cases as shown in figure I.

**Table No.I: Demographics (n= 50)**

Variables	Mean $\pm$ SD	Range
Age (years)	$55.67 \pm 13.31$	35-78
BMI ( $\text{kg}/\text{m}^2$ )	$23.67 \pm 3.91$	20-31
Gravida	$4.57 \pm 1.12$	0-9
Parity	$3.11 \pm 1.01$	0-7
Duration of symptoms (months)	$7.45 \pm 1.61$	4-24

**Table No.2. Study variables (n= 50)**

Variables		Number	%
Educational status	Educated	16	32
	Uneducated	34	68
Residential status	Rural	42	84
	Urban	08	16
Smoking	Yes	5	10
	No	45	90
Family h/o malignancy	Yes	6	12
	No	44	88



**Figure No.1: Type of malignancy detected (n= 50)**

## DISCUSSION

Gynecological malignancies are one of the leading causes of morbidity and mortality in females and

amongst then 2<sup>nd</sup> common causes after breast malignancies. They have equal distribution all across the globe; however, the prevalence and distribution of various malignancies varies. Overall incidence ranges from 30 to 35% of over all malignancies detected in females. The major risk factors are age, family history and parity.<sup>11-12</sup>

In the present study, out of 50 cases cervical malignancy was the most common and it was seen in 26 (52%), followed by ovarian cancer seen in 15 (30%) and endometrial or uterine which was observed in 9 (18%) of the cases.

These results were comparable to the findings of the studies done in the past regarding evaluation of various gynecological malignancies where cervical lesion was the most common. According to a study carried out by Nkyekyer K et al, revealed that the most common malignancy in their biopsies was cervical cancer, which was seen in 57.8% of their cases and was close to 52% in the present study.<sup>11</sup>

Ugwu et al, carried out a similar study in an African country, and also found cervical cancer as most common one which 78% of their cases and this was followed by ovarian cancer seen in 17% of the subjects, and in the present study ovarian CA was seen in 30% of the cases.<sup>12</sup>

The findings of the study done by Kyari et al was also in conjunction to the finding of the present study as they found ovarian CA in 27% of their cases and 30% in present study. A little higher prevalence was seen in a study by Jamal et al where they found ovarian CA in 42.4% and cervical CA as 50%, where the latter was again the commonest one.<sup>13-14</sup>

According to the studies done by Salani et al and De Angelis Ret al, cervical cancer was most common and it was seen in more than 60% of their cases; and they further described that this has significant association of this with age of the patient and the parity. They also found ovarian CA as the 2<sup>nd</sup> most common malignancy detected.<sup>15-16</sup>

## CONCLUSION

Gynecological malignancies are not that rare and the cervical cancer is the commonest CA detected followed by ovarian carcinoma.

### Author's Contribution:

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

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# Fluoroquinolones Resistance to Esbl Positive Escherichia Coli Causing Urinary Tract Infection in Khyber Teaching Hospital Peshawar

Shandana Altaf<sup>1</sup>, Tayyaba Basharat<sup>2</sup>, Mariana Amer<sup>1</sup>, Waheed Iqbal<sup>1</sup> and Amer Azhar<sup>3</sup>

## ABSTRACT

**Objective:** To find the resistance of fluoroquinolones to ESBL producing E. coli causing urinary tract infection.

**Study Design:** Single center observational study.

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

**Materials and Methods:** Urine samples for culture and sensitivity were collected from patients having UTI. Urine cultures for ESBL positive E. coli were included in the study. We analyzed the resistance of fluoroquinolones in ESBL positive E. coli in urinary tract infection.

**Results:** Total of 104 patients were included in the study. Male to female ratio was 1:1.47. Age range was 15 to more than 60 years. Resistance to norfloxacin, ciprofloxacin and levofloxacin was found to be 81.7%, 84.6% and 80.8% respectively.

**Conclusion:** The age group and the gender did not make any statistically significant difference in resistance pattern. There was more than 80% resistance to fluoroquinolones in ESBL positive E. coli urinary tract infection.

