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**ABSTRACT:** It should be structured, not more than 250 words, briefly mentioning under following sub-headings Objectives, Design, Place and duration of study, Methods, Results and Conclusion. Abstracts should be followed by 3-5 MeSH (Medical Subject Headings) words. Use appropriate terms to increase searchability of your study.

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**RESULTS:** Emphasize or summarize only the most important observations. Give numeric results not only as derivatives (for example, percentages) but also as the absolute numbers from which the derivatives were calculated, and specify the statistical significance attached to them giving degree of freedom, test of significance value and p-value (in brackets) if any. Do not duplicate data in graphs and tables if already mentioned in text.

**DISCUSSION:** The discussion should begin with a summary of the main results. These are then discussed



with results of other published studies either supporting or refuting your results. Any new findings of the research should be emphasized and the relevance should be stated. These can be used for future research or clinical practice. Details of methodology or introduction should not be included in the discussion. Do not repeat in detail data or other information given in other parts of the manuscript, such as in the introduction or the results section. Limitations of the study should be stated at the end of the discussion in a separate paragraph.

**CONCLUSION:** It should be provided under separate headings and highlight new aspects arising from the study. It should be in accordance with the objectives.

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## COMPARISON OF SERUM IRON AND FERRITIN STATUS IN BREAST FED AND BOTTLE FED INFANTS

Sajjad Haider

*Services Institute of Medical Sciences (SIMS) Lahore*

### ABSTRACT

**Aims and Objectives:** This study was conducted to see the iron and ferritin status in breast fed and bottle fed infants during weaning period. Second aim was to compare iron status between these groups and promote awareness regarding breast feeding.

**Methodology:** It was convenient non-probability study.

**Study population:** This study comprised of 90 subjects ranging from 6 months to 1 year of age of either sex.

**Subjects and methods:** It was a conventional and cross sectional study conducted on infants of either sex from 6 months to 1 year of age from preventive paediatric deptt. of Jinnah, Mayo and Children and Ganga Ram Hospital, Lahore. 30 cases were included in group I labeled as breast fed group, 30 in group II A (formula milk group) and 30 cases were included in group II B (animal milk fed group)

**Criteria:** Healthy infants (declared by concerned prevented pediatric department were included) on breast feed and weaning. Sick infants with any acute or chronic illness, those on iron supplements and those who stopped breast feeding after 6 months were not included.

**Data collection:** It was based on a Performa designed for this purpose and laboratory investigations.

**Results:** Serum iron in breast fed group was in the range of 87-102 $\mu\text{g}/\text{dl}$  with the mean of 94.43 (SD 3.68) while in the animal milk fed group and formula milk fed group it was in the range of 34-45 $\mu\text{g}/\text{dl}$  and the mean was 38.13 (SD 2.37) ( $P<001$ ) and 98-110 $\mu\text{g}/\text{dl}$  the mean was 104.0 (SD 3.06) respectively. Serum ferritin in breast fed group was 100-145 $\mu\text{g}/\text{dl}$  mean of 110.2 (SD 4.73), while in animal milk fed group and formula milk fed group it was 30-58 $\mu\text{g}/\text{dl}$  with the mean 43.83, SD 7.45 ( $P<001$ ) and 100-150  $\mu\text{g}/\text{dl}$  with the mean of 133.60 (SD 6.14) ( $P<001$ ) respectively.

**Conclusion:** Serum iron and ferritin levels in breast fed group were a little lower than formula fed group. This shows adequate iron supply in breast milk and no need of iron supplementation in breast fed infants. Moreover, much lower levels of iron and ferritin in animal milk fed infants is indicative of poor iron supply in commonly used animal milk (buffalo and cow). So breast feeding should be encouraged as human milk gives ample stores of iron for infants.

The present number of cases, in developing countries, for iron deficiency anemia in one- to three-year-old children is increasing. The real relationship between iron deficiency anemia and its effects on growth is not well understood, but these effects do not manifest until iron deficiency becomes marked and chronic enough to produce anemia. At that moment, treatment with iron can cure the anemia and replenish iron sufficiently, yet the poorer developmental functions remain persistent. Hence strategy should be to focus on the primary prevention of iron deficiency. In infancy, iron deficiency can be prevented by taking measures like complete avoidance of cow's milk, initiation of iron supplements at earlier age i.e. four to six months of age in breastfed infants, and using iron-fortified formula breastfeeding is discontinued. Low-iron formula should not be avoided. In the second year of life, iron

deficiency can be prevented by use of a diversified diet that is rich in sources of iron and vitamin C, minimizing cow's milk supplementation to minimal level i.e. less than 24 oz per day, and providing a daily iron-fortified vitamin. For those infants and toddlers who did not receive primary prophylaxis should be screened for iron deficiency. Screening is performed at nine to 12 months, six months later, and at 24 months of age. The hemoglobin/hematocrit levels determine degree of anemia in persons with enough iron deficiency to be anemic. Screening done with parameters eg erythrocyte protoporphyrin or red-cell distribution width will identify earlier stages of iron deficiency. A positive screening test is an indication for a therapeutic trial of iron, which remains the definitive method of establishing a diagnosis of iron deficiency<sup>(1)</sup>. Iron is fundamentally required by the body to form adequate number of

normal red blood cells. The key protein in red cells to which oxygen(O<sub>2</sub>) is attached is called haemoglobin. Haemoglobin is iron rich biochemical. Iron is also needed by other cells, especially muscle cells, which carry another oxygen binding protein myoglobin. Iron deficiency is the most prevalent single deficiency state on a worldwide basis. It is important economically because it diminishes the capability of individuals who are affected to perform physical labor, and it diminishes both growth and learning in children. In healthy people, the body concentration of iron (approximately 60 parts per million [ppm]) is regulated carefully by absorptive cells in the proximal small intestine, which alter iron absorption to match body losses of iron. Persistent errors in iron balance lead to either iron deficiency anemia or hemosiderosis. Both are disorders with potential adverse consequences<sup>(2)</sup>. Iron deficiency is the most common nutritional deficiency in the world. Infants and toddlers are especially susceptible because of their rapid growth, increased demands for iron, and variable dietary intake.. Iron deficiency is usually readily treated with dietary iron supplementation<sup>(3)</sup>. The risk of iron deficiency and iron deficiency anaemia appears to be greater in infants fed on whole cow's milk during first year of life. There is conflicting evidence regarding etiology of this phenomenon but the main postulated mechanism include the fact that whole cow milk is a poor source of iron and the possibility of decreased iron intake in alternate form is associated with poor absorption and bioavailability<sup>(4)</sup>.The cow's milk iron content is lower than human milk 1.5 mg versus 1.0 mg<sup>(5)</sup>. Adequate supplement feeding may not supply enough iron for infant who fed whole cow milk at age of 6 month<sup>(6)</sup>. Breast milk for 1-2 years supplies better source of food than the traditional weaning diet<sup>(7)</sup> and this is in line with Holy Quran (Surah Nisa) which directs mothers to feed their babies for two years (The Holy Quran, Sura Nisa). Despite the high incidence of iron deficiency, research in this area has been limited, perhaps, because iron deficiency is accepted as a relatively benign condition. However, improved understanding of food-iron absorption and availability of more effective fortification now makes it important to know the cost of iron deficiency in respect to ill health<sup>(8)</sup>.

### SUBJECTS AND METHODS

Present study comprised of 90 subjects and divided into three groups. Group I included 30 cases on breast feeding i.e. mostly on breast milk and weaning within 24 hours, 2-3 feeds other than human milk .Group IIA included 30 cases on formula milk and weaning. Group IIB comprised of 30 cases on animal milk and weaning. Apparently healthy infants (declared by respective preventive pediatrics department) were included in each group according to the type of feeding. The sick infants with any acute or chronic illness, on iron supplements or had stopped breast feeding after 8 months were not included in the study: Tests were performed at Postgraduate Medical Institute and Allama Iqbal Medical College, Pathology Department laboratory with due permission. Estimation of serum iron, TIBC and serum ferritin was done by ELISA. Different statistical tools were also applied such as number(n),mean,standard deviation(SD),t test and probability value(P value).

### RESULTS

Total 30 cases were included in each group designated as Group I (breast milk fed), group IIA (formula milk fed) and group IIB (animal milk fed) respectively. By estimation of serum iron, serum ferritin and TIBC following results have been obtained.

### DISCUSSION

In this study the iron level of breast fed infants (Group I) was found to be 87-102 µg/dl which is in accordance with the findings of <sup>(9)</sup>. Their studies showed iron range of 90-110 µg/dl and TIBC between 285-300 µg/dl. According to<sup>(10)</sup> the iron level of formula fed infants was higher than that in breast fed infants which is also shown in the present study. Serum iron level was in normal range along with TIBC in breast fed infants which is agreement with study by<sup>(11)</sup>. Infants on cows milk and animal milk had lower iron levels than that of breast-fed group while TIBC was raised, which is consistent with findings of this study (in group IIB). In this study serum ferritin was found to be higher in infants fed with fortified formula milk which is synchronous with finding of Lonnerdal and<sup>(12)</sup>. In their study they found serum ferritin concentration higher than the breast-fed groups and animal milk fed group, amongst infants of the similar age group. Compa-

parison of mean plasma ferritin concentration in iron

*Breast fed group (Group I)*

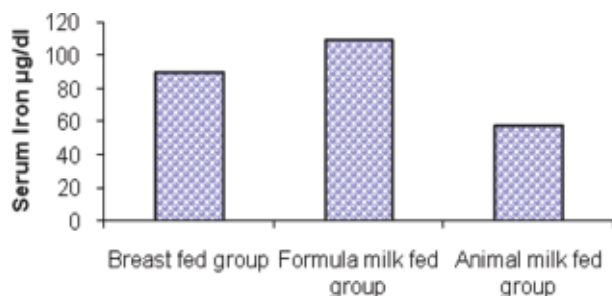
	Serum Iron	Serum TIBC	Serum Ferritin
Range	87-102 µg/dl	280-302 µg/dl	100-145 µg/dl
Mean	94.43	293.63	110.20
Standard deviation	3.68	4.73	8.60

*Formula milk fed group (Group IIA)*

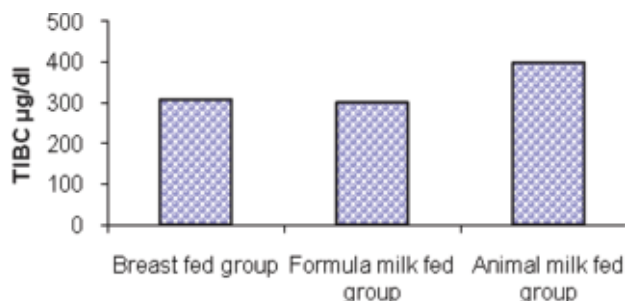
	Serum Iron	Serum TIBC	Serum Ferritin
Range	98-110 µg/dl	280-300 µg/dl	100-150 µg/dl
Mean	104.00	289.33	133.60
Standard deviation	3.06		

*Animal milk fed group (Group IIB)*

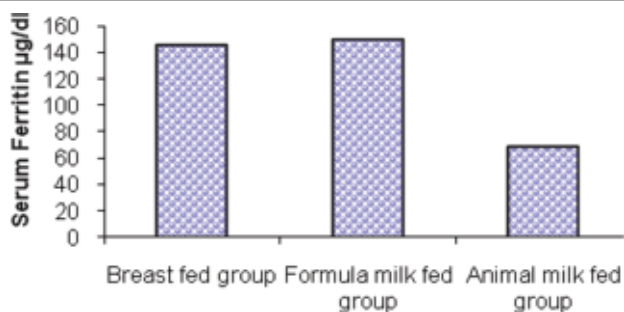
	Serum Iron	Serum TIBC	Serum Ferritin
Range	34-45 µg/dl	339-400 µg/dl	30 -58 µg/dl
Mean	38.13	386.60	43.83
Standard deviation	2.37	10.34	7.45



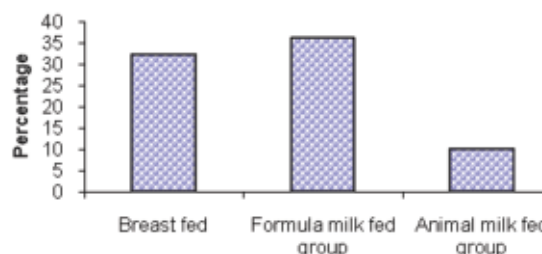
**Fig.2: Serum iron in three groups (mean values)**



**Fig.3: Serum TIBC in three groups (mean values)**



**Fig.4: Serum ferritin in three groups (mean values)**



**Fig.5: Transferrin saturation in three groups (mean values)**

fortified (supplemented) and nonfortified (non-supplemented) e.g. animal milk fed, infants was higher<sup>(13)</sup>, which is also seen in this study. The value of iron and ferritin which is comparatively higher in formula milk fed group may be due to iron content variation as some formula milk contain more than 6.7 mg/L of iron (more than average). Similarly low iron content of cow's milk than buffalos milk contributes to low iron status in cow's milk fed infants (buffalo milk contains 37.2% more iron than cow's milk)<sup>(14)</sup>. Although iron content of human milk is low but its bioavailability is 100%<sup>(15)</sup>. Interestingly parents of breast-fed infants need not worry, research in iron status of breast-fed infants documents adequate stores for well over 6 months of age<sup>(16)</sup>. In conclusion the study highlights iron status of breast milk fed infants which is higher than animal milk fed infants and equal to or slightly lower than fortified formula milk fed infants. Further research is required in this field, keeping in view feeding and dietary practices prevailing in our country, socioeconomic conditions of the people at large and iron deficiency prevalence in infants and toddlers.

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## AN AUDIT OF HIGH RISK PATIENTS REFERRED IN CRITICAL CONDITION TO LABOUR ROOM OF JINNAH HOSPITAL LAHORE

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### ABSTRACT

**Objective:** To highlight the factors responsible for higher maternal morbidity and mortality in patients referred to JHL labour room in critical condition.

**Study Design:** Prospective Descriptive Study.

**Methodology:** It was a prospective descriptive study conducted in Gynae unit I Jinnah Hospital Lahore for a period of one year i.e. 1-3-16 to 28-2-17. All patients who were referred in critical condition in emergency of Gynae unit I after initial management at lower levels of healthcare were included in the study.

**Results:** During the study period of one year there were 113 patients who were referred in critical condition. In majority of these patient (35%), the primary care providers are Traditional Birth Attendant. The common cause of referral in critical condition was life threatening haemorrhage and hypertensive disorders of pregnancy. Emergency Laprotomy was done in 35 of these referred patients (31%). ICU care was required in 29 patients and EUA and repair of genital tract tears was done in 22 patients. However Emergency C-section was required in 19 patients and postpartum hysterectomy was done in 8 patients.

**Conclusion:** Childbirth is a physiological process but complications can arise anytime. The TBAs should be trained in Emoc and they should be able to recognize early danger signs for timely referral. Strengthening and improving quality of services, infrastructure and availability of trained manpower at peripheral health centers will definitely reduce maternal & perinatal morbidity & mortality

Obstetrics patients are usually healthy and free from co morbidities.

However pregnancy and childbirth is not free from complications, some of which if not diagnosed and managed timely may prove to be life threatening. Identification of high risk cases and their prompt referral to a centre well equipped to tackle such cases may improve fetomaternal outcome.

Maternal mortality is one of the greatest health and development challenges facing the world, especially in developing world. Two of the most significant contributory factors to maternal mortality are non availability of trained health professional at the time of delivery and lack of access to effective referral/support services. Delivery conducted by untrained birth attendants has 4.67 times higher

mortality rate as compared to one conducted by SBAs. Recent figures indicate that worldwide 303,000 women die in pregnancy and childbirth each year.<sup>1</sup> Every day, approximately 830 women die from preventable causes related to pregnancy and 99% of these deaths occur in developing countries.<sup>2</sup>

Due to lack of awareness and absence of regular antenatal care, the critically ill patients are referred late and sometimes in moribund conditions with multiple organ damage. Timeliness and appropriateness of referral is an important factor in the ultimate outcome of the patients. Linking the primary, secondary and tertiary levels of care are an essential element of primary health care. A referral should rather be conceptualized as an active process which begins at door step of the patient's household and which in theory would end at the same place after transitory journey to referral facility. It offers women some degree of health care at every level of

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health care system while linking the different levels through an established communication transport system.

Pakistan has been struggling to make improvements in maternal and neonatal health including a nationwide health infrastructure with first level care facilities and community based health workers for providing maternal and child health care to the rural population. Despite a large national and donor investment national survey and research evidence from several rural regions of Pakistan suggests that the utilization of maternal care through community midwives is still very low, contributing to high MMR and poor progress in other maternal health indicators.<sup>3</sup>

The emergency admissions to tertiary health care centre contain large number of patients referred from rural areas. The condition of patient on admission to such referral hospitals and institutions reflects the quality of health services in that particular area, availability of transport facility and efficiency on the part of medical personnel in screening high risk patients who require referral to better equipped and specialized institution.

So the present study was undertaken to evaluate cases which were referred in critical condition and to highlight the importance of timely referral in such cases by the primary care.

## MATERIALS AND METHODS

It was a prospective descriptive study conducted in Gynae unit I Jinnah Hospital Lahore for a period of one year. All patients who were referred in critical condition in emergency of Gynae unit I after initial management at primary and secondary healthcare were included in the study. A detailed proforma was designed to collect information on demographic characteristics, reason for referral, condition on arrival and primary care provider. Management of patient was documented whether conservative or interventional. Duration of hospital stay, need for blood transfusions and final outcome was noted. Descriptive statistics like percentages are used for analysis. The comparison was made between these findings and conclusions were drawn after comparing and discussing with similar type of work carried out by other authors.

## RESULTS

During the study period of one year there were 113 patients who were referred in critical condition. It was found that majority of patients were referred from district Okara, Sahiwal, Bahawalnagar, Qasur and Lahore. However common areas of referral from

Lahore are Township, Thokar Niaz Baig, Chung,

**Table 1:** Age range of patients

Age Range	Patient No.	Percentages<
<20yrs	10	9%
20-30yrs	52	46%
30-40yrs	37	33%
>40yrs	14	12%

kangan Pur and KotRhadaKishan.