**Key Words:** fluoroquinolones resistance, ESBL positive E. coli, urinary tract infection.

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## INTRODUCTION

Urinary tract infection (UTI) is considered as the fourth leading cause of infection with a very high consumption of medications<sup>1</sup>. Many microorganisms are involved in the etiology of UTI including Staphylococcus aureus, Pseudomonas aeruginosa, proteus species and streptococcus species<sup>2,3</sup>, but Escherichia coli is considered as the predominant cause, in 80% of urinary tract infections (UTI) worldwide<sup>4</sup>.

The prevalence of Multi-drug resistance species of micro-organisms upsurges recently with special concern about the gram-negative bacteria that produces extended spectrum  $\beta$ -lactamase (ESBL) and are resistant to many classes of drugs which are not limited to penicillin, cephalosporin, monobactams excluding carbapenems.

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The ESBL is produced by bacteria of enterobacteriaceae family including E. coli<sup>4,5,6</sup>.

The fluoroquinolones are a group of antibacterials with major clinical importance, being one of the most frequently prescribed classes of antimicrobial agents in the world especially for UTIs because of their availability in both oral and intravenous forms. Resistance to fluoroquinolones emerges recently due to the intensive use of these drugs worldwide and is high in developing countries due to poor hygiene, illiteracy and poverty. Furthermore, fake and spurious drugs are also prevalent in the surroundings that attract patients because of low cost. Self-medication and easy availability of drugs without prescription is also common in the developing countries<sup>7</sup>.

The recent guidelines recommend the reservation of fluoroquinolones to severe and resistant infections and need to be prescribed following proper antimicrobial susceptibility testing to identify microorganism involved<sup>8</sup>.

The prescription of fluoroquinolones for UTI is very high with limited data availability on its resistance in our population. The aim of this study is to know about the resistance of fluoroquinolones in ESBL producing E. coli in patients with UTI in the department of nephrology Khyber Teaching Hospital Peshawar Pakistan irrespective of their disease status.

## MATERIALS AND METHODS

A single-center cross-sectional study was carried out to meet the objective of the study. This study was conducted in the department of nephrology, Khyber Teaching Hospital Peshawar. Urine samples for culture and sensitivity were collected from the patients having UTI from Sept 2018- Feb 2019. A mid-stream urine sample was collected in pre-sterilized container. For catheterized patients, urine sample was collected using sterile syringe after washing the tip of the catheter with boric acid. The collected samples were inoculated on MacConkey agar medium and incubated for 24-48 hours. Antibiotic susceptibility test was done using the Kirby-Bauer disk diffusion method that is based on the Clinical and Laboratory Standards Institute (CLSI)<sup>9</sup>. The commercially available antibiotic discs including ciprofloxacin, levofloxacin and norfloxacin were used. E. coli ATCC 25922 was used as a control organism. Double disc method following CLSI guidelines for confirmation of ESBL was used. An increase in zone of inhibition (5-12mm) for ceftriaxone and/or ceftazidime and/or cefotaxime confirmed the production of ESBL<sup>10,11</sup>. Total 104 confirmed ESBL E.coli samples were included in the study. The data was analyzed using SPSS version 20.0. All the numerical data was expressed as Mean  $\pm$  standard deviation (SD). The chi-square test was used for categorical data with p value  $<0.05$  was considered significant. The graph was constructed using graphed Prism version 7.0.

## RESULTS

In all 104 patients, 42 (40.4%) were males while 62 (59.6%) were females. Resistance to norfloxacin, ciprofloxacin and levofloxacin was found to be 81.7%, 84.6% and 80.8% respectively, while these drugs were sensitive only to 19(18.3%), 16(15.4%) and 20(19.2%) cases as shown in table 1. The age group were categorized as group 1, 2, 3 and 4. Group 1 includes patients which age range from 15-30 years, group 2 age range is from 31-45 years, group 3 age range is from 46-60 years and group 4 age range is above 60 years graphically presented in figure 1. The number of patients in group 1, 2, 3 and 4 are 16, 22, 30 and 33 respectively.

**Table No.1: frequency distribution**

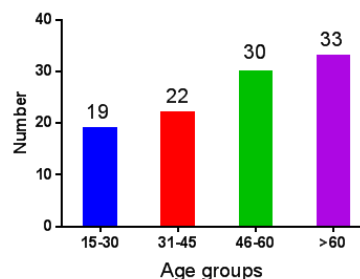
Variables		Frequency	% age
Gender	Male	42	40.4
	Female	62	59.6
Norfloxacin	Sensitive	19	18.3
	Resistant	85	81.7
Ciprofloxacin	Sensitive	16	15.4
	Resistant	88	84.6
Levofloxacin	Sensitive	20	19.2
	Resistant	84	80.8

**Table No.2: Association of Gender with resistance pattern**

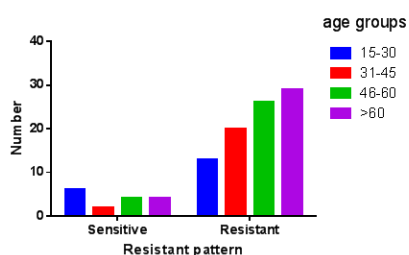
	Sensitive	Resistant	X <sup>2</sup> -value	p-value
	Ciprofloxacin			
Males	7	35	0.08	0.78
Females	9	53		
	Levofloxacin			
Males	8	34	0.002	1.0
Females	12	50		
	Norfloxacin			
Males	7	35	0.12	0.80
Females	12	50		

**Table No.3: Association of different age categories with resistance pattern**

Ciprofloxacin				
Age Groups (years)	Sensitive	Resistant	X <sup>2</sup> -value	p-value
Group 1 (15-30)	06	13	4.86	0.18
Group 2 (31-45)	02	20		
Group 3 (45-60)	04	26		
Group 4 (>60)	04	29		
Levofloxacin				
Group 1 (15-30)	06	13	5.2	0.15
Group 2 (31-45)	01	21		
Group 3 (45-60)	07	23		
Group 4 (>60)	06	27		
Norfloxacin				
Group 1 (15-30)	05	14	2.49	0.47
Group 2 (31-45)	03	19		
Group 3 (45-60)	07	23		
Group 4 (>60)	04	29		



**Figure No.1: UTIs cases in different age groups**



**Figure No.2: Resistant pattern with age groups in number of patients.**

## DISCUSSION

Fluoroquinolones are the only broad-spectrum antimicrobial agents that target bacterial DNA thereby inhibiting two enzymes, DNA gyrase and topoisomerase IV. Resistance to quinolones develop by chromosomal genes mutation that encodes the DNA gyrase and topoisomerase IV leading to modifications in target site and membrane permeation channels. Several other mechanisms of resistance to quinolones have also been reported<sup>12</sup>, and these occur due to multiple exposure of a patient to antimicrobial agents. Hospital acquired infections and admissions in intensive care unit are also associated with ESBL producing fluoroquinolone resistant UTI<sup>13</sup>. It has been reported that for one prescription of ciprofloxacin per month, the resistance was 3%, but with practices having 10 prescriptions per month resistance increased to 5.5%<sup>14</sup>. In Israel after restricting the use of Ciprofloxacin, resistance decreased from 12 % to 9%<sup>15</sup>. Fluoroquinolones are extensively used to treat UTI which is one of the most common bacterial infection that includes frequent relapses that may lead to pyelonephritis, kidney damage as well as complications caused by use of drugs for its eradication<sup>16</sup>. The emergence of ESBL mediated resistance in E.coli is alarming where the treatment option is very limited and is only sensitive to imipenem and meropenem but recently due extensive use of quinolones empirically, the resistance has increased<sup>17</sup>. In Our study resistance to norfloxacin, ciprofloxacin and levofloxacin to ESBL producing E.coli was 81.7%, 84.6% and 80.8%, respectively. This is similar to the study done six years back in our hospital looking for antibiotic susceptibility pattern to E.coli in UTI<sup>18</sup>. Our results show that gender doesn't make any difference in resistance pattern to norfloxacin (p value = 0.80), ciprofloxacin (p value = 0.78) and levofloxacin (p value = 1.0). Previous studies have shown that in E. coli UTI there was a lower incidence of resistance to fluoroquinolones in children as compared to adults and with increasing age the resistance to fluoroquinolones increased<sup>19</sup>. The same results were also shown in another study conducted in our hospital, showing resistance to fluoroquinolones up to 85% with increasing age<sup>18</sup>. Our study was about ESBL positive E.coli causing urinary tract infections the age

groups did not make any statistically significant difference to norfloxacin, ciprofloxacin and levofloxacin (table 3).