46% of patients were in the age group of 20-30yrs(table:1).The maximum number of patients were multigravida show ever 27% of patients were primiparas. In majority of these patients (35%), the primary care providers were Traditional Birth Attendants (table 2)

Emergency Laprotomy was done in 35 patients

**Table 2:** Primary Care Providers

Primary Care Provider	Patient No.	Percentage
TBA	40	35%
LHV /CHW	10	9%
BHU/THQ	9	8%
DHQ	33	29%
Secondary Care	21	19%

(31%). On laprotomy 19 patients had uterine rupture, 11 patients had sepsis and gut injury was found in 5 patients. ICU care was required in 29 patients (26%) and EUA and repair of genital tract tears was done in 22 patients (19%). However Emergency C-sectionwasrequired in 19 patients and postpartumhystrectomywasdone in 8 patients.

## DISCUSSION

Jinnah Hospital is 1500 beaded tertiary care hospital in south of Lahore.

Referred cases from peripheral areas of Lahore district and other neighboring district form a major bulk of patients. Delayed referral of critically ill patients by community health workers (TBA, LHV, CMW), Private clinics and local public sector facilities (BHU, RHC, TH ,DHQ) put a great burden on the limited resources of tertiary care hospitals.

During the study period of one year around 113 patients were referred in critical condition. Overall age distributions in majority of patients were between 20-35years of age, 87% of patients were of obstetrics and 13% were of gynaecology. 70% of patients were multigravida. Similar was the finding

**Table 3:** *Diagnosis On Arrival*

Diagnosis On Arrival	Patient No.	Percentage
PPH	29	26%
Hypertensive Disorders	20	17%
APH	17	15%
Pregnancy with other medical disorders	14	12%
Induced Septic	12	11%
Obstructed Labour	10	9%
Post-Operative Complications	8	7%
Transfusion Reactions	3	3%

of R Vet al where 82.4% of referred cases were of obstetrics.<sup>4</sup>

Sources of referral were TBAs in 40 patients and DHQ hospitals in 33 patients (table 1). Most of the studies in different tertiary care hospitals have similar data and TBAs or family members attend even worldwide 70% of births.<sup>5</sup> Another study conducted in Lahore on referred cases after trial of labour showed that about 90% of patients never had any antenatal checkup and 94% were under care of TBAs and LHVs.<sup>6</sup> In a study conducted in Liaquat University Karachi on iatrogenic medical and surgical complications resulting in ICU admissions among obstetric patients also showed maximum referrals by TBA/LHV (41.17%).<sup>7</sup>

Pakistan Demographic and Health survey (PDHS) 1991 and 2006 data reveals that more than 50% of women prefer TBAs assistance for delivery.<sup>8</sup> TBAs play a significant role in maternal and child health care delivery system and are likely to continue to be major resource for the foreseeable future.<sup>9</sup> Most of these primary care providers in rural areas are not trained in Emoc and are unable to recognize high risk pregnancies so that timely referral could be made to a health facility. Another major cause is lack of professional ethics among service providers perilously compromising the quality of healthcare in Pakistan.

The common indications for referral in this study was Haemorrhage (41%), Hypertensive Disorders of Pregnancy (16%), Sepsis (11%), Obstructed labour (9%). In a study conducted in Uttarakhand India most patients in antenatal period were referred with Pregnancy induced hypertension and its complication.<sup>10</sup> Among postnatal patients PPH was the commonest reason for referral. Similar results were shown in an audit of obstetrics referrals to Abbasi Shaheed Hospital, Karachi.<sup>11</sup>

Most of the patients presented in shock with primary PPH, mostly requiring either exploration under anesthesia or laprotomy. On exploration

uterine rupture was found in 19 patients and Caesarian Hystrectomy had to be done in 8 patients because of failure of conservative measures to control hemorrhage.

## CONCLUSION

Childbirth is a physiological process but complications can arise anytime. Health education and awareness by mass media and non-government organizations can improve the health and social status of women in rural areas. The TBAs should be trained in Emoc and they should be able to recognize early danger signs for timely referral. Strengthening and improving quality of services, infrastructure and availability of trained manpower at peripheral health centers will definitely reduce maternal & perinatal morbidity & mortality.

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## FREQUENCY OF COMPLICATIONS AMONG CHRONIC KIDNEY DISEASE PATIENTS ON DIALYSIS

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### ABSTRACT

**Background:** It is widely accepted that patients chronic kidney disease (CKD) those who are on dialysis are at increased risk of infection. Possible complications may include low blood pressure, muscle cramps, irregular heartbeat, nausea, vomiting, headache and infections.

**Objective:** To find out frequency of complications of dialysis and its relationship with demographic and clinical variables

#### Subject and Methods:

Study design	Descriptive case series
Study duration	June 2015 December 2015
Sample size	35 CKD patients

**Data Collection and Analysis:** 35 patients of chronic kidney disease (CKD) were those fulfilling the inclusive criteria were selected from Nephrology Unit in tertiary care Hospital, Lahore. After informed consent frequency of complication and relate demographic and clinical factor were evaluated. Data was entered and analyzed in SPSS version: 19.0. Frequency and percentage were calculated chi-square test was used to compare complications among demographic variables with  $p < .05$  as statistical significance.

**Result:** A total of 35 selected patients were inducted in the study. 26 (74.3%) were on dialysis for less than 5 years and 9 (25.7%) for more than 5 years. 32 (91.4%) were suffering from chronic kidney disease. 3 (8.6%) were hepatitis B +ve and 26 (74.3%) were hepatitis C +ve. 12 (34.3%) became hepatitis C +ve after admission to hospital and 2 (5.7%) patient carried hepatitis B +ve, after having treatment in Bahria Hospital, Just 1 (2.85%) took hakeem medications for his treatment before coming to hospital. The association of duration of CKD with age, gender, hepatitis B +ve and hepatitis C +ve and hakeem medication was insignificant but risk of development of complications in patients of age more than 30 years and who were on dialysis for more than 5 years was significant ( $p=0.015$ ).

**Conclusion:** According to our study following factors Increasing age, duration of dialysis, duration of having chronic kidney diseases show increasing risk for development of the complications of dialysis.

**Keyword:** CKD, risk factor, dialysis, renal failure

Chronic kidney disease (CKD) is a complex disease impacting more than twenty million individuals in the United States. Progression of CKD is associated with a number of serious complications, including increased incidence of cardiovascular disease, hyperlipidemia, anemia and metabolic bone disease. CKD patients should be assessed for the presence of these complications and receive optimal treatment to reduce their morbidity and mortality. A multidisciplinary approach is required to accomplish this goal.<sup>1-3,12</sup>

As many as 25 million Pakistanis are suffering

from chronic kidney diseases (CKD) and Punjab has 19 % of such patients, threatening healthcare resources globally. Chronic dialysis may be indicated when a patient has symptomatic kidney failure and low glomerular filtration rate (GFR). During 1996 to 2008, there was a trend to initiate dialysis at progressively higher estimated GFR.<sup>4</sup> Risk factors for CKD include cardiovascular disease, diabetes, hypertension, and obesity. Hemodialysis was one of the most common procedures performed in U.S. hospitals in 2011, occurring in 909,000 stays (a rate of 29 stays per 10,000 population). There was an

increase of 68 % from 1997, when there were 473,000 stays. It was the fifth most common procedure for patients aged 45–64 years. The population of patients receiving dialysis is largely due to high prevalence of predisposing conditions such as diabetes and hypertension.<sup>8</sup> There were currently more than 240 million people with diabetes worldwide who were prone to kidney diseases. The prevalence of kidney diseases is increasing dramatically and the cost of treating chronic diseases represents a leading threat to healthcare resources worldwide.<sup>5,6</sup> Lack of registries makes an accurate estimation of the number of individuals needing renal replacement therapy (RRT) impossible. Published data are hospital-based or based on individual experience.<sup>7</sup> Reports prepared on the basis of those presenting to hospitals for RRT are likely to be significant underestimates. Many patients never come to medical attention. An Indian population-based study determined the crude and age-adjusted end stage renal disease (ESRD) incidence rates at 151 and 232 per million population, respectively. If validated in other parts of this region, it would mean that about 220,000–275,000 new patients need RRT every year in this part of the world. It is estimated that there are about 55,000 patients on dialysis in India, and the dialysis population is growing at the rate of 10–20% annually.<sup>1</sup>

Complications of dialysis include; low blood pressure (hypotension), muscle cramps, itching, sleep problems, anemia, bone diseases, high blood pressure (hypertension), fluid overload, inflammation of the membrane surrounding the heart (pericarditis), high potassium levels (hyperkalemia), access site complications, amyloidosis and depression<sup>9</sup> A potential serious complication in chronic hemodialysis patients is subclavian vein stenosis. One hundred and ninety patients, 61 with acute renal failure and 129 with chronic renal failure, underwent hemodialysis using a total of 302 subclavian vein catheters. Local hematomas and sepsis (seven events) were the only acute complications. Subclavian vein stenosis and/or thrombosis had occurred

and were shown in five of 44 patients who had arteriovenous access created distal to the venous outlet obstruction, resulting in the loss of three of five of these accesses.<sup>10</sup>

#### **METHODS:**

A total of 35 patients were selected from Nephrology Unit, in a tertiary care hospital, Lahore. This study was descriptive case series conducted during January to June, 2015. Informed written consent of each patient was taken. Patients having dialysis for more than three times per month were included. They were patients with male & female Stage 5 Chronic Kidney Disease Patients. Kidney diseases of first four stages were excluded. Sample Technique was non probability convenient sampling. A Structured questionnaire was developed to get related information (social, economic, demographic and confounders related to outcome variable i.e CKD). Data was entered in SPSS version 17. Frequency and percentages were calculated. Chi-square test was used to compare complications among demographic variables with  $p < .05$  as statistical significance.

#### **Objectives:**

To find out of complications among dialysis patients and its relationship with demographic factors.

#### **RESULTS:**

The present study was carried out among chronic renal disease patients in Nephrology Unit in tertiary care Hospital, Lahore. A total of 35 patients were inducted in the study. 10(28.6%) were male and 25 (71.4%) were female. 42.9% were illiterate 20% were below matric 14.3% was above matric and 22.9% were post graduate. 43.8% belongs to family having income less than Rs. 3000 per month. (Table-1) 74.3% were on dialysis for less than 5 years and 25.7% for more than 5 years. 8.6% have got hepatitis B. Out of these 2.9% were hepatitis B+ve after 4 months of dialysis and 5.7% after 2 months of



dialysis. Out of total 35 patients 5.7% have got hepatitis B+ve before coming to hospital and 94.3% after coming to hospital. 74.3% out of total 35 patients were hepatitis C +ve, 11.4% were hepatitis C + before dialysis and 34.3% were hepatitis C +ve

**Table 1:** Demographic and clinical profile of patients. (n=35)

Variables	Frequency	Percent
<b>Age</b>		
≤ 30	13	37.1
>30	22	62.9
<b>Gender</b>		
Male	10	28.6
Female	25	71.4
<b>Education</b>		
Ill literate	15	42.9
Below matric	7	20.0
Above matric	5	14.3
Post-graduation	8	22.9
<b>Income status</b>		
Rs: <3,000 / month	15	43.8
RS: >3,000 / month	9	56.2
<b>Duration of dialysis</b>		
< 5 years	26	74.3
> 5 years	9	25.7

before coming to hospital. The association of duration of CKD with age, gender, was insignificant but risk of development of complications in patients of age more than 30 years and who were on dialysis for more than 5 years was significantly ( $p=0.015$ ) more. (Table-2)

**Table 2:** Frequency of complication (n=35)

Complication	Yes	No
	Frequency (%age)	Frequency (%age)
Muscle cramps	18 (51.4)	17 (48.6)
Nausea, vomiting, headache	19 (54.2)	16 (45.8)
Irregular heartbeat	10 (28.5)	25 (71.5)
Fall in blood pressure	12 (34.2)	23 (65.8)
Infection Hepatitis B +ve	3 (8.6)	32 (91.4)
Infection Hepatitis C +ve	26 (74.2)	9 (25.8)

## DISCUSSION:

As 42.3% of patients found to have CKD were illiterate so increasing the awareness and training regarding self-care, 91.4% were suffering from

**Table 3:** Complications and demographic characteristics Cross tabular

Variables n=35	Yes		No		Chi-sq. P value
	Frequency	Percent	Frequency	Percent	
<b>Age</b>					$X^2=0.846$ $P=0.365$
≤ 30	5	38.4	8	61.6	
>30	12	54.4	10	45.6	
<b>Gender</b>					$X^2= 0.114$ $P=0.735$
Male	7	70.0	3	30.0	
Female	16	64.0	9	36.0	
<b>Education</b>					$X^2= 2.536$ $P=0.469$
Ill literate	12	80.0	3	20.0	
Below matric	4	57.1	3	42.9	
Above matric	3	60.0	2	40.0	
Post-graduation	4	50.0	4	50.0	
<b>Income status</b>					$X^2= 1.020$ $P=0.320$
Rs: <3,000 / mon	14	63.6	8	36.4	
RS: >3,000 / mon	6	41.1	7	58.9	
<b>Duration of dialysis</b>					$X^2= 0.296$ $P= 0.586$
< 5 years	19	73.0	6	37.0	
> 5 years	6	66.6	3	53.4	

chronic kidney disease. So Increase awareness among people about controlling their blood sugar levels and blood pressure can help prevent the kidney damage and obstruction.<sup>1</sup> According to the information gathered from the patients, they are not aware of the importance of exercise and balanced diet for healthy and normal functioning human organs. Moreover, they are using hakeem medication and OTC drugs without any prescription, leading to the irreversible kidney damage thus increasing duration of kidney disease which would increase risk of complication.<sup>11</sup> 102 patients with end-stage renal disease who underwent hemodialysis with dual-lumen cuffed catheters between 1 April 1995 and 1 January 1999. Forty-one patients (40%) developed 62 episodes of bacteremia (3.9 episodes per 1000 catheter-days [95% CI, 3.0 to 4.9 episodes per 1000 catheter-days]). Twenty-four catheters (39%) were removed immediately, and 38 (61%) were left in place during treatment. Only 12 (32%) of the 38 catheters were salvaged successfully. Salvage was less likely to succeed in patients with gram-positive bacteremia than in patients with gram-negative bacteremia, but this difference was not statistically significant ( $p=0.14$ ). Nine of the 41 patients (22%) who developed bacteremia had the following complications: osteomyelitis (6 patients), infective endocarditis (4 patients), and death (2 patients). Conclusions: Bacteremia frequently occurs in patients undergoing hemodialysis with dual lumen catheters.<sup>12</sup>

### CONCLUSION:

According to our study following factors, increasing age, duration of dialysis and duration of having chronic kidney disease, and development of Hepatitis B, Hepatitis C, increases chances of complications of dialysis.

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## A RETROSPECTIVE INSIGHT OF HEAD AND NECK TUMORS: AN EPIDEMIOLOGIC ASSESSMENT

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### ABSTRACT

**Introduction:** Head and neck tumors can lead to devastating cosmetic and functional deficits with resultant psychological, physical, and nutritional detriment. Despite recent advances in medicine, the overall survival for patients with head and neck cancer has remained static for the past 35 years.

**Objective:** This study aimed to determine the epidemiological characteristics of carcinomas of the head and neck in population, and the distribution of risk factors based on tumor locations.

**Material and Methodology:** It is a retrospective analysis of the data from January 2008 to March 2016. A total of 356 patients were taken into account.

**Results:** Epidemiological parameters and risk factors were obtained from a self-administered questionnaire, and tumor characteristics were obtained from clinical records. Among 356 head and neck cancers 147 oral cavity, 63 perioral, 60 scalp, 45 periorbital, 21 nose, 13 ear, 7 marjolin's ulcer. Most patients were males (78 %). Smokers (52 %) and betel nut/tobacco (16 %). 52% of the patients were from urban background and 48% from rural areas. Intra oral malignancy was more common in urban areas (71%) as compare to rural. While skin tumors were more common in rural area patients (80%) as compared to urban area patients. Tumor type was distributed as squamous cell carcinoma 200 (56%), basal cell carcinoma 93 (26%), recurrent tumor 14 (4%) dermatofibrosarcoma 14 (4%), adenocarcinoma 7 (2%), angiosarcoma 6 (2%), Carcinoma expleomorphic adenoma 6 (2%), Miscellaneous 16 (4%).

TNM Stage IV was 114 (32%), III was 135 (38%), II was 71 (20%) and I was 36 (10%). Three co morbidities were taken in to account 85 patients (24%) were hypertensive, 64 (18%) were diabetics, 35 (10%) had Hepatitis C and rest had no co morbidities.

**Conclusions:** Squamous cell carcinoma is the leading tumor type of head and neck malignancies. The distribution of these tumors differs between the sexes, with a higher proportion of oral cavity in men. Skin cancers were more strongly associated with rural areas, although less strongly associated with smoking and intraoral malignancy common in urban. Patients mostly presented with advanced stage of malignancy.

**Keywords:** Head and neck cancer, squamous cell carcinoma, risk factors, smoking, betel nut, recurrence.

We are one of the largest centers for plastic and reconstructive surgery in Pakistan, a country of over 180 million people, and receive cases from all over the country. Every year we enter 70 new cases of malignancy. We are a major referral center for difficult and challenging cases from all over the country and malignant tumors constitute a major chunk of our practice. Even today, there is no 'cancer registry' in Pakistan and there is no definite data regarding the incidence of various cancers. This state of affairs is very depressing since cancer takes a

heavy toll of human life in this extremely populous country and incurs a huge cost in terms of morbidity and mortality. The majority of the population is poor, and has little access to even basic necessities of life. Not only are accurate figures regarding the incidence and prevalence of cancers unknown, the diagnosis and management of malignant tumors is extremely suboptimal (in terms of facilities, qualified physicians, therapeutic options etc.). The majority of patients cannot afford the cost of treatment. Cancer patients often die painful and miserable deaths.

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Little to no facilities is available in remote areas and people need to travel to larger cities in order to get treatment which is very expensive. Although the government and private sector have taken a number of initiatives to improve cancer care in the country, the overall situation remains bleak. An important step in achieving better cancer care is to determine the incidence of various cancers in the country. A Plastic Surgery department cannot accurately determine overall cancer incidence, however can add a bit to solve the problem.

### **MATERIALS AND METHODS:**

After the protocol had been approved by the institutional review board, we retrospectively studied the questioners and clinical records of 356 patients who attended head and neck OPD and were at different stages of workup from January 2008 to March 2016. Questioners were filled by residents in OPD and ward. Data was compiled and analyzed with SPSS. 17. The reports were manually reviewed, and the following information was extracted: date of biopsy, medical record number, age, sex, city, pathologic diagnosis, and anatomic location. The data were rechecked manually to delete duplications. All the patients with biopsy proven malignancies in the head and neck region both intraoral and skin malignancies were included. All stages of malignancies and patients who accepted the course of treatment were included. Terminal cases were excluded and those who lost to follow up.