A study published in 2001, reported 55.8% resistance to ESBL producing E.coli to 55.8% to fluoroquinolones<sup>17</sup>. Another study published in 2009 reported fluoroquinolones resistance to ESBL producing E.coli was 62.9%<sup>20</sup>. In a study published in 2011, showed that 54% of the UTIs were caused by ESBL producing E. coli in which 85% were resistant to ciprofloxacin<sup>21</sup>. Jang WH et al have shown that E. coli resistance to levofloxacin was 29.49% by year 2005 which has increased to 43.2% by the year 2009<sup>22</sup>. According to the recent study published in 2019, 44% of the UTIs caused by E.coli of ESBL group shows 93.3% resistance to fluoroquinolones<sup>23</sup>. WHO data from five regions reveal 50% resistance to fluoroquinolones in E.coli UTI<sup>24</sup>.

The emergence of ESBL mediated E.coli is indeed a threat worldwide and especially to Pakistan where self-medication and misuse of antimicrobial agents is a major problem. A meta-analysis by Fasugba O et al showed that in Asia and Africa the pooled resistance was highest to ciprofloxacin compared to America and Europe<sup>19</sup>. The drugs can be directly purchased from the market without proper prescription which urges a proper policy in the country for the rational use and selling of drugs. In Countries having policies to control drug prescription, there's evidence of decline in use of antimicrobials and their resistance rates<sup>25</sup>. Another reason for increase in antimicrobial resistance globally and specially in Asia is extensive use of antimicrobials in animal food<sup>26</sup>. The health care providers must choose proper antimicrobial agent through authentic laboratory investigations rather than empirical treatment for these infections as well as public awareness is needed to discourage misuse and self-medication to limit antimicrobial resistance and health care burdens. New IDSA guidelines suggest using trimethoprim-sulphamethoxazole, nitrofurantoin and Fosfomycin as first line treatment for acute uncomplicated cystitis and advocate that fluoroquinolones should not be used for acute cystitis and can be reserved for complicated cases<sup>27</sup>.

## CONCLUSION

The prevalence of ESBL producing E.coli is increasing day by day therefore, decreasing the drug susceptibility and increasing resistance pattern. Fluoroquinolones should not be used as first line treatment in UTIs. The use of antibiotics in animal food for their growth should also be limited, as it has positive correlation with increasing resistance to antibiotics. New strategies need to be defined properly for prescribing as well as selling of these drugs to further limit the resistance patterns. Infection control units need to be developed in every tertiary care hospital to guide clinicians and health care



providers in selection of proper antimicrobial agents for specified infections.

#### Author's Contribution:

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 Revisiting Critically: Shandana Altaf, Tayyaba Basharat  
 Final Approval of version: Shandana Altaf

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# Postmortem Interval Estimation by Sturner's Equation Based Upon Vitreous Potassium Level

Postmortem  
Interval &  
Vitreous  
Potassium

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## ABSTRACT

**Objective:** To determine the level of postmortem vitreous Potassium and to correlate it with known postmortem interval by using Sturner's equation and develop a new equation if the above mentioned equation does not work in our set up.

**Study Design:** Confirmatory Analytical study

**Place and Duration of Study:** This study was conducted at the medicolegal autopsies in the Mortuary of King Edward Medical University, Lahore and samples were analyzed in the Pathology Department of same institution from December 2012 to May 2013.

**Materials and Methods:** 102 samples were obtained just before the commencement of autopsy. Cases with known cause and time of death were included in the study. Head injury, unknown, putrefied and poisoning cases were not included. Sample collection took 06 months. Relevant information were collected on a detailed Proforma for each case.