### **RESULTS:**

Among 356 head and neck cancers 147 oral cavity, 63 perioral, 60 scalp, 45 periorbital, 21 nose and 13 ear, tumors were presented anatomically (Table 1). Most patients were males 78% (Figure 1). 52 %smoked cigarette and 16 % chewed betel nut/tobacco. 52% of the patients were from urban background and 48% from rural areas. Intra oral malignancy was more common in urban areas (71%) as compare to rural. Cutaneous malignancies were more common in rural area patients (80%) as

compared to urban area patients. Tumor type was distributed as squamous cell carcinoma 200 (56%), basal cell carcinoma 93 (26%), recurrent tumor 14 (4%), Melanoma 14(4%), dermatofibrosarcoma 14 (4%), adenocarcinoma 7 (2%), angiosarcoma 6 (2%), Carcinoma expleomorphic adenoma 6 (2%), Miscellaneous 16 (4%) (Figure 3). TNM Stage IV was 114 (32%), III was 135 (38%), II was 71 (20%) and I was 36 (10%) (Figure 2).

### **DISCUSSION:**

Head and neck is a vast anatomical entity. We considered it as a single location because of dedicated outdoor and indoor facility for this region at Jinnah Burn and Reconstructive Surgery Center, and included tumors of scalp, face, neck and oral cavity.

In 2006, more than 3.5 million BCCs and SCCs were diagnosed in the United States<sup>1</sup>. Eighty-eight per 100,000 BCCs and 29 per 100,000 SCCs calculated in an Italian cancer registry for the period 1993–1998<sup>2</sup>. BCC is the most common skin cancer in Caucasians, Hispanics, Japanese, and Chinese Asians, while SCC is the second most recorded cutaneous malignancy in the former races. In Asian Indians and black people, SCC is the most common cutaneous malignancy followed by BCC<sup>2-6</sup>. Our data showed that SCC was the commonest cancer among Pakistanis followed by BCC. Our results were similar to results published by colleagues in other geographic areas. Malignant melanoma is the third most common cutaneous malignancy among Asians, Hispanics, black people, and Caucasians<sup>7-9</sup>. It is the fifth leading cancer in American men and the seventh leading cancer in American women. The overall age-adjusted incidence of melanoma in the United States was 19.7 per 100,000 in 2011<sup>10,11</sup>. In 2000, there were 35,000 new cases of melanoma diagnosed in Europe.<sup>12</sup> Looking at the results of other studies published, in our study the malignant melanoma was also the third most common cutaneous malignancy and shares itself with dermatofibrosarcoma protuberans. Dermatofibrosarcoma protuberans in our

center ranked after all the former cutaneous malignancies with similar ranking in other geographical areas.

Our most of the cutaneous malignancies were from residents of rural areas probably they are farmers and have long sun exposed hours of working. UV light imposes great risk of triggering cutaneous malignancies. Ultraviolet (UV) light in its different wavelengths induces different types of DNA damage generating DNA photoproducts. The biological effects of UV light include erythema, tanning, immunosuppression, mutagenesis, and carcinogenesis.<sup>14, 15</sup> Cancers induced by intense or repeated exposure to UV light include BCC and SCC in sun-exposed skin of both Caucasians and black people and melanoma in Caucasians and black males<sup>16-19</sup>. A congenital disorder with DNA damage repair defects also predisposes to sun-induced malignancies, and this was observed in one of our subject with xeroderma pigmentosum.

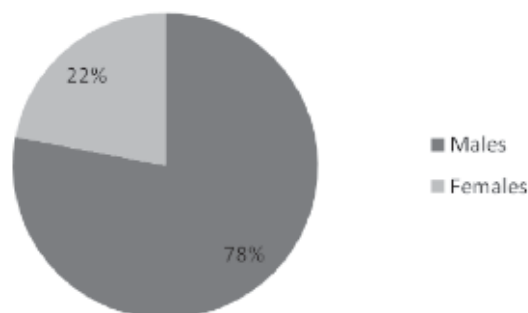
Cancer of the oral cavity was overall the second commonest type of malignant tumor. Carcinoma of the oral cavity, lymphoma (Non Hodgkin and Hodgkin combined) and esophageal carcinoma were among the top five malignancies in both males and females. The high incidence of oral cancer in both sexes is related to the widespread ingestion of paan (betel quid), chalia, naswaar; cigarette, cigar and hooka smoking; poor oral hygiene etc.<sup>20</sup> Human Papilloma Virus (HPV) associated intra oral malignancies are rear in our setup. Mouth and tongue cancer is very common in the subcontinent, where many of the major risk factors such as cigarette or bidi smoking, betel quid chewing, tobacco chewing etc are rampant.<sup>20</sup> It is no wonder that the highest incidence rates of oral cancer in females are found in the Indian subcontinent<sup>21</sup>. In India, studies have shown regional differences in the incidence rates of oral cancers in both males and females according to data from registries in different regions of the country. In our study males predominated in intra-oral malignancies (71%). The US National Cancer Institute's SEER data showed that incidence rate as

well as five year survival rate from oral cancer had remained constant inspite of advances in surgery and radiation<sup>22</sup>. The study emphasized that early detection of localized lesions with appropriate treatment and aggressive counseling of the public to prevent betel nut use and give up smoking were extremely important in decreasing the morality rates from oral cancer. Recurrent tumors also sprouted in our OPDs, partially because of poor compliance of the patient and partly due to suboptimal treatment instituted. Most of the tumors were in advanced stage of disease as per TNM guidelines.

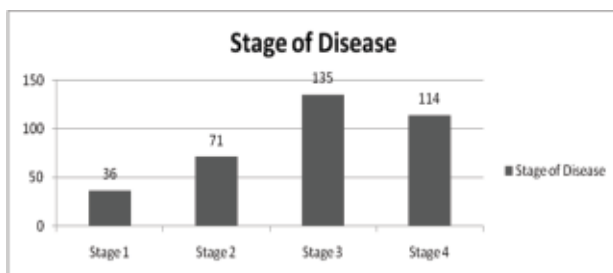
## TABLES AND CHARTS

**Table 1:**

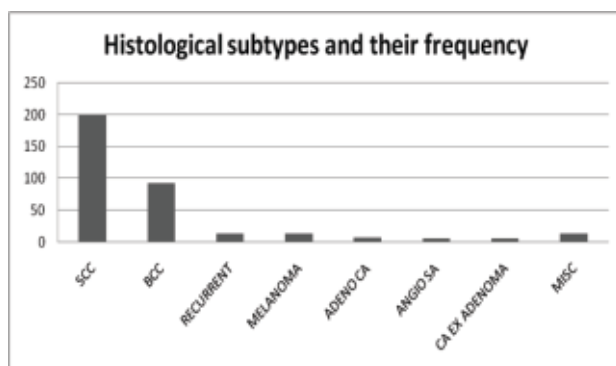
Location	Frequency
Oral Cavity	147
Perioral	63
Scalp	60
Periorbital	45
Nose	21
Ear	13



**Figure 1:**



**Figure 2:**



**Figure 3:**

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## DIAGNOSTIC ACCURACY OF NEUTROPHIL LYMPHOCYTE RATIO AS A PREDICTOR OF IN-HOSPITAL MORTALITY AFTER STROKE

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### ABSTRACT

Stroke being second leading cause of death worldwide, has been investigated extensively. Clinicians are often asked to predict outcome after stroke by the patient, family and other care givers. This study had been conducted to test diagnostic accuracy of Neutrophil lymphocyte ratio (NLR) in predicting in-hospital mortality after stroke. It was a cross sectional study conducted in a tertiary care teaching hospital over a period of six months. A total of 200 stroke patients were enrolled and divided into 2 groups as acute ischemic stroke, and acute hemorrhagic stroke. Admission NLR levels were taken. Patients were given standard treatment & followed for outcome that was taken as mortality within a week or discharged in that period. Data analyzed using SPSS version 17. Cross tabulation was done for In-patients mortality and NLR ratio and diagnostic accuracy of NLR was calculated for in-hospital mortality. Results show that there is higher NLR in patients who died during hospital stay. The sensitivity of NLR of  $>5$  for in-hospital mortality is 94.9% with PPV 90.2%. We concluded that the NLR has a high diagnostic accuracy and predictive values in detecting in patient mortality from strokes and may be used as a simple and easy to measure marker for prediction of in-hospital mortality in both ischemic and hemorrhagic stroke patients.

**Key words:** Neutrophil lymphocyte ratio (NLR), ischemic stroke, hemorrhagic stroke, mortality.

Stroke is second most common cause of death worldwide and a major cause of acquired disability in adults. Despite tremendous progress in understanding the pathophysiology of stroke, translation of this knowledge into effective therapy has largely failed, with exception of thrombolysis, which only benefits a small proportion of patients. Systemic and local immune responses have important roles in causing stroke & are implicated in primary and secondary progression of ischemic lesions, as well as in repair, recovery, and overall outcome.<sup>1</sup>

The neutrophil-to-lymphocyte ratio (NLR) has recently been described as a predictor of clinical outcomes in patients with acute coronary syndrome.

A study assessed the clinical significance of NLR as a new predictor of the outcome in patients with acute ischemic stroke. NLR was higher in patients with an unfavorable outcome than in those with a favorable outcome (3.88 vs. 2.27 at 3 months,  $p < 0.01$ ; 3.67 vs. 2.31 at 1 year,  $p < 0.001$ ).<sup>2</sup>

Another study on patients with acute cerebral infarction who presented within 24 hours of symptom onset the NLR was calculated and the median NLR was significantly increased among the mortality group compared with the survival group. The sensitivity for short-term mortality when the NLR was  $>5$  was 83.10%, and the specificity was 62.00%. The positive predictive value of a NLR  $>5$  was 45.7%, and negative predictive value was

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90.50%.<sup>3</sup>

As inflammatory mechanisms play an important role in acute brain ischemia and they contribute to the functional outcome. NLR has been studied as a measure of systemic inflammation in prevalent chronic diseases in Asian population.<sup>4</sup> It remains to be established whether the inflammatory response is a truly independent risk factor in general, or whether specific anti-inflammatory interventions are beneficial either in prevention or acute treatment.<sup>5</sup> Stroke is the third most common cause of death and the first leading cause of disability in developed and developing countries. No large scale epidemiological studies are available to determine the true incidence of stroke in Pakistan. Estimated annual prevalence is 2.5/1000, translating to 350,000 new cases every year.<sup>6</sup>

The rationale of my study is to assess diagnostic accuracy of NLR as a predictor of in-hospital mortality among patients with acute stroke. The measurement of this ratio may serve as a clinically accessible and useful biomarker for patient survival as no such study has been carried out in Pakistan before and it will serve as adjuvant to other diagnostic modalities.

#### **W.H.O Definition of Stroke<sup>7</sup>:**

Stroke is defined by clinical findings and symptoms, rapidly developed signs of focal (or global) disturbance of cerebral function lasting more than 24 hours (unless interrupted by surgery or death), with no apparent cause other than a vascular origin. WHO definitions are:

#### **Definite focal signs:**

- unilateral or bilateral motor impairment
- unilateral or bilateral sensory impairment
- aphasia/ dysphasia
- hemianopia / diplopia / forced gaze
- acute onset of dysphagia / apraxia / ataxia / perception deficit.

#### **Not acceptable as sole evidence of focal dysfunction:**

- dizziness, vertigo, localized headache
- blurred vision of both eyes
- dysarthria
- impaired cognitive function or impaired consciousness
- seizures.

Neuroimaging is needed for classification of stroke by subtypes: subarachnoid hemorrhage, intracerebral hemorrhage and brain infarction. Thrombotic and embolic strokes are responsible for about 80–85% of all strokes in the Indo-European populations, and as low as 65% in some Asian populations. Subarachnoid hemorrhage represents 5–10% of all strokes, and occurs more often in younger patients, while both intracerebral and especially thrombotic and embolic stroke increase markedly with age.

#### **NLR AS PREDICTOR OF MORTALITY IN STROKE:**

NLR at the time of admission may be an important predictor of short term mortality in acute stroke patient<sup>3</sup>. In another retrospective study on 151 patients with first acute ischemic stroke that occurred within 24 hours of symptom onset, it was seen that NLR at the time of hospital admission maybe a predictor of short-term mortality (within 30 days) independent from infarct volume in acute ischemic stroke patients.<sup>8</sup> Many previous studies showed that leukocyte, neutrophil, and lymphocyte counts play a role in peripheral inflammatory response and atherosclerotic processes.<sup>9,10</sup> Neutrophils, in particular, may cause neutrophil invasion and plaque rupture by secreting some mediators (Proteolytic enzymes, arachidonic acid, elastase, free oxygen radicals).<sup>11,12</sup> Another recent study on 868 stroke patients shows prognostic value of NLR. Overall mortality rate was 10.7%. NLR was significantly higher in patients who died ( $p < 0.001$ ). NLR levels were significantly higher in both ischemic & hemorrhagic stroke patients who died compared to both groups of patients who survived suggesting the value of NLR level in predicting mortality.<sup>13</sup>



**OBJECTIVES:**

To assess the diagnostic accuracy of NLR for predicting in-hospital mortality among stroke patients.

**OPERATIONAL DEFINITIONS:****Stroke:**

Any patient with sudden loss of neurological function due to cerebrovascular accident diagnosed on the basis of neurological examination of patient and confirmed on findings of CT scan as ischemia or hemorrhage at the time of admission was labeled as stroke.

**In-hospital mortality:**

It was defined as death of patients within 7 days of admission.

**Neutrophil lymphocyte ratio:**

It is the ratio of absolute neutrophil count to absolute lymphocyte count taken within 24 hours of presentation of patient with stroke. NLR of  $>5$  will be taken as indicator of poor prognosis and NLR  $\leq 5$  was taken as indicator of good prognosis.

**Diagnostic accuracy:**

Diagnostic association of NLR with stroke was calculated as:

TP = In hospital mortality occurred among stroke patients with NLR  $> 5$ .

TN = In hospital mortality not occurred among stroke patients with NLR  $\leq 5$ .

FP = Mortality not occurred among stroke patients with NLR  $> 5$ .

FN = Mortality occurred among stroke patients with NLR  $\leq 5$ .

**Study setting:** Department of medicine, Jinnah Hospital Lahore.

**Study design:** Cross sectional study

**Study duration:** Six months from July 2014 to December 2014.

**Sample size:** It is estimated as 200 cases using 95% confidence level, with an expected sensitivity of 83% with 9% margin of error, specificity 62% with 8% margin of error taking a percentage of mortality

in strokes as 30%.

**Sample technique:** Non-probability purposive sampling.

**SAMPLE SELECTION:****Inclusion criteria:**

- Newly diagnosed patients with stroke within 24 hours of event
- Age 50–75 years
- Both genders

**Exclusion criteria:**

- Patient with previous strokes and transient ischemic attacks.
- History of head trauma and other cerebral disease.
- Immunosuppressive drug users.
- Infection history in the last two weeks determined on fever  $>100^{\circ}$  F.
- History of malignancy.

**DATA COLLECTION PROCEDURE:**

After informed consent, a total of 200 patients fulfilling the criteria were enrolled in this study from medical emergency. Demographic information including name, age & address were documented. Peripheral venous blood sample taken at the time of admission. The NLR was calculated as the ratio of neutrophils to lymphocytes. A CT scan was carried for each subject as a routine procedure for diagnosing ischemic and hemorrhagic stroke. Patients were given appropriate treatment as required. Patients were kept in hospital as long as the in-patient treatment needed. Information entered in a structured questionnaire.

**DATA ANALYSIS:**

Data were analyzed using SPSS version 17. Mean and + S.D calculated for age. Frequency tables and percentages was calculated for gender, in hospital mortality.  $2 \times 2$  table was generated for mortality and NLR ratio and diagnostic accuracy of NLR was calculated for in-hospital mortality. Data stratified for type of stroke.

**RESULTS:**

A total of 200 patients were enrolled, 105 (52.5%) were males and 95(47.5%) were female, with mean age of 62years (50-75). Among stroke patients 154(77%) had acute ischemic stroke, & 46(23%) had hemorrhagic stroke. Overall mortality rate was 20% although it was less in ischemic stroke patients. Mean time of event of stroke was 7.9+2.48 hours.

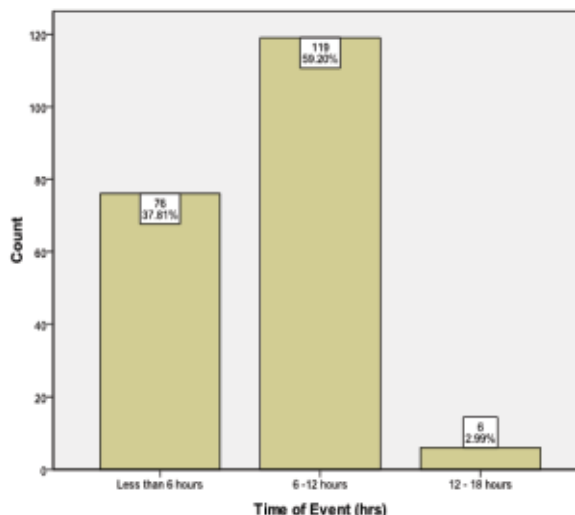
Among all, 41 patients died and 159 survived. Total patients with NLR > 5 were 39 out of which 37 died and 2 survived with sensitivity of high NLR 94.9% and PPV of 90.2%.

Patients with NLR ≤ 5 were 161, among them 157 survived and 4 died, with specificity of NLR ≤ 5 97.5% and NPV of 98.7%.

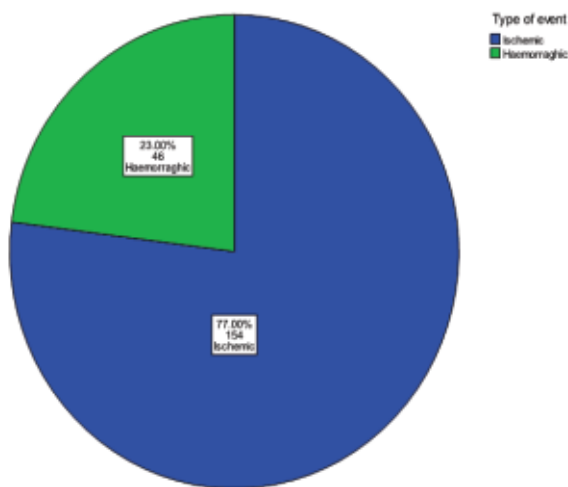
Total patients with ischemic stroke were 154, among them 129 survived and discharged, and 25 died. Out of total Ischemic stroke 23 had NLR > 5, 22 died and 1 survived showing sensitivity of high NLR for in-hospital mortality in ischemic stroke of 95.7% and PPV of 88%.

131 patients had NLR ≤ 5, 3 of them died and 128 were survived, with specificity of NLR 97.7% and NPV of 99.2%.

Total patients with hemorrhagic stroke were 46, among them 30 were survived and 16 died. Total patients who had hemorrhagic stroke and NLR >5 were 16, out of them 1 was survived and 15 died during hospital stay, with sensitivity of high NLR for in-hospital mortality after hemorrhagic stroke of 93.8% and PPV of 93.8%. 30 patients with hemorrhagic stroke had NLR ≤ 5, 1 died and 29 survived showing specificity of NLR 96.7% and NPV of 96.7%.



Graph no.1: Time of stroke event in hours



Graph no.2: Type of stroke

Table 1: NLR \* In hospital mortality Diagnostic Accuracy Cross tabulation

			In hospital mortality		Total
			Yes	No	
NLR	> 5	Count	37	2	39
		Sensitivity	94.9%	5.1%	100.0%
		PPV	90.2%	1.3%	19.5%
NLR	< 5	Count	4	157	161
		Specificity	2.5%	97.5%	100.0%
		NPV	9.8%	98.7%	80.5%
Total	Count		41	159	200
	% within Neutrophil lymphocyte ratio		20.5%	79.5%	100.0%
	% within In hospital mortality		100.0%	100.0%	100.0%

**Table 2:** NLR \* In-hospital mortality \* Type of event Diagnostic accuracy in type of events

Type of event			In hospital mortality		Total	
			Yes	No		
Ischemic	NLR	>5	Count	22	1	23
			Sensitivity	95.7%	4.3p%	100.0%
			PPV	88.0%	.8%	14.9%
	<5	Count	3	128	131	
		Specificity	2.3%	97.7%	100.0%	
		NPV	12.0%	99.2%	85.1%	
Total		Count	25	129	154	
		% within NLR	16.2%	83.8%	100.0%	
		% within In hospital mortality	100.0%	100.0%	100.0%	
Hemorrhagic	NLR	>5	Count	15	1	16
			Sensitivity	93.8%	6.3%	100.0%
			PPV	93.8%	3.3%	34.8%
	<5	Count	1	29	30	
		Specificity	3.3%	96.7%	100.0%	
		NPV	6.3%	96.7%	65.2%	
Total		Count	16	30	46	
		% within NLR	34.8%	65.2%	100.0%	
		% within In hospital mortality	100.0%	100.0%	100.0%	

## DISCUSSION:

To our knowledge this is the first study in Pakistan which investigated the diagnostic accuracy of neutrophil lymphocyte ratio as measure of in-hospital mortality in stroke patients.

Stroke is a major cause of premature mortality, responsible for over 8,500 deaths a year.<sup>14</sup> According to world health organization 1 in 6 people around the world will have a stroke in their lifetime.<sup>15</sup> Two third of stroke deaths occur in less developed countries.<sup>16</sup>

Acute ischemic stroke (AIS) treatment is limited to parenteral tissue plasminogen activator (tPA) and mechanical endovascular therapies. These strategies benefit eligible patients, but carry inherent risks, thereby making determination of individual risk versus benefit important when considering recanalization therapies. The most commonly assessed stroke risk factors are age, infarct volume, and baseline National Institutes of Health Stroke Scale (NIHSS) score.<sup>17-18</sup>

The neutrophil-lymphocyte ratio (NLR) is an established marker of systemic inflammation,<sup>19</sup> and has been recently reported as a predictor of 60 day mortality following AIS.<sup>3</sup> NLR is an indicator of

prognosis for cancer, cardiac disease, and sepsis,<sup>20-23</sup> and has been associated with both the presence and severity of coronary artery disease<sup>24</sup> and metabolic syndrome.<sup>25</sup> There is no widely used point of care biomarker proven to predict who will benefit from endovascular therapy, but white blood cell (WBC) counts are routinely obtained during acute stroke triage, making NLR a readily available biomarker. Our results suggest that NLR significantly predicts outcome and could be used in addition to these variables to identify which patients may benefit from an interventional procedure. NLR may also serve as a tool to help clinicians counsel patients and families when consenting for these procedures.

NLR may also be useful as an inclusion/exclusion criterion when considering patients for enrollment in clinical trials. NLR predicts outcome independently of intervention, including treatment with IV tPA; this would indicate that patients with an elevated NLR may fare poorly during a clinical trial, regardless of treatment, thus adversely impacting the outcome measures of the clinical trial. This is especially important when considering the results of recent clinical trials, such as Interventional Management of Stroke (IMS) III, in which patients were randomized to either IV tPA or IV tPA and endovascular therapy<sup>26</sup>. Our results suggest that NLR can predict outcome regardless of IV tPA treatment and could therefore be used as an exclusion criterion when considering patient eligibility for a future trial. The NLR at the time of hospital admission may be a predictor of short-term mortality in acute stroke patients. Because of the routine use and inexpensive nature of hemogram analysis, the NLR should be investigated in future prospective, randomized controlled trials investigating acute stroke.

In our study, we found out the sensitivity and specificity of NLR in predicting in-hospital mortality is 94.9% and 97.5% respectively. No study has yet been done so far in local settings in which NLR is studied in patients with stroke in Pakistan. Our findings support the hypothesis that the NLR as an inflammatory marker is associated with poor outcome. NLR levels were significantly higher in both Ischemic stroke and hemorrhagic stroke patients who died compared to both groups of patients who survived. This situation suggests that NLR level is valuable in predicting in-hospital mortality whatever the stroke type is.

## CONCLUSION:

We concluded that neutrophil lymphocyte ratio

has a high diagnostic accuracy and predictive values in detecting in-patient mortality from stroke and it can be routinely used for predicting outcome among stroke patients.

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## TO COMPARE THE OUTCOME OF SEPTOPLASTY VERSUS SUBMUCUS RESECTION(SMR) IN PATIENT PRESENTING WITH NASAL SEPTAL DEVIATION

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### ABSTRACT

**Background:** Nasal septum deviation or deviated nasal septum is a physical disorder of the nose, involving a displacement of the nasal septum. A deviated septum occurs when the thin wall between your nasal passages is displaced to one side. Submucous Resection (SMR) of the nose is a surgical procedure during which the bony and cartilage of nasal septum are partially removed from below the muco-perichondrium.

**Objective:** To compare the outcome of septoplasty versus submucous resection (SMR) in patients presenting with septal deviations.

**Material & Method:**

**Study Design:** It was randomized control trial

**Setting:** Unit I, Department of ENT, Jinnah hospital Lahore

**Duration:** 6 months from 01-09-2017 to 31-09-2017.

**Data collection:** After meeting the inclusion criteria 250 patients were enrolled. Informed consent and demographic information was taken from all the patients. Then patients were divided into two groups. One is treated with SMR and other is treated with septoplasty. Then outcome of the patients was noted. All the collected data was entered and analyzed on SPSS version 21.

**Results:** In our study the mean age of the SMR group was  $34.63 \pm 9.04$  years, and its mean value in septoplasty group was  $33.37 \pm 8.91$  years. Male to female ratio of the patients was 0.8:1. The septal perforation was found in 9(3.60%) patients. Statistically insignificant difference was found between the study groups with septal perforation condition.

**Conclusion:** SMR showed significantly better functional outcomes than septoplasty in patients of septal deviations.

**Keywords:** Septal Deviations, Perforation, Sub-Mucous Resection, Septoplasty

Nasal septum deviation or deviated nasal septum (DNS) is a physical disorder of the nose, involving a displacement of the nasal septum. Some displacement is common, affecting 80% of people, most unknowingly. Nasal septal deviation (NSD) is a common diagnosis made by otolaryngologists but is one that is not usually based on objective measurements. As a result, there can be a significant inter-observer variability in terms of diagnosing the condition, verifying its precise location, quantifying the degree of deviation, and assessing its clinical impact on patients.

Septoplasty and Submucous resection (SMR) are two commonly employed surgical procedures to correct symptomatic deviated nasal septum. The SMR was first described by Freer in 1902 and by Killian in 1904. This technique requires removal of the most of the septal cartilage with only sparing a strip of 5 to 10 mm of cartilage from the caudal and dorsal part of the septum. Septoplasty and SMR can be performed alone or frequently resection of the turbinates may be required as well to correct the nasal obstruction. Septoplasty and SMR are the two successive methods for management of NSD but

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also associated with some complications and morbidity. It has been reported in a study that the SMR has better outcome than septoplasty i.e. relieve of nasal obstruction (83.3% vs 70%), rhinorrhea (20% vs 16.5%), snoring (73% vs 50%), and Nasal speech (67.5% vs 50%) but SMR also showed almost equal Septal perforation (3.4% vs 2.5%). It was concluded that the success of SMR in relieving the symptomatic nasal obstruction is higher than septoplasty. But it has been reported in another study that the SMR has better outcome than septoplasty i.e. nasal obstruction relieved (74% vs 72%), rhinorrhea (32% vs 30%), snoring (60% vs 51%), and Nasal speech (65% vs 60%) and SMR also showed almost equal Septal perforation (2.5% vs 2%). The study revealed no significant difference between the functional outcome and complication rates of the two procedures i.e. SMR and septoplasty for symptomatic deflected nasal septum.

The purpose of my study is to compare the outcome of septoplasty versus SMR in patients presenting with septal deviations. It has been observed through literature that SMR is more successful than septoplasty but the controversial results have been reported in literature. So we want to confirm through this study that which method is more successful in relieving NSD and has less complications associated with NSD surgery. This will improve our practice and in future we will be able to implement the more successful method for management of NSD in local setting.

### **OBJECTIVE:**

To compare the outcome of septoplasty versus sub-mucous resection (SMR) in patients presenting with septal deviations.

### **Operational Definitions**

#### **Septal deviations**

It was defined as a displacement of the nasal septum detected on clinical examination and confirmed through nasal x-ray

#### **Outcome**

It was measured within 1 month after as follows:

1. Relieved Nasal obstruction: If patient didn't complaint of problem in breathing and nothing impedes the flow of air into and out of the nose on subjective assessment
2. Relieved Rhinorrhea: If patient didn't complaint of nasal cavity is filled with a significant amount of mucus fluid
3. Relieved Snoring: If patients or their attendants didn't complaint of grunting sound while asleep.
4. Septal perforation: If there was a hole or fissure in nasal septum develops after surgery

### **Hypothesis:**

There was a difference in outcome with SMR versus septoplasty in patients presenting with septal deviations.

## **MATERIALS AND METHODS:**

### **Study Design**

Randomized Controlled Trial

### **Setting**

Unit I, Department of ENT, Jinnah hospital Lahore

### **Duration**

6 months from 01-03-2017 to 31-08-17.

### **Sample size**

Sample size of 250 cases was calculated with 80% power of test, 5% level of significance and expected percentage of snoring i.e. 73% with SMR vs 50% with septoplasty for management of patients with NSD.

### **Sampling Technique**

Non-probability, consecutive sampling

### **Sample selection:**

#### **a. Inclusion criteria:**

1. Age range between 18-50 years of either gender
2. Patients having symptomatic DNS (on x-ray record)
3. Patient fit for General anesthesia (ASA I & II)

#### **b. Exclusion criteria**

1. Patient having nasal obstruction e.g. nasal



- polyps, nasal allergies, benign and malignant lesion of the nose, hypertrophy of the turbinates, adenoid hypertrophy (medical record)
2. Patient undergoing revision nasal septal surgery (on medical record)
  3. Patient having any form of bleeding diathesis (medical record)

### Data collection Procedure

After taking approval from the ethical committee, 250 patients fulfilling the selection criteria were admitted in ENT wards through OPD of Department of ENT, Jinnah Hospital, Lahore. Informed consent was taken before patients under-going surgery. Patient's demographics (name, age, gender and contact) was noted.

Then patients were randomly divided in two groups by using random number table. In group A, patients were undergone Septoplasty while in group B, patients were undergone SMR. All surgeries were done by researcher himself.

Both procedures were performed under GA with intranasal splints and nasal packing placed after the surgery. Patients were shifted to post-surgical wards after surgery and was followed-up there for 3 days. Nasal pack was removed at first post-operative day.

After 3 days patients were discharged and were advised to follow-up in OPD. Intranasal splints to be removed after 1 week. Patient was followed-up in OPD for 1 month after surgery. After 1 month, patients were evaluated for presence of outcome i.e. nasal obstruction relieved, rhinorrhea, snoring, nasal speech, and septal perforation.

### Data analysis

Data analysis was entered and analyzed through SPSS version 21. Quantitative variables such as age was presented as means and standard deviation. Qualitative variables such as gender and outcome (nasal obstruction relieved, rhinorrhea, snoring, nasal speech, and septal perforation) was presented as frequency and percentage. Chi-square test was used to compare the complications between

both groups. P-value  $\leq 0.05$  was considered as significant. Data was stratified for age and gender to deal with effect modifiers. Post-stratification, chi-square test was applied. P-value  $\leq 0.05$  was considered as significant.

### RESULTS:

In this present study total 250 patients participated. The mean age of the group A patients was  $34.63 \pm 9.04$  years and its mean value in group B was  $33.37 \pm 8.91$  years. Table#1

In this study 115(46%) patients were male and 135(54%) patients were females. Male to female ratio of the patients was 0.8:1. Fig#1

In our study the male patients were 115 in which 54 were from group A and 61 were from group B, similarly the female patients were 135 in which 71 were from group A and 64 were from group B. Table#2

In our study the mean value of duration of the symptoms of the group A patients was  $14.03 \pm 6.99$  months and its mean value in group B was  $12.10 \pm 6.86$  months. Statistically significant difference was found between the study groups with duration of symptoms i.e. p-value=0.029.

According to our study results the nasal obstruction relieved was noted in 187 patients in which 110 were from group A and 77 were from group B, similarly the nasal obstruction relieved was not found in 63 cases in which 15 were from group A and 48 were from group B. Statistically significant difference was found between the study groups with nasal obstruction relieved condition i.e. p-value=0.001. Table#3

According to our study results the rhinorrhea was noted in 70 patients in which 22 were from group A and 48 were from group B, similarly the rhinorrhea was not found in 180 cases in which 103 were from group A and 77 were from group B. Statistically significant difference was found between the study groups with rhinorrhea condition i.e. p-value=0.001.

According to our study results the snoring

TO COMPARE THE OUTCOME OF SEPTOPLASTY VERSUS SUBMUCUS RESECTION(SMR)

condition was noted in 66 patients in which 14 were from group A and 52 were from group B, similarly the snoring was not found in 184 cases in which 111 were from group A and 73 were from group B. Statically significant difference was found between the study groups with snoring condition i.e. p-value=0.001.

In our study the nasal speech condition was noted in 59 patients in which 6 were from group A and 53 were from group B, similarly the nasal speech was not found in 191 cases in which 119 were from group A and 72 were from group B. Statically significant difference was found between the study groups with nasal speech condition i.e. p-value= 0.001.

In this study septal perforation was found in 9(3.60%) patients and it was not found in 241 (96.40%) patients. Fig#2

In this study the septal perforation condition was noted in 9 patients in which 4 were from group A and 5 were from group B, similarly the septal perforation was not found in 241 cases in which 121 were from group A and 120 were from group B. Statistically insignificant difference was found between the study groups with septal perforation condition i.e. p-value>0.09.

The study results showed significant difference between the study groups with nasal obstruction relieved stratified by age, female patients and duration of symptoms i.e. p-value<0.05.

The study results showed significant difference between the study groups with rhinorrhea stratified by age, female patients and duration of symptoms i.e. p-value<0.05.

The study results showed significant difference between the study groups with snoring stratified by age, gender and duration of symptoms i.e. p-value<0.05.

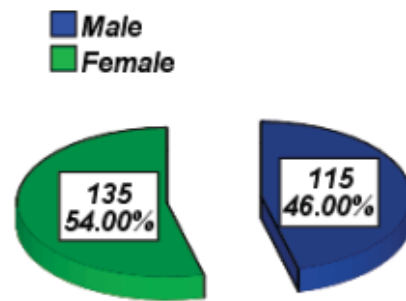
The study results showed significant difference between the study groups with nasal speech stratified by age, gender and duration of symptoms i.e. p-value=<0.05.

The study results showed insignificant difference between the study groups with septal perforation stratified by age, gender and duration of symptoms i.e. p-value>0.05.

**Table 1:** Comparison of age with study groups

		Study Groups	
		Group A	Group B
Age (years)	n	125	125
	Mean	34.63	33.37
	SD	9.04	8.91

Group A=SMR  
Group B=Septoplasty



**Fig#1:** Frequency distribution of gender

**Table 2:** Comparison of gender with study groups

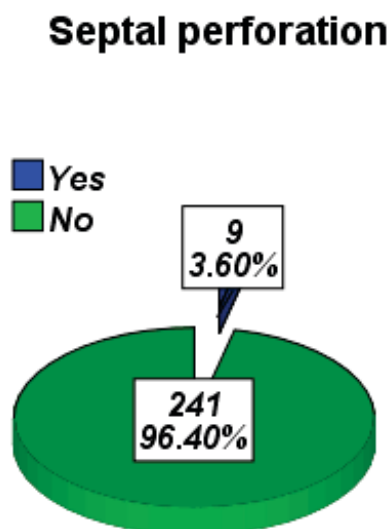
		Study Groups		Total
		Group A	Group B	
Gender	Male	54	61	115
	Female	71	64	135
Total		125	125	250

Group A=SMR  
Group B=Septoplasty

**Table 3:** Comparison of duration of nasal obstruction relieved with study groups

		Study Groups		Total
		Group A	Group B	
Nasal obstruction relieved	Yes	110	77	187
	No	15	48	63
Total		125	125	250

Group A=SMR  
Group B= Septoplasty  
Chi value=23.11  
p-value=0.001



**Fig#2:** Frequency distribution of septal perforation

## DISCUSSION:

This present randomized control trial was carried out at Unit I, Department of ENT, Jinnah hospital Lahore to compare the outcome of septoplasty versus SMR in patients presenting with septal deviations.