**Results:** Linear correlation between vitreous potassium level and time since death ( $r=0.428$ ,  $P<0.001$ ) was significant. An Ordinary Regression equation was developed which measured more accurate PMI as compared to other well-known equations and seemed to be a more appropriate model for our settings.

**Conclusion:** Our analysis has shown that the formula (equation number 5) developed in this research is comparatively more helpful for our setup than other well-known formulae for the estimation of PMI.

**Key Words:** Postmortem Interval (PMI), Vitreous Humor, Potassium, Ordinary Regression Equation, Inverse Regression Equation, Sturner's equation.

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## INTRODUCTION

It is the duty of police officer under section 174 CrPC to investigate death under suspicious circumstances.<sup>1</sup> Authorized Medical officers are asked to perform medicolegal autopsy and give the opinion regarding time since death besides fatal period and cause of fatality. After death numerous chemical variations occur in different fluids in a sequential way till the body is totally fragmented.<sup>2,3</sup> Vitreous potassium concentration is known to be widely used bio marker in the estimation of time since death.<sup>2</sup>

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Many researchers have highlighted a linear relationship between the postmortem interval and vitreous potassium level.<sup>4</sup>

After death, cell membrane of retinal cells converts into a semi permeable. Consequently, potassium starts to come out into vitreous humor steadily up to 120-125 hours after death. This potassium leakage appears to provide a form of biological clock that provides a mean to assess time since death.<sup>5,6</sup> Many formulae are available to estimate the relation between the vitreous potassium and the postmortem interval.<sup>7</sup>

Sturner conducted a study on 91 autopsies and noticed a linear rise in Vitreous potassium. On the basis of his data he proposed a formula to find out postmortem interval.<sup>6,8</sup>

Death Time [Hrs] =  $7.14 [K^+ \text{level (mEq/L)}] - 39.1$

In our study Postmortem interval is calculated through the Sturner's equation by using potassium level in vitreous humor<sup>5,8,9</sup> and if it is not applicable in our setup then develop our own equation base upon our own demographics. Thus, the following are the objectives of this study.

### Research Objectives:

- 1- To find out vitreous Potassium level
- 2- To use Sturner's equation in estimation of postmortem interval (known); and

- 3- To develop a new equation if the above mentioned equation does not work in our set up.

## MATERIALS AND METHODS

102 vitreous Potassium samples from the mortuary of KEMU, Lahore and analyzed in Pathology Department by Auto analyzer. Sampling was started from 20<sup>th</sup> December 2012 and continued up to 15<sup>th</sup> May 2013. The postmortem interval range was from 5 hours and 30 minutes to 36 hours.<sup>10</sup> The causes of the death included firearm injuries, asphyxial deaths, blunt and sharp edge weapon injuries, and complication arising from myocardial diseases. All the dead bodies were grouped into four groups depending upon the time since death. So group I was with Postmortem interval of 0-12hrs, group II 12.01-24hrs, group III 24.01-36hrs and group IV more than 36hrs.

Scleralpuncture was performed for each sample just before autopsy by retracting the lid near the outer canthus of left eye. 20 gauge needle attached with 10ml syringe was used. Needle tip was kept directed toward the globe center. Procedure was carried out with care to avoid any damage to the retina.<sup>3,11</sup>

In most of the cases 2-3 ml of fluid was collected. Normal saline was reintroduced to restore the tension in the globe for cosmetic reasons. Clear samples not containing any piece of slough tissue contamination were used. Samples were kept at -20°C temperature before analysis.<sup>12-15</sup>

**Inclusion Criteria:** Dead bodies with known cause and time of death.

**Exclusion Criteria:** Putrefied dead bodies, poisoning cases, damaged eyes due to injury and unknown dead bodies were not included in the study.

## RESULTS

In the present study data of 102 cases were obtained. In all these cases exact death time or postmortem interval was known. Data analysis was carried out on SPSS statistical software version 16. Mean PMI in hours was  $16.35 \pm 5.20$  hours and range was 5.30 hrs. to 32 hrs. Mean of the potassium was  $7.10 \pm 2.15$  mEq/L and range was 1.7 to 14.7 mEq/L. Correlation between potassium and PMI was significant ( $r=0.4280$ ,  $P<0.001$ ). Male cases were 81.37% and females 18.63% only.



Figure No.1: Obtaining vitreous humor for analysis<sup>6</sup>

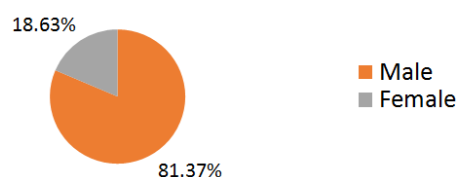


Figure No.2: Gender Distribution of the study cases

The main causes of death in studied cases were Firearm Injuries (FAI), Asphyxia (AD), Blunt Weapon Injury (BWI), Cardio vascular Diseases (CVD), and Sharp Weapon Injury (SWI).

Statistical analysis also showed that vitreous potassium level significantly is not dependent upon cause of death generally.

Total cases were divided into four groups based upon time since death. However, the range of PMI was 5.30 to 32 hours so there were only following three groups shown in Table 2. The results indicate that the vitreous potassium level increases after death with the passage of time.

A wide range of age distribution was also observed in the studied cases and range was 14 years to 70 years. It had no significant effect on vitreous potassium level. Scatter plot was used to display the relation between PMI and  $K^+$  values. Estimated regression line for PMI in hours by the Direct Method (Ordinary Regression) with graph is given in equation shown here:

$$PMI(Y) = 1.036 K^+(X) + 8.973$$

Estimated PMI (in Hours) was also calculated by the Inverse Regression Method as, the fitted line of  $K^+$ , when PMI was taken as independent variable. Estimated regression line for potassium level  $K^+$  is given in equation given below

$$K^+(Y) = 4.225 + 0.1768 PMI(X)$$

$$PMI(X) = -23.90 + 5.66 \times K^+(Y)$$

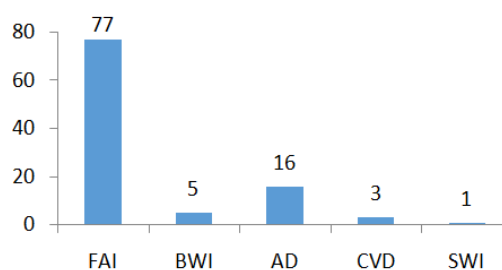


Figure No.3: Distribution of the studied cases based on the cause of death

### Application of Sturmer's and Regression Equations:

All the vitreous  $K^+$  values of the samples were used to determine PMI by utilizing both Regression Equations (Ordinary and Inverse) and Sturmer's Equation. The PMI in most of the cases was very wrong with inverse regression and Sturmer's equations. Whereas with

ordinary regression equation not even a single calculation of PMI was in negative and the deviations between the estimated PMI and actual PMI were much less than 06 hours in more than 80% samples. The mean error of the estimated PMI for with all three equations is given in Table 3.