The nose represents the entrance of the respiratory tract and has several functions the passageway for the air stream. It harbours chemical sensory functions, it warms and moistens the air and it plays a role in the defence against foreign bodies of the surrounding environment. Nasal obstruction is one of the most common problems bringing a patient to the ENT OPD and septal deviation is a frequent structural etiology.<sup>(7,8)</sup>

In our study the nasal obstruction relieved was noted in 187 patients in which 110 were from group A [SMR] and 77 were from group B [septoplasty] (p-value=0.001). Rhinorrhea was noted in 70 patients in which 22 were from group A and 48 were from group B (p-value=0.001). Snoring condition was noted in 66 patients in which 14 were from group A and 52 were from group B (p-value=0.001). Nasal speech condition was noted in 59 patients in which 6 were

from group A and 53 were from group B (p-value=0.001). While on the other hand septal perforation condition was noted in 9 patients in which 4 were from group A and 5 were from group B. i. e p-value=(1.000). Some of the studies are discussed below showing their results as

Septoplasty and SMR are the two successive methods for management of NSD but also associated with some complications and morbidity. It has been reported in a study that the SMR has better outcome that septoplasty i.e. relieve of nasal obstruction (83.3% vs 70%), rhinorrhea (20% vs 16.5%), snoring (73% vs 50%), and Nasal speech (67.5% vs 50%) but SMR also showed almost equal Septal perforation (3.4% vs 2.5%). It was concluded that the success of SMR in relieving the symptomatic nasal obstruction is higher than septoplasty.<sup>9</sup>

It has been reported in another study that the SMR has better outcome that septoplasty i.e. nasal obstruction relieved (74% vs 72%), rhinorrhea (32% vs 30%), snoring (60% vs 51%), and Nasal speech (65% vs 60%) and SMR also showed almost equal Septal perforation (2.5% vs 2%). The study revealed no significant difference between the functional outcome and complication rates of the two procedures i.e. SMR and septoplasty for symptomatic deflected nasal septum.<sup>10</sup>

Phillips noted changes in 21% cases after SMR<sup>11</sup> and Samad et al found it in 8.5% cases after septoplasty.<sup>12</sup> Altered dental sensations in the upper incisors teeth were seen in 6.6% cases after SMR and 5% after septoplasty. In a local study, higher rates of altered dental sensation were noted in 11% cases after septoplasty and 31% after SMR<sup>13</sup>. Septal perforation occurred in 2.5% cases after SMR and 2% after septoplasty. Zia and Butt noted septal perforations in 2% of their cases.<sup>14</sup> while Haraldsson et al found septal perforations in 1.6% after septoplasty and 8% after SMR.<sup>15</sup>

On the other hand study done by K. Padma and M. Prabhakar<sup>16</sup> concluded that 84% of patients had relief of nasal obstruction in Septoplasty compared to 81% in SMR. Three patients in SMR, two in

Septoplasty had complications. There was no significant difference between SMR and Septoplasty with respect to symptomatic relief and complications following the surgery.

A study by Kamran Iqbal et al<sup>6</sup> revealed no significant difference between the functional outcome and complication rates of the two procedures i.e. SMR and septoplasty for symptomatic deflected nasal septum. Nasal obstruction was relieved in 89/120(74%) patients after SMR and 72/100 (72%) after septoplasty (p>0.05). The overall complication rate was 37/120(31%) in SMR and 24/100(24%) in septoplasty group(p>0.05).

### CONCLUSION:

It has been proved in our study that SMR showed significantly better outcomes than to septoplasty in patients presenting with septal deviations except in septal perforation outcome.

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## OUTCOME OF ENDOSCOPIC OESOPHAGEAL DILATATION IN PATERSON BROWN KELLY SYNDROME

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### ABSTRACT

**Introduction:** Paterson Brown Kelly syndrome is association of esophageal dysphagia, upper esophageal web and iron deficiency anemia. It is common in middle-aged women and can lead to carcinoma of post-cricoid region.

**Objectives:** The objective of my study is to find the frequency of success in dysphagia in Paterson Brown Kelly syndrome after endoscopic dilatation relieving dysphagia in patients of Paterson Brown Kelly Syndrome.

**Study design:** Descriptive case series.

**Setting:** The study was carried out in ENT department, Jinnah Hospital, Lahore.

**Duration:** One year from 1-Jan-2016 to 31-Dec 2017.

**Subjects and methods:** Sixty-four number of patients were selected on the basis of non-probability sampling technique with 79 % had improvement in dysphagia, presenting in outpatient department of all ages and both gender having dysphagia, microcytic hypochromic anaemia and web formation in upper part of esophagus seen on barium swallow were selected through non-probability technique. Patients having dysphagia due to neurogenic causes or any malignancy were excluded from the study. All the patients underwent blood complete examination, barium swallow examination. The outcome was discussed for esophagoscopy and web dilatation with Endoscopic bougies as an optimal surgical approach in patients of Paterson Brown Kelly Syndrome in terms of safety, efficacy, recurrence and complications.

**Results:** Upper esophageal web dilatation with bougies was found to be efficacious in the management of Paterson Brown Kelly Syndrome in my study.

**Conclusion:** Upper esophageal web dilatation with bougies is a safe and cost-effective procedure in early detection and treatment of Paterson Brown Kelly Syndrome.

**Key words:** Esophagus, Paterson Brown Kelly Syndrome, Esophagoscopy, Esophageal web

Paterson brown Kelly syndrome is also called sideropenic dysphagia or Plummer vinson syndrome<sup>1</sup>. This syndrome commonly affects middle aged women in the 4th to 7th decades of life due to high incidence of iron deficiency although it can occasionally present in children<sup>2</sup>.

The exact pathogenesis of this syndrome remains unknown. The most important possible etiological factor is iron deficiency. This theory is primarily based on the finding that iron deficiency is a part of the classic triad of Paterson brown kelly

syndrome together with dysphagia and esophageal webs and that dysphagia can be improved by iron supplementation. Other etiologic factors including malnutrition, genetic predisposition or even autoimmune processes have been proposed.<sup>3</sup> It is presented as a classical triad of dysphagia, iron deficiency anemia and upper esophageal web. The main complaint is dysphagia<sup>4</sup>.

### OBJECTIVE:

The objective of my study is to:

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- Find the frequency of success in dysphagia in Paterson Brown Kelly syndrome after endoscopic dilatation.

**OPERATIONAL DEFINITION:**

**Paterson brown Kelly syndrome:** Difficulty in swallowing solids or liquids for 1 month at least with all the following

Presence of one or more esophageal webs contraction more than 50% on barium swallow.

1-Ferritin	Serum	<15-200 ng/mL
2-Hematocrit:		
Females	Blood	<36-47%
Males	Blood	<41-51%
3-Hemoglobin:		
Females	Blood	<12-16 g/dL
Males	Blood	<14-17 g/dL

**Outcome:**

Outcome will be assessing on Barium swallow 1-month post endoscopic dilatation. Absence of web (constriction less than 50%) on barium swallow will be labeled as success in dysphagia

**MATERIAL AND METHODS**

**STUDY DESIGN:** descriptive case series.

**STUDY SETTING:** ENT Department, Jinnah hospital Lahore.

**STUDY DURATION:** one year from 1 Jan 2016 to 31 Dec 2017.

**SAMPLE SIZE:** My sample size is 64 using 79 % had improvement in dysphagia, 95% confidence level and 10% margin of error under software for sample size determination.

**SAMPLING TECHNIQUE:**

Non probability / consecutive sampling technique is used in the study.

**SAMPLE SELECTION:**

Inclusion criteria

1. Age: 15 -60 years
2. Either gender
3. All Patients presenting in OPD diagnosed as Paterson Brown Kelly syndrome as per operational definition with difficulty in swallowing

solids or liquids for at least 1 month.

**Exclusion criteria**

1. Patients having dysphagia due to trauma i.e head injury, blunt trauma or iatrogenic diagnoses on history and clinical examination.
2. Patients having dysphagia due to esophageal motility disorder, drug induced and ageing diagnosed on previous medical record.
3. Patients with dysphagia due to tumor involving oral cavity, pharyngeal and esophageal diagnosed on history clinical examination and endoscopy.
4. Patient with dysphagia due to neurological disease i.e. CVS ,CP angel tumor etc. on medical record.

**DATA COLLECTION PROCEDURE:**

64 subject those fulfilling the inclusion criteria are recruited for the study. Ethical committee approval is taken. After an informed consent a detailed history is taken about dysphagia from patients presenting in OPD

Patients are informed about the procedure and also morbidity of the procedure after explaining risk benefit ratio. Patients diagnosed of having PBKS are admitted in ward and esophagoscopy is done on elective list under general anesthesia. Boogies of different sizes were used for dilatation depending upon the size of the web.

All the procedures were performed by a single consultant ENT surgeon having 5 years experience. All patients, if stable are discharged on first post operative day. All the patients are advised to follow up at one month to determine the success of intervention.

Strict exclusion criteria were followed to control confounders and bias in study. A Performa was filled after one months of the procedure containing question regarding the relief of dysphagia.

**DATA ANALYSIS PROCEDURE:**

Data is entered and analyzed in SPSS version 18.0. Mean ± S.D is calculated for age. Frequency

and percentages were presented as gender, success of endoscopic dilatation. Data is stratified for age, gender, duration of dysphagia, number of webs to deal with effect modifiers. Post stratification chi square test is applied, P value less than or equal to 0.05 will be considered significant.

## RESULTS

A total of sixty four patients were included in the study over a period of one year. All the patients underwent esophagoscopy under general anesthesia and esophageal bougies of different sizes were used to dilate the upper esophageal web.

Mean age of subjects were 40.9 years SD 15.26, minimum age was 15 years and maximum age was 60 years. 50.0% of subjects were between 15 – 37 years and 50.0% of subjects were between 38-60 years. (Table no: 1). Gender distribution of the patients is shown 67% of subjects were female and 33% of subjects were male. (Graph no: 1). 95.3% of subjects has duration of disease less than 5 years and 4.7% had duration of disease > 5 years.

96.9% had one web and 3.1% had two webs. (Table no: 2).

71.9% of subjects has no dysphagia one month after intervention i.e. success in endoscopic dilatation and only 28.2% had dysphagia one month after intervention. (Graph no: 3).

Dysphagia after one month of intervention was crosstabulated with age, 54.3% had no dysphagia in 15 – 37 years age group as compared to 45.7% among 38-60 years and was statistically non significant. (Table no: 3). (chi-square = 1.237 P= .266)

Success in endoscopic dilatation was cross tabulated with gender, 71.7% had no dysphagia among males as compared to 28.3 % among females and was statistically non significant. (Table no: 4). (chi-square = 1.537 P= .215)

Success in endoscopic dilatation was cross tabulated with duration of disease, 97.8% had no dysphagia among < 5 years as compared to 2.2 % among > 5 years duration and was statistically non

significant. (chi-square = 2.313 P= .128)

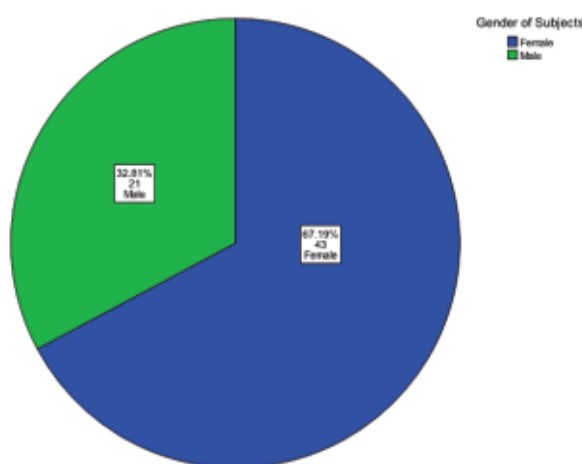
Success in endoscopic dilatation was cross tabulated with no of webs, 97.8% had no dysphagia among patients with one web as compared to 2.2 % among patients' with two webs and was statistically non significant. (chi-square = .489 P= .485)

**Table 1:** Age of subjects (yrs)

Age	Frequency	Percent
15 - 37 years	32	50.0
38 - 60 years	32	50.0
Total	64	100.0

Mean = 40.9 years SD = 15.26 Minimum = 15 years  
Maximum = 60 years

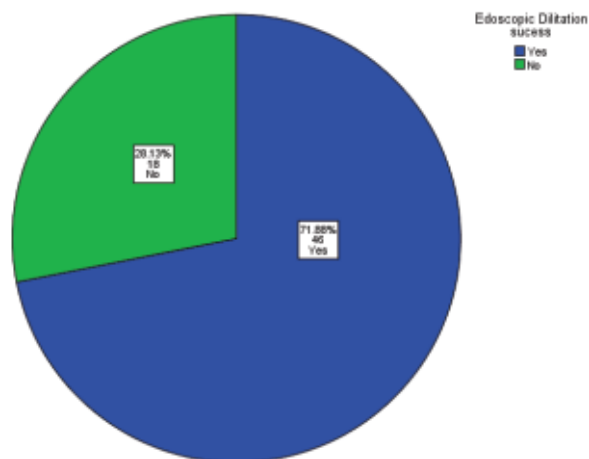
## Results and main findings:



**Graph no: 1** Gender distribution of subjects

**Table 2:** Number of webs

Number of Webs	Frequency	Percent
One web	62	96.9
Two webs	2	3.1
Total	64	100.0



**Graph no:3-** Success of endoscopic dilatation. (n=64)

**Table 3:** Age \* Success of endoscopic dilatation  
Cross tabulation

		Success of endoscopic dilatation		Total	Chi-square
		Yes	No		P value
Age of Subjects	15 - 37 years	25	7	32	X <sup>2</sup> = 1.237 P = .266
		54.3%	38.9%	50.0%	
	38 - 60 years	21	11	32	
		45.7%	61.1%	50.0%	
Total		46	18	64	
		100.0%	100.0%	100.0%	

**Table 4:** Gender \* Dysphagia after one month  
Cross tabulation

		Success of endoscopic dilatation		Total	Chi-square
		Yes	No		P value
Gender of Subjects	Female	33	10	43	X <sup>2</sup> = 1.537 P = .215
		71.7%	55.6%	67.2%	
	Male	13	8	21	
		28.3%	44.4%	32.8%	
Total		46	18	64	
		100.0%	100.0%	100.0%	

**DISCUSSION**

In my study total 64 patients were included. 33% male and 67% females. Male to female ratio

was 1:3. This shows high incidence of PBKS in females. Mean age was 40.9. In a study done by Novacek most of the patients were females and in fourth to seventh decade of life.<sup>3</sup> This syndrome is associated with high incidence of post cricoid carcinoma. So follow up of the patients is essential.<sup>5</sup> In a study 15% of patients developed esophageal or pharyngeal cancer.<sup>3</sup> In my study we excluded the patients of malignancy.

The triad of Paterson Brown Kelly Syndrome consists of dysphagia for solids, upper esophageal web and iron deficiency anemia. In the past it was common in Scandinavian population, especially in rural areas of Sweden but nowadays it is rare over there.<sup>3</sup> It is still common in developing and under developed countries. In world its incidence is falling. This is because of better nutrition. But it is still high in Pakistan especially in women of child bearing age. Their diet is deficient in essential vitamins and minerals. They have gynaecological problems like menorrhagia. They are diagnosed late and don't take treatment properly and develop anemia and esophageal web formation.

Sometimes double membrane may be detected in cervical esophagus like in study of Castro in which a 27 year old patient had PBKS with double membrane.<sup>6</sup> In my study no double membrane was detected.

In my study all 64 patients underwent esophagoscopy and web dilatation. All the patients were given oral iron therapy. All patients were free of any symptoms after 4 months of therapy. In a study done by FikretDemirci it was seen that most common cause of dysphagia was esophageal web. These webs were present in 15-20% of patients. They presented two cases of PBKS who underwent esophagoscopy and web dilatation. Post operatively they were given oral iron therapy until their serum ferritin level became normal. Both patients were in good health after two years.<sup>7</sup>

Congenital esophageal webs are very rare. George F et al reported a case of congenital esophageal web in a 21 year old man who complained of

dysphagia for solids since the age of 7.8 In my study there was no congenital esophageal web seen.

Makharia GK reported three cases of PBKS in which there was clubbing instead of classical kiolonycia.<sup>9</sup> It is unusual presentation. In my study no patient had clubbing.

Kitabayashi studied a 59 year old female patient. She had advanced gastric cancer.<sup>10</sup> This is very rare. None of my patient had any malignancy.

There is statistically significant difference in all the parameters measured before and after procedure. In stickiness of food in throat, feeling of lump in throat, intake of solids with help of liquid and dysphagia for solids p value was .000, which is statistically significant. This statistically significant difference validates my hypothesis.

#### CONCLUSION AND RECOMMENDATIONS:

Endoscopic esophageal web dilatation is a safe and cost-effective procedure in treatment of PBKS. If diagnosed earlier can be treated completely if we are able to maintain normal hemoglobin and iron levels. Epidemiological studies with large sample size are required to assess the efficacy of esophageal web dilatation.”

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## ASSOCIATION OF MATERNAL HEMOGLOBIN LEVELS WITH INTRAUTERINE GROWTH RESTRICTION

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### ABSTRACT

**Background:** During human pregnancy, inadequacy of fetal growth is a matter of great concern as it can lead to intrauterine growth restriction which is a potential cause of neonatal morbidities and mortalities. IUGR is defined as an estimated fetal weight at one point in time at or below 10th percentile for gestational age. WHO classifies anemia in pregnancy as mild anemia (10-11 g/dL), moderate anemia (7-10 g/dL) and severe anemia (< 7g/dL). Low hemoglobin levels leading to decreased oxygen concentration in blood can ultimately result in chronic hypoxia, hence contributing to intrauterine growth restriction.

**Objective:** The objective of this study was to compare maternal hemoglobin levels in pregnancies with adequate for gestational age fetuses and pregnancies with IUGR.

**Material and method:** It was a cross sectional comparative study, conducted in Federal Post Graduate medical institute, after taking permission from Ethical review board, from January 2015 to January 2016, with a sample size of 60 pregnant women. They were divided equally among pregnant women with adequate for gestational age pregnancies and pregnant women with intrauterine growth restricted pregnancies confirmed by ultrasonography at 28-35 weeks of gestation, with 30 women in each group.