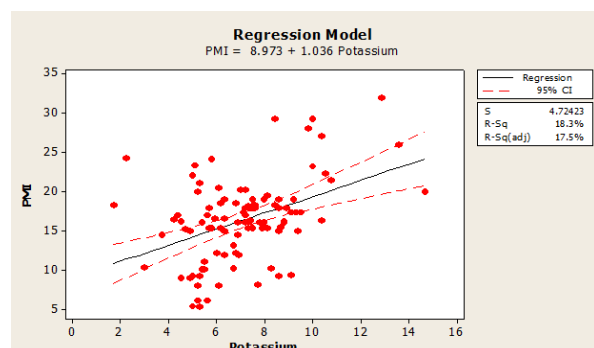


Figure No. 4: Regression Model for PMI

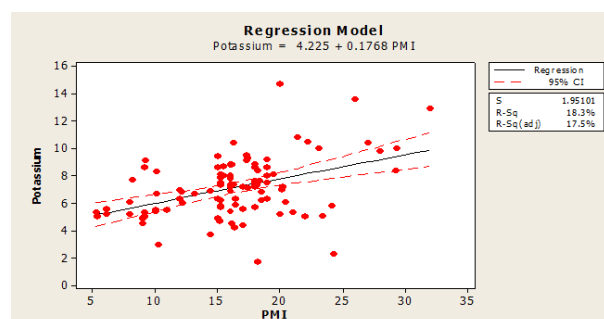


Figure No.5: Regression Model for Vitreous Potassium Level

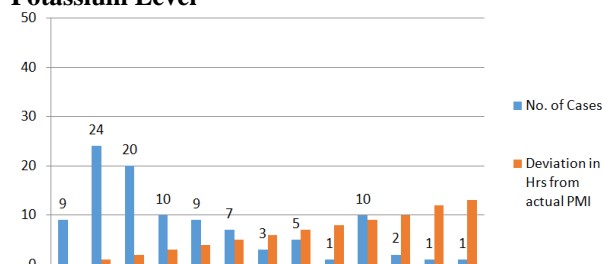


Figure No.6: Deviations (in hours) between estimated PMI and actual PMI utilizing the vitreous  $K^+$  by Ordinary Regression Equation

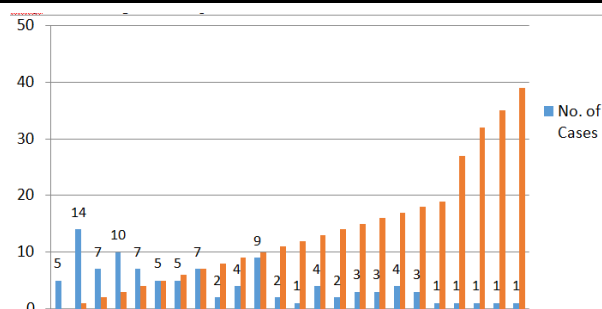


Figure No.7: Deviations (in hours) between estimated PMI and actual PMI utilizing the vitreous  $K^+$  by Inverse Regression Equation

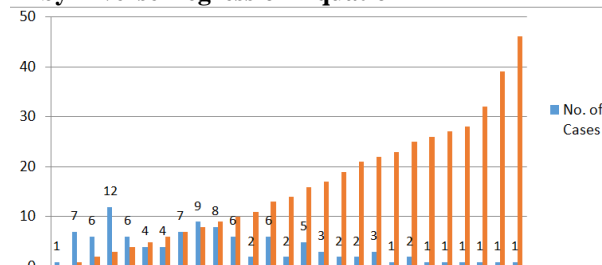


Figure No.8: Deviations (in hours) between estimated PMI and actual PMI utilizing vitreous  $K^+$  by equation of Sturmer

Table No.1: Vitreous Potassium level in male and female cases

Distribution of Cases based on Gender				
Sex	No of Cases	Range $K^+$ (mEq/l)	Mean $K^+$ (mEq/l)	SD
Male	83	1.73 - 10.4	6.84	1.76
Female	19	2.26 - 14.7	8.27	3.16
Statistical Analysis				
Comparison	t value	p value	Significance	
Male & Female	1.902	$p < 0.05$	Significant	

Effect of sex was significant on the levels of vitreous  $K^+$  (higher in females).

The margin of mean error with Ordinary Regression and Inverse Regression is Zero. (The regression model has the basic first assumption that mean of the error should be zero. In the Table 3, for equation of Sturmer, mean of the error is not equal zero. So Ordinary Regression and Inverse Regression Model seem to be a better good equations according to this analysis.

Table No.2: Distribution of Cases based on PMI

Distribution of Cases based on PMI						
S No	TSD / PMI	No of Cases	Percentage of Cases	Range $K^+$ (mEq/l)	Mean $K^+$ (mEq/l)	SD
Group I	0-12 Hours	19	18.63%	3 - 9.1	5.89	1.54
Group II	12.1 to 24 Hours	77	75.49%	1.73 - 14.7	7.13	1.96
Group III	24.1 to 36 Hours	6	5.88%	8.4 - 13.6	10.85	1.99
Statistical Analysis						
Comparison		t value	p value	Significance		
Group I & Group II		2.958	$P < 0.005$	HS		
Group I & Group III		5.6	$P < 0.005$	HS		
Group II & Group III		4.421	$P < 0.005$	HS		

**Table No.3: Descriptive Statistics of Errors**

Descriptive Statistics of Errors		
	No. of Cases	Mean
Error due to Ordinary Regression	102	.0025
Error due to Inverse Regression	102	.0215
Error due to Sturmer equation	102	4.6492

Ordinary Regression, Inverse Regression and Sturmer's Equation were used to estimate the PMI by utilizing vitreous  $K^+$  values.

In case of Ordinary Regression Equation, 82% cases had 06 hours deviations from real PMI (Figure 6). Vitreous  $K^+$  rise was fairly consistent in early hours of postmortem interval but scatter range increased after 20 hours. Moreover with this equation not even a single case of estimated PMI was in negative.

The inverse regression equation use with all the samples showed deviations of -14 to 40 hours from the actual PMI. These deviations were quite erratic and depicting no relation with the actual PMI. The estimated PMI was negative for four cases (as it can't be so).

With equation of Sturmer estimated PMI was in negative for twenty two cases (as it cannot be). In most of the cases either overestimation or underestimation of PMI showed no comparison with real PMI. Range of deviations was -27 to 53 hours from the real PMI.

## DISCUSSION

During criminal investigation of death, the authorized medical officer (working in the ministry of health) conducting autopsy has to find out the cause and manner of death and probable estimate of the postmortem interval. Postmortem vitreous humor is stable fluid as it is inert, isolated and protected from sudden biochemical changes taking place in the body and process of putrefaction after death.

Postmortem vitreous potassium showed a fairly linear increase with the passage of time. Potassium rise was consistent during the early hours and scatter range increased after 20 hours. Same pattern of PMI vitreous potassium rise is seen in various studies.<sup>8,12,14-20</sup>

Significant effect of gender variation was observed on the levels of potassium. Male cases showed the mean vitreous potassium level of 6.84 mmol/l; whereas, the female cases showed the mean vitreous potassium level of 8.27 mmol/l - slightly higher vitreous potassium levels were observed in the female cases.

The data analysis of the female cases revealed that the cause of death in more than 60% cases was asphyxia. The analysis results showed that the vitreous potassium

level is fairly higher in asphyxial death cases (7.63 mmol/l). Our study included 19 female samples.

The slopes of line of linear regression for PMI and postmortem vitreous potassium rise in literature varies and range is 0.14 mmol/L per hour<sup>19</sup> to 0.332 mmol/l per hour.<sup>20</sup> The zero hour intercept vary from 4.2 to 8.0 mmol/l is reported.<sup>21</sup> In the present study, the rise of regression slope line is 0.1768 mmol/l per hour and it is in close agreement to the slope line of 0.17 mmol/l per hour which was obtained in a combined original data for vitreous potassium of six studies.<sup>4,22-26</sup> It is believed that the regression line slope should be relatively steeper. Relatively flat slopes have tendency to give higher readings for postmortem interval.

The mean error of Ordinary Regression and Inverse Regression was almost Zero thus fulfilling the first basic assumption for regression model,  $E(e) = 0$ . It was not zero for Sturmer's equation. Therefore, Ordinary Regression equation appeared to be a more appropriate model for our demographics.

## CONCLUSION

Postmortem vitreous humor biochemistry is significant. Postmortem vitreous  $K^+$  level has important role in determination of PMI. Thus, it can solve the major problem faced by the authorized medical officer conducting autopsy to precisely estimate the postmortem interval of the deceased, assist the Police investigation and the courts of law in finalizing the just verdict.

This study showed that the Ordinary Regression Equation is relatively more helpful for our setup than other well-known formulae for the estimation of PMI.

### Author's Contribution:

Concept & Design of Study:	Nasreen Akhtar
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Data Analysis:	Nasreen Akhtar
Revisiting Critically:	Azhar Masud Bhatti, Wardah Anwar, Anam Iqbal
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**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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