**Results:** Maternal hemoglobin levels were raised but not statistically significantly (p value 0.296) raised in pregnant women with adequate for gestational age fetuses as compared to that in pregnant women with IUGR. Mean maternal hemoglobin levels were  $10.2 \pm 1.0$  g/dL in pregnant women with AGA fetuses and  $9.9 \pm 1.2$  g/dL in pregnant women with IUGR.

**Conclusion:** It is concluded that decreased maternal hemoglobin levels are not significantly associated with IUGR.

During human pregnancy, inadequacy of fetal growth is very serious matter as it can result in intrauterine growth restriction which is not only a reason of neonatal morbidities and mortalities but also of life-long complications.<sup>(1)</sup> IUGR is defined as an estimated fetal weight at one point in time at or below 10th percentile for gestational age.<sup>(2)</sup> Birth weight is one of the most significant and easily measurable predictor of morbidity and mortality of infant as well as developmental problems of children, yet this variable is the most ignored one. Infant mortality is believed to be inversely related to birth weight.<sup>(3)</sup> In the 19th century, the birth weight was broadly categorized into low birth weight (less than 2500 g) and normal birth weight (more than

2500 g). The idea of intrauterine growth restriction was totally ignored which was taken into light by the introduction of the concept of intrauterine growth restriction by WHO in 1961.<sup>(4)</sup> American college of gynecology (ACOG) and Royal college of obstetrics and gynecology (RCOG) has been unanimous about the limit of 10th percentile as cutoff value to declare IUGR. Moreover, umbilical artery Doppler scan helps in establishing difference between intrauterine growth restriction, constitutionally small fetus and normal pregnancy.<sup>(5)</sup>

The outcomes of IUGR are not only important clinically but also for public health services as it increases burden on public health resources. The survivors of IUGR may have to face complications



like premature birth, low APGAR score and hypoxic brain injury.<sup>(6)</sup> They are more likely to encounter hyperlipidemia, type 2 diabetes mellitus and non-alcoholic fatty liver disease<sup>(7)</sup>, retinopathy of prematurity,<sup>(8)</sup> thrombocytopenia, necrotizing enterocolitis<sup>(9)</sup>, neurodevelopment delays in adult life.<sup>(10)</sup>

Most of the available data on IUGR is collected from the West which cannot be fit on Asian population as it has its own genetic makeup and risk factors. Annually approximately thirty million babies get affected by IUGR and out of them about 75% are Asians. Unfortunately, in Pakistan there is 10-25% incidence of IUGR which is not a healthy sign.<sup>(11)</sup> WHO classifies anemia in pregnancy as mild anemia (10-11 g/dl), moderate anemia (7-10 g/dl) and severe anemia (< 7g/dL).<sup>(12)</sup> According to criteria based on CDC, anemia in pregnancy is labeled by a hemoglobin value less than 11.0 g/dL in both the first and last trimesters and less than 10.5 g/dL in the second trimester.<sup>(13)</sup> Hemodilution which occurs physiologically during pregnancy alters maternal hemoglobin levels. Plasma volume expansion plays a significant role to facilitate fetal circulation.<sup>(14)</sup> Because of expansion of plasma, hemoglobin concentration falls till 7 weeks and then increases slightly.<sup>(15)</sup>

Stressful conditions in body stimulate various hormonal, autonomic and behavioral responses which are helpful in short term and long-term adaptation to stress. Low hemoglobin levels leading to decreased oxygen concentration in blood can ultimately result in hypoxia, hence contributing to growth restriction.<sup>(13)</sup> Another proposed mechanism is that iron deficiency leads an increased production of norepinephrine, which in turn stimulates production of corticotropin-releasing hormone and in turn possibly restricts fetal growth.<sup>(16)</sup> The chronic hypoxia results in failure of fetus to grow up to his genetically determined growth potential. Hence resulting in intrauterine growth restriction.<sup>(17)</sup> In contrast to this another possible mechanism is in favor of the idea that hemoconcentration due to failure of plasma expansion can cause IUGR.<sup>(18)</sup>

## MATERIAL AND METHOD:

It was a comparative and cross-sectional study, conducted in the Department of Physiology, Federal Postgraduate Medical Institute, Lahore and Obstetrics and Gynecology department, Shaikh Zayed hospital, Lahore after taking permission from the respective head of departments and Ethical review board. The study span was one year.

A target population of 60 pregnant women was chosen who were fulfilling the inclusion and exclusion criteria, and was distributed into 2 groups, as follows:

**Group A:** 30 Pregnant women (between 28-35 weeks of gestation) with adequate for age uncomplicated normal pregnancy

**Group B:** 30 pregnant women (between 28-35 weeks of gestation) with intrauterine growth restricted pregnancy

Convenient sampling was done.

The subjects with following conditions were excluded:

- Diabetes Mellitus
- Oligo/polyhydramnios
- Chronic Hypertension
- Twin pregnancies or multifetal gestation

Pregnant women were selected from the outpatient department and obstetric ward of Shaikh Zayed medical complex meeting the inclusion criteria. Written informed consent was taken from all the participants. Then every individual was assessed by taking history and using specially designed questionnaire. Blood sample was taken. Hemoglobin levels were estimated in Pathology Laboratory of Shaikh Zayed Medical Complex.

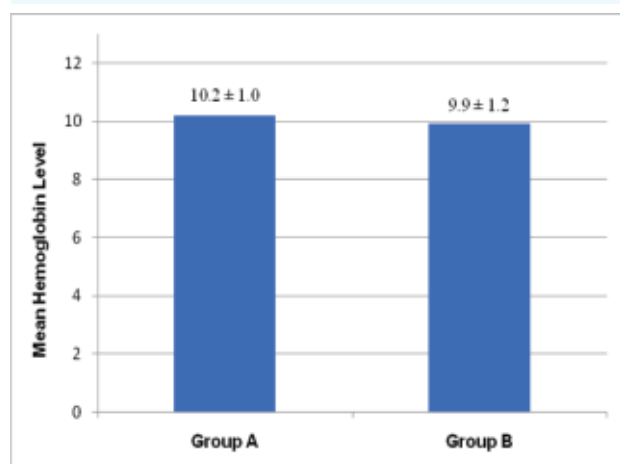
The data was entered into and analyzed by SPSS (Statistical Package for Social Sciences) version 17.0. Shapiro Wilk test was used to check normality of data. Independent sample t-test was performed to compare the mean hemoglobin level in both groups. Mann Whitney U test was performed to compare the gravida score of both groups. p value less than 0.05 was taken statistically significant.

## RESULTS

Following results were obtained:

**Table 1:** Comparison of Hemoglobin Level between both groups

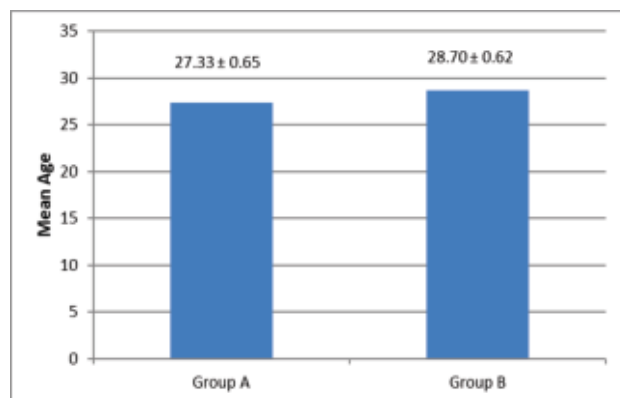
	Hemoglobin Level g/dl			p- value
	Mean $\pm$ SD	Minimum	Maximum	
Group A	10.2 $\pm$ 1.0	7.9	12.2	0.296
Group B	9.9 $\pm$ 1.2	7.9	13.0	



**Figure 1:** showing comparison of Hemoglobin Level between both groups

**Table 2:** Comparison of age between both groups

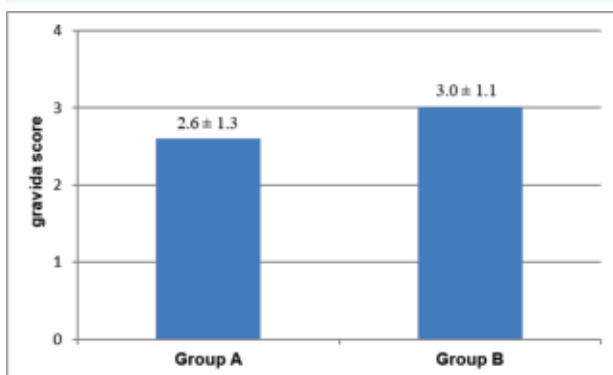
Age	Group A	Group B
Mean	27.33	28.70
Standard Deviation	0.65	0.62
Minimum	20	22
Maximum	34	36
p-value	0.134	



**Figure 2:** Comparison of age between both groups

**Table 3:** Comparison of Gravida Score between both groups

	Gravida score				p- value
	Mean $\pm$ SD	Median (Inter-Quartile Range)	Minimum	Maximum	
Group A	2.6 $\pm$ 1.3	2.5(2.0 - 3.0)	0	6	0.166
Group B	3.0 $\pm$ 1.1	3.0(2.0 - 4.0)	1	3	



**Figure 3:** Comparison of Gravida score between both groups

## DISCUSSION:

In our study we evaluated the effect of maternal age, gravida score and hemoglobin levels in pregnant women between the age of 20-40 years with evidence of intrauterine growth restriction by physical examination and ultrasound at 28-35 weeks of gestation with age and duration of pregnancy matched group of pregnant women with evidence of adequate for gestational age fetuses confirmed by both physical examination and ultrasound.

In this study the mean age of pregnant women with AGA fetus was 27.33  $\pm$  0.65 years and mean age of pregnant women with IUGR fetus was 28.70  $\pm$  0.62 years. Khan et al., Anjum et al. and Ferraz et al. pointed out that maternal age < 20 years was a risk factor for IUGR and LBW.<sup>(19,20,21)</sup> The p value of 0.134 in our study depicted that the effect of age on both groups was insignificant. This insignificance can be explained by the fact that none of the women participated in our study was below the age of 20 years. According to our study, the mean gravida score of group A was 2.6  $\pm$  1.3 and mean gravida score of group B was 3.0  $\pm$  1.1 (p < 0.166). In a study Moh W et al. suggested that primigravida woman has more chances to have LBW child as compared to her children in subsequent pregnancies.<sup>(22)</sup> In another study, Motghare D et al. pointed out that as gravida score increases, chances of IUGR decreases.<sup>(23)</sup> Our study however, has not supported the effect of gravida score on frequency of IUGR.

According to this study, the mean hemoglobin level of group A was higher as compared to the mean hemoglobin level of group B. However, this difference was not found to be significant. ( $p$  value = 0.296). This low level of hemoglobin is in accordance with the results of studies carried by Acharya et al. and Lone F et al which described strong and inverse relation of hemoglobin level with intrauterine growth restriction.<sup>(24,25)</sup> In a study conducted by Bencaiova G and Breymann C, pregnant women with hemoglobin in a range of 8-9g/Dl are at a higher risk of having intrauterine growth restricted babies as compared to pregnant women with hemoglobin 10-11.9g/dL.<sup>(13)</sup> However Kozuki et al and Scanlon et al pointed out that anemia is not a significantly associated with adverse pregnancy outcomes which favors our results that moderate anemia is not associated with IUGR.<sup>(12,26)</sup> In a research, Rondo P and Tomkin A found out that mean hemoglobin levels in pregnant women with intrauterine growth restricted pregnancy(16.4g/dL) was higher than pregnant women with adequate for gestational age pregnancy(15.7g/dL).<sup>(27)</sup> According to Scholl both extremes of the maternal hemoglobin levels result in adverse pregnancy outcomes.<sup>(18)</sup>

### CONCLUSION:

As anemia and intrauterine growth restriction is a very prevalent condition in Pakistan, this study can be very helpful to study the association of hemoglobin levels with IUGR. In this study, it is concluded that decreased maternal hemoglobin levels are not significantly associated with IUGR.

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## FREQUENCY OF INFECTION AFTER IMMEDIATE INTRAMEDULLARY NAILING VERSUS EXTERNAL FIXATOR IN OPEN TIBIAL SHAFT FRACTURES

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### ABSTRACT

**Objective:** To compare the frequency of infection with immediate intramedullary nailing (IMN) versus external fixator (EF) in open tibial shaft fractures.

**Design:** It was a randomized controlled trial.

**Place and Duration of Study:** This study was conducted at the Department of Orthopedic Surgery, Sir Ganga Ram Hospital Lahore over 1 year period from January 2017 through December 2017.

**Patients and Methods:** This study involved 40 patients of both genders aged between 20-50 years who presented with open tibial shaft fractures falling under Gustilo Type II. These patients were randomly divided in two groups by lottery method. Patients in Group-A underwent fracture fixation with unipolar external fixator with 4 half pins while those in Group-B underwent immediate intramedullary nailing. Outcome variable was frequency of infection in first 4 weeks after surgery which was noted and compared between the groups. A written informed consent was taken from each patient.

**Results:** The age of the patients ranged from 20 years to 50 years. There were 32 (80.0%) male and 8 (20.0%) female patients in the study cohort with a male to female ratio of 4:1. Infection was observed in 3 (7.5%) patients. The frequency of infection with IM nail was lower than that of external fixator (5.0% vs. 10.0%;  $p=0.759$ ). Similar insignificant difference was observed across various age and gender groups.

**Conclusion:** Frequency of infection after immediate intramedullary nailing of open tibial shaft fractures was lower to that of external fixator. Immediate intramedullary nailing thus appears method of choice for the management of such patients in future practice.

**Keywords:** Tibial Shaft, Open Fractures, External Fixator, Intramedullary Nail

Tibial shaft fracture is a common injury largely owing to superficial location and the subcutaneous characteristics of tibial antero-medial aspect, frequently resulting in open fractures causing painful and prolonged recovery, frequently associated with complications<sup>1</sup>. The overall rate of open tibial fractures in Pakistan has been reported as 44% being commonest (62%) between 20-40 years of age<sup>1</sup>. Current practice in management of open tibial shaft fractures is application of external fixator and wound management followed by open reduction and internal fixation when wound healing has been

satisfactory thus to reduce infection of subsequent implant<sup>2</sup>. The current practice of initial external fixation and wound management is aimed at providing enough soft tissue coverage and reducing infection of subsequent internal fixation. But it comes with its own drawbacks of patient's tackiness, pain, prolonged hospital stay and complications.<sup>3</sup> However, recent studies have documented a very low and acceptable infection rate of 1.6% to 4% with immediate internal fixation which is comparable to that of external fixator<sup>4,6</sup>. The results of this study claim immediate internal fixation to be at least as

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safe as external fixator as far as infection is concerned. In another study, Kumar et al.<sup>7</sup> found that the rate of infection was even lower with IM nail (10.0% vs. 20.0%) as compared to external fixator. In the light of this evidence, immediate internal fixation with IM nail appears to be better or at least comparable to external fixator in terms of infection, yet avoiding external fixator and its associated demerits.

It was important to understand that the results of these studies couldn't be applied in Pakistani population where the microbial profile and antibiotic sensitivity in such patients differed from other populations.<sup>1</sup> At the moment no such study was available in Pakistan. Therefore the purpose of this study was to determine infection rate of immediate intramedullary nailing in open tibial fractures among Pakistani population which if found satisfactory would help to avoid external fixator in future thus improving patient's satisfaction and reducing hospital stay and complications in such patients.

## PATIENTS AND METHODS

**Study Design:** It was a randomized controlled trial.

**Study Setting:** Research was conducted at Department of Orthopedic Surgery, Sir Ganga Ram Hospital Lahore.

**Duration of Study:** Duration of study was 1 year from January 2017 through December 2017.

**Sample Size:** Sample size of 40 cases; 20 cases in each group was calculated with 80% power of test, 5% level of significance taking expected frequency of infection to be 43% with IM nail and 50% with external fixator in open tibial shaft fractures.

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

### Sample Selection:

#### *Inclusion criteria*

Patients of both sex groups with ages in the range of 20-50 years presenting with Gustilo Type II open tibial shaft fractures were included.

#### *Exclusion criteria*

Patients presenting more than 6 hours after

injury, poly trauma patient having other skeletal or visceral injuries, fractures of the diaphysis which extended into the articular surface or fractures too distal or proximal in the diaphysis not suitable for intramedullary nailing and pathological fractures were not included in the present study. Patients with diabetes (BSR > 200 mg/dl), osteoporosis, osteoarthritis, osteomalacia, positive RA factor and those unfit for anesthesia (ASA class  $\geq$  III) were also excluded.

**Data Collection Procedure:** Patients presenting with open tibial shaft fractures falling under Gustilo Type II were included in the study. These patients were randomly divided in two groups by using lottery method. In Group-A a unipolar external fixator was used with 4 half pins (AO External Fixator,). In Group-B intramedullary nailing was used. Fixator pins were placed through an anterior stab incision, using a manual drill. Then patients were followed-up in OPD. On each visit, Clinical evaluation was done for assessment of infection during first 4 weeks. Infection was labeled if there was pus, redness and pain around the wound and body temperature  $\geq$  100°C during 4 weeks of surgery.

### Data Analysis Procedure:

Numerical variables; age of patient has been presented by mean  $\pm$  SD. Categorical variable i.e gender and infection have been presented by frequency and percentage. Chi-square test has been applied to compare the frequency of infection in both the groups taking  $p \leq 0.05$  as significant. Data has been stratified for age and gender to address effect modifiers. Post-stratification chi-square test has been applied taking  $p \leq 0.05$  as significant.

## RESULTS

The age of the patients ranged from 20 years to 50 years. 8 (40.0%) patients in Group-A and 9 (45.0%) patients in Group-B were aged between 20-35 years while 12 (60.0%) patients in Group-A and 11 (55.0%) patients in Group-B were aged between 36-50 years. There were 32 (80.0%) male and 8 (20.0%) female patients in the study cohort with a

male to female ratio of 4:1. Both the study groups were comparable in terms of age ( $p=0.749$ ) and gender ( $p=0.429$ ) groups distribution as shown in Table 1.

Infection was observed in 3 (7.5%) patients overall out of 40 patients. The frequency of infection

**Table 1:** Baseline Characteristics of the Study Groups

Characteristics	Ex. Fix n=20	IM Nail n=20	X <sup>2</sup>	P value
Age (years)				
• 20-35 years	8 (40.0%)	9 (45.0%)	0.102	0.749
• 36-50 years	12 (60.0%)	11 (55.0%)		
Gender				
• Male	17 (85.0%)	15 (75.0%)	0.156	0.693
• Female	3 (15.0%)	5 (25.0%)		

Chi-square test (df=1), observed difference was statistically insignificant

was insignificantly lower with IM nail (5.0% vs. 10.0%;  $p=0.548$ ) as compared to external fixator as shown in Table 2. Similar insignificant difference was observed across various age and gender groups.

## DISCUSSION

**Table 2:** Comparison of Frequency of Infection between the Groups

Infection	Ex. Fix n=20	IM Nail n=20	P value
Yes	2 (10.0%)	1 (5.0%)	0.548
No	18 (90.0%)	19 (95.0%)	

Chi-square test  $\chi^2=0.360$ , df=1, observed difference was statistically insignificant

Tibia, the second largest bone of the skeleton, is located on the anteromedial side of the leg. The commonest cause of tibialdiaphyseal fractures in most areas is road-traffic accidents, and the most difficult tibial fractures occur in motorcycle riders — over 60% of all such tibial fractures are open.<sup>10</sup> The choice of treatment for tibial shaft fractures has changed during the past decade, IM nailing having become more popular due to good results obtained as regards functional outcome<sup>11</sup>.

In recent years, there has been a greater acceptance of the use of IM nailing also in the

treatment open tibial shaft fractures. Earlier it was believed that external fixation is safer for severe open tibial shaft fractures because the vasculature of the tibia is better preserved. The blood supply to the tibia comes mainly from a nutrient artery, and it is highly unlikely that the tibial nutrient artery would survive a high-energy injury. The endosteal blood supply of the tibia is already compromised, and nailing significantly worsens the situation<sup>12</sup>.

Many studies have directly compared the two methods of management.<sup>13</sup> Overall, un-reamed tibial nailing (UTN) reduced the incidence of reoperations, superficial infections, and mal-unions when it was compared with the use of external fixators. Early internal fixation is safe and has several benefits. Available evidence supports the current trend towards the earlier coverage and closure of open fracture wounds.<sup>14</sup> In addition; a high rate of infection occurs if secondary IM nailing has to be performed.<sup>15</sup> The timing of secondary nailing is important to avoid infection. Recently, a large prospective series of open tibial shaft fractures treated with immediate IM nailing without reaming showed that UTN appears to be safe and effective in the treatment of open tibial fractures.<sup>13</sup>

In the present study, 3 patients acquired wound

**Table 3:** Frequency of Infection after External Fixator in Existing Literature

Author	Year	Population	Infection
Ostermann et al. <sup>16</sup>	1993	USA	3.7%
Marsh et al. <sup>9</sup>	1991	USA	5.0%
Park et al. <sup>17</sup>	2007	Japan	7.0%
Stojiljkovic et al. <sup>18</sup>	2007	Europe	8.3%

infection within 30 days of surgery yielding the frequency of infection of immediate intramedullary nailing of open tibial shaft fractures to be 5.0%. The results of our study match with those of Craveiro-Lopes et al. in 2016 (5.0%), Sing et al.<sup>5</sup> in 2011 (4%) and Bhattacharjya et al.<sup>6</sup> in 2012 (2.38%). A similar frequency of infection was observed with external fixator where it was found to be 10.0%. Our results are comparable to those of Stojiljkovic et al.<sup>18</sup> and

Park et al.<sup>17</sup> who reported similar frequency of 8.3% and 7.0% for infection after external fixator for open tibial shaft fractures. Marsh et al.<sup>9</sup> (5.0%) and Ostermann et al.<sup>16</sup> (3.7%) however reported relatively lower frequency of infection with external fixator.

Thus immediate intramedullary nailing was not associated with any increased frequency of infection in open tibial shaft fractures when compared with external fixator, but it avoided the drawbacks of patient's tuckiness, pain, prolonged hospital stay and complications associated with external fixator. The results of the present study are similar to those of other studies in this regard. A very important limitation of our study is that we only considered infection as the outcome variable and other parameters like post-operative pain, length of hospital stay and non-union were ignored which are however important and must be considered before a change of practice. Future studies considering these parameters are therefore highly recommended.

## CONCLUSION

Frequency of infection after immediate intramedullary nailing of open tibial shaft fractures was comparable to that of external fixator. Immediate intramedullary nailing thus appears method of choice for the management of such patients in future practice.

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## COMPARISON OF MEAN DURATION OF FIRST STAGE OF LABOUR IN PRIMIGRAVIDAS WITH PHLOROGLUCINOL VERSUS DROTAVERINE HYDROCHLORIDE AT TERM

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### ABSTRACT

**Background:** Labour is defined as painful uterine contraction that brings about demonstrable effacement and dilatation of the cervix. The latent phase of labour is also called prodromal labour or pre-labour. The most prominent sign of labour are the strong contractile waves that move the fetus down the birth canal. Cervical change occurs at a slow, gradual pace during the latent phase of the first stage of labor. Different drugs are available which can help in reducing the duration of first stage which may help in reducing complications of prolonged first stage and number of cesarean sections and complications associated with it. Phloroglucinol and Drotaverine are two successful drugs but due to controversy, they are not in much use. So we conducted this study to compare both of these drugs and find the most effective drug which can reduce duration of first stage of labour.

**Objective:** To compare the mean duration of first stage of labour with intravenous Drotaverine versus intravenous phloroglucinol in primigravidas presenting in active phase of labor at term.

**Material and Methods:** A randomized control trial was conducted at Unit II, Department of Obstetrics & Gynecology, Jinnah hospital, Lahore. The study was conducted in the six months from April to September 2015; the non-probability purposive sampling technique was used in this study. Informed consent and demographic profile (name, age, gestational age,) was obtained. Females were randomly divided into two groups by using lottery method. In group P, females were administered i/v phloroglucinol 40mg and in the group D, females were administered i/v drotaverine 40mg. Injection was repeated every 60 minutes till fully cervical dilatation and 2nd stage starts. Duration of labour was noted. Both groups were compared for mean duration of first stage of labor by using independent sample t-test. P-value <0.05 was considered as significant.

**Results:** The mean age of the patients was 27.24±4.64 years while the mean gestational age was 38.82±1.35 weeks. The mean duration of first stage labor of the patients was 177.18±40.48 minutes. Statistically there is highly significant difference was found between the study groups and duration of labour at first stage labour of the patients i.e. p-value=0.000

**Conclusion:** This study concluded that both phloroglucinol and drotaverine appears to be effective in the acceleration of labour but phloroglucinol is superior which further shortens the duration of labour.

**Keywords:** First Stage of Labour, Phloroglucinol, Drotaverine, Duration of labour, Gestational age, Primigravida.

Labour is defined as painful uterine contraction that bring about demonstrable effacement and dilatation of the cervix.<sup>(1)</sup> Defining normal and abnormal labor progression has been a long-standing challenge.<sup>(2)</sup>

All these causes increased physiological burden for the mother and may eventually cause complications in the 2nd stage and the puerperium. A

short 1st stage of the labor is naturally of dual advantage, both to the obstetrician and the patient.<sup>(3)</sup>

In a large, contemporary population, the rate of cervical dilation accelerated after 6 cm and progress from 4 to 6 cm was far slower than previously described. Allowing labor to continue for a longer period before 6 cm of cervical dilation may reduce the rate of intrapartum and subsequent repeat

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cesarean deliveries.<sup>(2)</sup>

The active phase of labor may not start until 5cm of cervical dilation in multiparas and even later in nulliparas. Given that cervical dilation accelerates as labor advances, a graduated approach based on levels of cervical dilation to diagnose labor protraction and arrest is proposed.<sup>(4)</sup>

As a serious circumstance, prolonged labor contributes to increased perinatal loss and infant mortality and morbidity apart from causing psychological trauma to the mother. In recent decade, Spasmolytics and spasmo-analgesics combinations are frequently administered to facilitate dilatation of the cervix during delivery and to shorten first stage of labor as an attempt to speed up the process of labor.<sup>(5)</sup>

Drotaverine hydrochloride, has been found to be superior than valethamate in augmenting first stage of labour. Drotaverine is a phosphodiesterase (PDE) inhibitor and is selective for type IV isoenzyme. It relieves muscular spasm and this is thought to facilitate cervical dilatation.<sup>(6)</sup>

Phloroglucinol is one of spasmolytics, primarily used for gastrointestinal tract colic. The drug was extensively used during 1970s and early 1980s for augmentation of labour.<sup>(7)</sup>

A study reported the significant reduced mean duration of first stage of labour with phloroglucinol i.e.  $144.40 \pm 30.78$  minutes as compared to drotaverine hydrochloride i.e.  $191.25 \pm 76.89$  minutes (p-value=0.000).<sup>(8)</sup>

The rationale of this study is to compare the mean duration of first stage of labour with intravenous Drotaverine versus intravenous phloroglucinol in primigravidas presenting in active phase of labor at term. There is not much literature present in which both of these drugs are compared. The literature which is available that is controversial. But the studies that were reported earlier had small sample size as well. This study is designed to be conducted with large sample size so that we may achieve more précised results.

There are various definitions of the onset of labour, including:

- Regular uterine contractions at least every six minutes with evidence of change in cervical dilation or cervical effacement between consecutive digital examinations.<sup>(9)</sup>
- Regular contractions occurring less than 10 min

apart and progressive cervical dilation or cervical effacement.<sup>(10)</sup>

- At least 3 painful regular uterine contractions during a 10-minute period, each lasting more than 45 seconds.<sup>(11)</sup>

In order to avail for more uniform terminology, the first stage of labour is divided into "latent" and "active" phases, where the latent phase is sometimes included in the definition of labour<sup>(12)</sup>, and sometimes not.<sup>(13)</sup>

Some reports note that the onset of term labour more commonly takes place in the late night and early morning hours. This may be a result of a synergism between the nocturnal increase in melatonin and oxytocin.<sup>(14)</sup>

Phloroglucinol is an organic compound that is used in the synthesis of pharmaceuticals and explosives. It is a phenol derivative with antispasmodic properties that is used primarily as a laboratory reagent.<sup>(15)</sup>

Austrian chemist Heinrich Hlasiwetz (1825-1875) is remembered for his chemical analysis of phloroglucinol.<sup>(15)</sup>

Phloroglucinol is also generally found in the flavonoid ring A substitution pattern.<sup>(15)</sup>

Phloroglucinol is one of spasmolytics, primarily used for gastrointestinal tract colic. The drug was extensively used during 1970s and early 1980s for augmentation of labor. There has been a resurgence of interest in the subject. 18% incidence of Post-Partum Haemorrhage was reported due to uterine atony with the use Drotaverine hydrochloride. This incidence is statistically significant and limits the use of Drotaverine in labor.

Although the number of patients with these complications were not large enough but still it is suggested that phloroglucinol can be used in patients with above mentioned complications with no toxic effects and a good outcome. Phloroglucinol shortens the duration of labor, is non toxic to both mother and foetus and does not cause uterine atony. It also has an analgesic action. As Spasmolytic, phloroglucinol have a definite role in obstetrics.<sup>(16)</sup>

Drotaverine (INN, also known as drotaverin) is an antispasmodic drug structurally related to papaverine. Drotaverine is a selective inhibitor of phosphodiesterase 4, and has no anticholinergic effects. Drotaverine has been shown to possess dose-dependant analgesic effects in animal models.



Drotaverine is sold under the brand name “No-Spa” (Chinoin Pharmaceutical and Chemical Works, Hungary, a member of the Sanofi S.A.) and under many other names in the states of former Soviet Union (such as Russia and Kazakhstan), mainly “Но-шпа” (pronounced nosh-pa).<sup>(17)</sup>

#### **Operational Definition:**

**Duration of first stage of labour:** It was measured in minutes after administration of drugs till complete dilatation i.e. from 3cm to full dilatation with palpable uterine contractions of active labour.

#### **MATERIALS AND METHODS:**

This present randomized control trial was conducted at Unit II, Department of Obstetrics & Gynecology, Jinnah hospital, Lahore. The study was conducted in the six months from April to September 2015; the non-probability purposive sampling technique was used in this study.

Sample size of 200 females; 100 females in each group is calculated with 95% confidence interval, 80% power of test and taking magnitude of mean duration of first stage of labour i.e.  $144.40 \pm 30.78$  minutes with phloroglucinol and  $191.25 \pm 76.89$  minutes with drotaverine hydrochloride in primigravidas presenting in active phase of labor at term.

#### **Sample selection:**

##### **Inclusion criteria:**

- Females with gestational age >37 weeks (assessed through USG and antenatal record)
- Primigravidas of reproductive age group (20-35 years)
- In spontaneous active labour undergoing normal vaginal delivery (cervical dilatation >3cm fully effaced with regular uterine contractions and  $\geq 1$  in 10 minutes).

##### **Exclusion criteria:**

- Multiple pregnancy (assessed through USG).
- Macrosomic babies or Malpresentation (assessed through USG).
- Cephalopelvic disproportion or contracted pelvis (assessed through USG).
- Fever ( $>100^{\circ}\text{C}$ ), cardiac problems (assessed through ECG), migraine and any other psychiatric disorder (assessed through history and medical record).
- Females having allergy to any content of any of drugs using in trial (through history).
- High risk patients (BP>140/90mmHg, BSR>200gm/dl, pre-eclampsia (BP>14-/90, protein urea+1 on dipstick), and/or eclampsia (pre-eclampsia with convulsions).

#### **Data collection procedure**

200 primigravidas, who fulfil selection criteria, were enrolled in study from Labor room of Jinnah hospital, Lahore. Informed consent and demographic profile (name, age, gestational age, contact number) was obtained. Females were randomly divided into two groups by using lottery method. In group P, females were administered i/v phloroglucinol 40mg and in the group D, females were administered i/v drotaverine 40mg. Injection was repeated every 60 minutes till fully cervical dilatation and 2nd stage starts. Duration of labour was noted (as per operational definition). All this information was collected through a pre-designed proforma.

#### **Data analysis procedure**

Data was analyzed by SPSS version 16. Quantitative variables like age, duration of first stage of labour and gestational age was presented as mean+SD. Both groups were compared for mean duration of first stage of labor by using independent sample t-test. P-value<0.05 was considered as significant.

#### **Results:**

Total 200 cases were presented in Unit II, Department of Obstetrics & gynecology, Jinnah hospital, Lahore. The mean age of the patients was  $27.24 \pm 4.64$  years with minimum and maximum ages of 20 & 35 years respectively. Table#1

In this study the mean gestational age of the patients was  $38.82 \pm 1.35$  weeks with minimum and maximum gestational ages of 37 & 41 weeks respectively. Table#2

The study results showed that the mean duration of first stage labor of the patients was  $177.18 \pm 40.48$  minutes with minimum and maximum duration of 101 & 240 minutes respectively. Table#3

In this study the mean duration of first stage labor in Drotaverine group was  $212.25 \pm 18.58$  minutes and in Phloroglucinol group it was  $142.11 \pm 21.57$  minutes. Statistically there is highly significant difference was found between the study groups and Duration of first stage labor of the patients. i.e p-value=0.000 Table#4

#### **Discussion:**

Labour is a multifactorial process which involves myometrial contraction, cervical ripening and dilatation and the expulsion of fetus and placenta in an orderly manner. The first stage of labour in primigravida lasts about 12-16 hours and in a parous woman 6-8 hours.<sup>(18)</sup>

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Phloroglucinol and drotaverine are commonly used pharmacological agents in labour room in many hospitals, to decrease the duration of first stage of labour in order to prevent the prolonged labour. Because the morale of most women start to deteriorate after six hours in labour and after twelve hours the rate of deterioration significantly accelerates, there is a greater incidence of operative vaginal deliveries, Caesarean section and also fetal hypoxia.<sup>(19)</sup>

In our study the mean duration of first stage labor of the patients was 177.18±40.48 minutes. In comparison of both groups mean duration in Drotaverine group was 212.25±18.58 minutes and Phloroglucinol group it was 142.11±21.57 minutes. Highly significant difference was found between the

**Table 1:** Descriptive statistics of age (years)

<b>Age (Years)</b>	n	200
	Mean	27.24
	SD	4.64
	Minimum	20.00
	Maximum	35.00

study groups and duration of first stage labour of the patients. Our study showed that Phloroglucinol group significantly reduces the duration as compared to Drotaverine group. i.e p-value=0.000

Naqvi, demonstrated that the duration of first

**Table 2:** Descriptive statistics of gestational age (weeks)

<b>Gestational age (weeks)</b>	n	200
	Mean	38.82
	SD	1.35
	Minimum	37.00
	Maximum	41.00

stage of labour in group A (phloroglucinol) was 144.40 ± 30.78 minutes and group B (drotaverine) was 191.25 ± 76.89 minutes, difference was statistically significant (p < 0.05) so duration of first stage of labour was 46.85 minutes (24.49%) faster in group A.<sup>(19)</sup>

**Table 3:** Descriptive statistics of duration of first stage labor

<b>Duration of first stage (Minutes)</b>	n	200
	Mean	177.18
	SD	40.48
	Minimum	101.00
	Maximum	240.00

A study reported the significant reduced mean duration of first stage of labour with phloroglucinol i.e. 144.40±30.78minutes as compared to drotaverine hydrochloride i.e. 191.25±76.89minutes (p-value=0.000).<sup>(18)</sup> While another study reported that with phloroglucinol the mean duration of first stage of labour was 227.74±13.60minutes.<sup>(7)</sup> While with drotaverine hydrochloride mean duration of first

**Table 4:** Descriptive statistics of duration of first stage labor in accordance with study groups

		Study Groups	
		Drotaverine	Phloroglucinol
Duration of first stage labor (Minutes)	n	100	100
	Mean	212.25	142.11
	SD	18.58	21.57

t-value=24.63  
p-value=0.000 (Significant)

stage of labour was 134.23±80.02.<sup>(9)</sup>

Our study findings are consistent with the study conducted by Tabassum<sup>(20)</sup> who concluded that total duration of first stage of labour and rate of cervical dilatation in phloroglucinol group was 227.74±13.60 and 2.14±0.36 cm per hour respectively, in our study it was 144.40 ± 30.78 and 2.86 cm per hour respectively.

Study conducted by Sharma<sup>(21)</sup> who concluded that duration of first stage of labour and rate of cervical dilatation in drotaverine group was 194±57.04 minutes and 2.04±0.68 cm per hour and in our study it was 212.25±18.58 minutes. Similar results have been reported by Himangi.<sup>(22)</sup>

Bindiya Gupta et al concluded in their study that Drotaverine hydrochloride and hyoscine-N-butylbromide do not have a role in augmentation of labor. They showed that the mean duration of the active phase of labor was 4.48±2.26 h, 3.9±2.42 h, and 3.6±2.07 h in groups 1, 2, and 3, respectively. The mean rate of cervical dilation was 2.6 cm/h, 2.4 cm/h, and 2.5 cm/h, respectively.<sup>(23)</sup>

In our study the mean age of the patients was 27.24±4.64 years and the mean gestational age of the patients was 38.82±1.35 weeks with minimum and maximum gestational ages of 37 & 41 weeks respectively.

Naqvi, et al in their study showed the Mean period of gestation was 38.6 ± 1.16 weeks and 38.6 ± 1.05 weeks and mean age in years was 27.3 ± 3.71 and 27.3 ± 3.82 in group A and B respectively and were not statistically significant.<sup>(19)</sup>

Tabassum et al demonstrated that all patients in their study were with <37 weeks gestation, delivered

healthy babies showing that phloroglucinol can be used in patients with preterm labour without any risk of respiratory depression of fetus.<sup>(16)</sup>

## CONCLUSION:

It has been concluded through results of this study that Phloroglucinol is more effective than Drotaverine in reducing duration of first stage of labour. Thus in future we will implement the use of Phloroglucinol to reduce first stage of labour. This will help in reducing complications of prolonged first stage of labour and number of unnecessary cesarean sections.

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## UNCONTROLLED HYPERTENSION AND CANCER SURGERY: WHETHER TO ANESTHETIZE OR NOT?

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### ABSTRACT

Uncontrolled Hypertension remains one of the commonly encountered problems in surgical patients. It poses multiple complications in peri-operative time depending upon duration and severity of disease along with end organ damage. Various classifications and treatment guidelines have been devised in literature for control of hypertension. Hypertension can lead to different problems in peri-operative period especially in patients with uncontrolled disease. However, in cancer surgery, the dilemma of delaying cancer patients to achieve optimum control of blood pressure, still remains questionable because delay in the cancer surgical procedure to achieve optimum level of blood pressure can adversely affect the prognosis of disease. We have reviewed different guidelines and protocols available for the classification of hypertension, looked for various complications of uncontrolled hypertension and their impact on different body organs, and most importantly the impact of delay while optimizing blood pressure on overall patient outcome.

**Key words:** Hypertension, peri-operative complications, JNC 8, delay in cancer surgery, time sensitive procedures.

Hypertension is one of the most common medical conditions affecting about 73 million people in United States alone.<sup>(1)</sup> According to data from the Centers for Disease Control and Prevention (CDC), hypertension is prevalent in 30.4% of the world population and out of these 53.5% of population do not have their hypertension controlled.<sup>(2)</sup> It is the most common condition in pre-anesthesia visits for postponing elective surgery.<sup>(3)</sup> Surgical patients may have different stages of increasing blood pressure and possible end organ damage as well. Hypertension is a risk factor for myocardial infarction, chronic kidney disease, retinopathy, stroke including infarction and hemorrhage.<sup>(4,5)</sup> There are different classifications available to describe severity of disease as well as various treatment options depending upon severity of disease and associated comorbid conditions and end organ damage. Randomized controlled trials show improved outcome in presence of antihypertensive drug treatment in

patients with hypertension<sup>(6)</sup>.

Cancer patients are unique that, they can't wait a lot of time for optimization before surgery as delays in surgical procedures in these patients can lead to worsening of their prognosis with regards to cancer. Further there may be further spread of cancer or even metastasis while these patients wait for their hypertension to be optimized. Various studies have been done showing that hypertension may not even be up to optimal level in 6-8 weeks while waiting for surgery in these patients<sup>(7,8)</sup>.

In this article we have reviewed various classifications of hypertension, different treatment options, peri-operative concerns in patients with uncontrolled hypertension, its possible complications as well as various concerns of delay in surgical procedures in cancer patients.

### METHODOLOGY:

Literature related to hypertension, its multiple

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problems and concerns of delay in cancer surgery was searched since 1980 to 2016 from Pub med and Medscape using the mentioned key words.

**CLASSIFICATION OF HYPERTENSION:**

Different classifications have been described by different societies dealing with health care problems.

**Joint national committee (JNC 7) Classification<sup>(9)</sup>:**

Classification	Systolic blood pressure (mmHg)		Diastolic blood pressure (mmHg)
Normal	<120	and	<80
Prehypertension	120-139	Or	80-89
Stage 1 Hypertension	140-159	Or	90-99
Stage 2 hypertension	>160	Or	>100

**British Hypertension Society NICE /NHS guidelines (2011)<sup>(10)</sup>:**

Classification	Clinic Blood Pressure (mmHg)	Ambulatory/ Home BP (mmHg)
Stage 1 hypertension	≥ 140/90	≥ 135/85
Stage 2 hypertension	≥ 160/100	≥ 150/95
Severe hypertension	Systolic BP ≥ 180 Or Diastolic BP ≥ 110	

**WHO Classification International Society of Hypertension (ISH)<sup>(11)</sup>:**

Grade of hypertension	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)
Grade 1	140-159	90-99
Grade 2	160-179	100-109
Grade 3	≥ 180	≥ 110

**Blood pressure goals: Evidence-Based Guideline 2014: JNC 8<sup>(12)</sup>:**

The panel members appointed to the eighth Joint National Committee (JNC 8) has given following blood pressure goals in different age groups and disease status.

**General population aged > 60 years:** Target blood pressure <150/90 mmHg (Grade A evidence).

**General population aged < 60 years:** Target blood pressure <140/90 mmHg (Grade E evidence).

- Diastolic BP goal in aged 30-59 years: Grade A evidence
- Diastolic BP goal in aged 18-29 years: Grade E evidence
- Systolic BP goal: Grade E evidence

**Patients with DM and CKD:** Target blood pressure <140/90 mmHg (Grade E evidence)

**COMPLICATIONS OF HYPERTENSION:**

Hypertension is associated with multiple complications and end organ damage including heart, kidney, brain and eyes. It is a risk factor for atherosclerosis and ultimately can lead to ischemic heart disease, heart failure, left ventricular hypertrophy due to structural changes in heart, diastolic dysfunction and peripheral arterial disease. Patients with left ventricular hypertrophy are on risk for developing congestive heart failure, stroke and sudden death<sup>(13,14,15,16)</sup>. The impact of hypertension on kidney is also well understood, it leads to kidney injury and end stage renal disease. These changes are actually due to atherosclerotic patches affecting glomerular capillaries and post glomerular structures ultimately leading to ischemia.<sup>(17)</sup> Regarding brain, the incidence of cerebral hemorrhage increases with increased level of blood pressure, also it is risk factor for brain infarction<sup>(18,19)</sup>. In eyes, retinal vessels undergo certain micro vascular changes in correspondence with increasing level of blood pressure causing vasospasm and retinal ischemia<sup>(4)</sup>.

**Pre-op considerations in a patient with Hypertension<sup>(20)</sup>:**

- Duration and severity of disease.
- Compliance with medications and number and type of drugs for treatment.
- BP control: Uncontrolled or resistant hypertension.
- Association with systemic complications.
- Association with other medical disease e.g. Diabetes mellitus, Obesity, hyperlipidemia.
- Target organ damage including heart, brain,



kidneys and peripheral vessels.

- Side effects and complications of drug treatment.

### PERIOPERATIVE PROBLEMS:

#### High readings of blood pressure in pre-operative period in spite of medication:

This is precipitated by pre-operative anxiety related to surgical procedure and it is usually isolated systolic hypertension and gets settle with anxiolytic medications<sup>(21)</sup>. Anyhow, if patient has missed the routine medications in morning time, then it can lead to high reading readings of blood pressure. Therefore, it is advised to continue antihypertensive medications in pre-operative period especially the beta blockers and nitrates, although few have concerns in continuing ACE inhibitors, angiotensin receptors blockers, and diuretics to avoid severe hypotension after induction of general anesthesia<sup>(22,23)</sup>.

#### Blood pressure swings on induction of anesthesia:

Hypertensive patients show variable responses after induction of general anesthesia, laryngoscopy and intubation. Adequate control of blood pressure is required to avoid responses and changes in blood pressure after induction of general anesthesia including initial hypotension followed by increased blood pressure secondary to sympathetic activation during laryngoscopy. This response is more pronounced in patients with uncontrolled and untreated hypertension.<sup>(24)</sup> It includes rise of even more than 90 mmHg rise in systolic blood pressure in hypertensive patients as compared to 20-30 mmHg in non-hypertensive individuals. Hypertensive patients face more lability in blood pressure<sup>(25)</sup> in peri-operative time which may lead to myocardial ischemia as mentioned by Roberts et al<sup>(26)</sup>. Recovery from general anesthesia leads to changes in blood pressure and heart rate that slowly increase it affects more to the hypertensive patients<sup>(27)</sup>.

#### Requirement of high mean arterial pressure to maintain end organ perfusion<sup>(28,29)</sup>:

Hypertension shift the mean arterial pressure and peripheral organ perfusion curve to right side

and raised level of blood pressure is required to maintain peripheral perfusion especially of vital organs. Lower mean arterial pressure can lead to hypoperfusion of these vital organs and ultimately ischemia and its disastrous effects.

#### Hypotensive anesthesia for neurosurgery and maxillofacial surgery<sup>(30,31)</sup>:

Induced hypotension is usually required by surgical team to decrease surgical site bleeding and optimized condition for ongoing surgery. This can cause hypoperfusion of the end organs. Brief periods of hypotension can be compensated by stable patients but in patients with already having end organ damage, it further leads to deterioration of organ functions. Multiple strategies may be required for optimized surgical conditions including regional anesthesia, vasodilators, limiting period of induced hypotension, invasive monitoring, diagnosis and management of ongoing metabolic acidosis as well as experienced surgical handling.

#### Risk of surgical site hemorrhage & exaggerated response to pain<sup>(32,33)</sup>:

Peri-operative hypertension can be one of the reason for more surgical site hemorrhage prolonged duration of surgery, requirements of blood transfusion. In recovery room, post-operative pain can be common cause of increasing blood pressure and it requires appropriate management.

Various other studies show concerns of hypertension on patient outcome. A multi centered study in Swiss Hospitals, 125,000 patients in which 27881 (22%) hypertensive, at least 1 cardiovascular event occurred in 6 % patients<sup>(34)</sup>. Another review of 45 different papers, different complications in hypertensive patients in peri-operative period documented<sup>(35)</sup>. Regarding cancellation of surgery, patients with end organ damage and stage 3 hypertension, cancellation is justified to achieve optimum level of blood pressure<sup>(36)</sup>.

### CANCER SURGERY AND HYPERTENSION CONTROL:

In cancer surgical patients, the benefits of

optimization have to be balanced against the risk of spread and dissemination of disease. Most cancers are rapidly growing and the treatment of any cancer depends upon the stage at which it is diagnosed and treatment instituted. For those cancers for which the primary treatment is surgery, it has to be done in optimum time period. This issue has been identified by the American Heart Association which in its 2014 update has used the term “time sensitive procedure”. This time sensitive procedure is defined as a procedure in which delays of more than one week to six weeks for evaluation and optimization can negatively affect outcome<sup>(37)</sup>.

This “time sensitive” nature of cancer surgery has been highlighted for many cancers. Smith and colleagues showed that young women with breast cancer with a longer treatment delay time have significantly decreased survival time compared with those with a shorter treatment delay time.<sup>(38)</sup> Kulkarni et al found that treatment delay between transurethral bladder tumor resection and radical cystectomy resulted in worse overall survival.<sup>(39)</sup> They further stated that the suggested maximum wait time from transurethral bladder tumor resection to cystectomy was 40 days. The literature on head and neck cancers is not that different as found by Stefanuto and colleagues who found that a professional delay exceeding 1 month was associated with an increased risk of the patient having late-stage disease for upper gastrointestinal and respiratory tract cancers<sup>(40)</sup>.

All these studies highlight the importance of minimizing the delay between diagnosis and treatment of cancer, a delay which can be offset by delays for optimization and treatment of hypertension.

#### **PROCEEDING WITH SURGERY IN THE UNCONTROLLED HYPERTENSION:**

Traditionally anesthesia providers are reluctant to proceed with surgery in case of high blood pressure readings in view of the increased risk of cardiovascular complications in these patients. Recent evidence suggests that uncontrolled hyper-

tension is not as big a risk factor as we are lead to believe.

A meta-analysis of 30 observational studies done by Howell and colleagues concluded that the likelihood of experiencing an adverse peri-operative cardiac event is on average only 1.31-fold higher in hypertensive patients than in normotensive patients.<sup>(41)</sup> In addition Wexler and colleagues studied uncontrolled hypertensive patients and compared patients who underwent surgery and those who were postponed. They found no difference in mortality in both groups of patient.<sup>(42)</sup> All these findings were acknowledged by the American Heart Association when they downgraded uncontrolled hypertension to “low risk” in their 2007 guidelines for peri-operative risks<sup>(43)</sup>.

Another concern for most anesthetists, the high intra-operative blood pressure recordings in the uncontrolled hypertensive patient have been addressed by Monk and colleagues who found that it was intra-operative hypotension not hypertension that was one of the factors that led to increased one year mortality in patients undergoing non-cardiac surgery<sup>(44)</sup>.

#### **THE POSTPONED PATIENT FOR OPTIMIZATION:**

The rationale behind postponing any patient for surgery is optimization and compliance with medication so that his body and physiological parameters will be in a better position to cope with the stresses of surgery<sup>(45)</sup>. However, it has yet to be studied whether delay of 4-6 weeks as proposed by most guidelines leads to better control of hypertension. Wax et al found that, patients who returned for surgery days to years later, blood pressure was still high. The results of this study give a clue that the benefits of postponement are overestimated and need to be further investigated<sup>(46)</sup>.

#### **CONCLUSION:**

The debate of anesthetizing patients with uncontrolled hypertension still stays in clinical

practice in spite of keeping in mind the perioperative problems posed by untreated and uncontrolled hypertension. Patients with cancer disease especially in advanced disease and at risk of developing metastasis in case of delays prove difficult and challenge in making a decision of their procedure to be postponed or going ahead. As for as keeping in mind all guidelines and concerns of delay, we conclude that decision should be individualized in every patient considering the pros and cons of uncontrolled hypertension and underlying surgical and medical problems and overall patient outcome. Still there is need of large multi centered study especially in cancer patients regarding hypertension and their disease outcome if delayed anyhow. However, we conclude that we should go ahead for surgery to have better outcome in terms of avoiding cancer dissemination until it is very clear evidence that hypertension can adversely affect their outcome.

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# THE HERLYN-WERNER- WUNDERLICH (HWW) SYNDROME OHVIRA SYNDROME RARE CONGENITAL MULLERIAN ANOMALY

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## ABSTRACT

Herlyn-Werner-Wunderlich syndrome is a rare congenital anomaly of a urogenital tract, uncommon variant of mullerian duct anomalies. This is consisting of uterus didelphys, obstructed hemivagina and ipsilateral renal agenesis. It is also known as OHVIRA syndrome (obstructed hemivagina with ipsilateral renal agenesis).<sup>1</sup> It usually present at puberty with pelvic pain, dysmenorrhea, vaginal or pelvic mass.

This article reports a case of 11 years old student of class four who presented with severe lower abdominal and perineal heaviness, diagnosed as case of Herlyn-Werner-Wunderlich syndrome. Resection of septum obstructing the vagina was done and mucous was drained out.

**Key words:** Uterus didelphys, Herlyn-Werner-Wunderlich syndrome (HWW), OHVIRA syndrome, mullerian anomaly.

Mullerian duct abnormalities cover a wide range of developmental anomalies resulting from defective fusion, non-development or defects in regression of the septum during fetal development.

Herlyn-Werner-Wunderlich syndrome is a rare disease in which there is triad of; uterus didelphys, obstructed hemivagina and renal agenesis (most often ipsilateral). It is also called OHVIRA (obstructed hemivagina with ipsilateral renal agenesis) syndrome.<sup>1</sup>

It is classified as a type III Mullerian duct anomaly (MDA). Accounts for 5% of MDAs.<sup>2,3,4</sup> The estimated overall prevalence of MDA is 2-3% of woman; uterus didelphys constitutes 11% of MDAs. Associated renal anomalies are present in approximately 43%.<sup>5,6</sup>

The most common presentation is pain and dysmenorrhea, pain and abdominal or vaginal mass secondary to haematocolpos or haematometra.

Early detection and treatment is very important, result in good prognosis with preservation of fertility. Early detection and intervention is necessary as

surgical resection of obstructing vaginal septum can provide pain relief and prevent further complications like endometriosis and infertility. Uterine surgery is not recommended. About 80% of patients are able to conceive with didelphys uterus.

We present a case of 11 years old student of class four who presented with severe lower abdominal and perineal heaviness, diagnosed as case of Herlyn-Werner-Wunderlich syndrome (obstructed hemivagina uterus didelphys and ipsilateral renal agenesis). Resection of septum obstructing the vagina and marsupialization was done and moderate amount of mucous was drained out.

## Case Report

Presentation of a clinical case of 11 year old unmarried girl, student of class four with chief complaint of severe pain in lower abdomen and heaviness in the lower abdomen and perineum on the left side since 1-2 years. She had not started menstruation yet. There is history of occasional vomiting. She had appendectomy one year back. There was no urinary or bowel complaints. Pain was refractory to analgesics. She was admitted in several hospitals for the same complaint where conservative

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management was done without any diagnosis and referred to Jinnah Hospital.

**Examination:**

Secondary sex characters well developed, Adrenarche and thelarche Tanner's Stage III

Abdominal Examination: Abdomen was soft and non tender. There was no mass palpable.

Rectal Examination; Firm bulge was present on left half of vagina, rectal mucosa was free from the bulge.

PV examination was not done.

Ultrasonography of abdomen and pelvis revealed didelphys uterus, right side uterus 5x2.3 cm with central endometrium 0.3 cm. Left uterine horn measured 5.8x3.5x4.2 cm. Left endometrial canal showed fluid/ blood extending into left fallopian tube and downward into cervix and vaginal canal. Both ovaries were normal looking. No free fluid in pelvis. Right kidney normal in size and texture (compensatory hypertrophy). Left kidney absent.

MRI of abdomen & pelvis revealed two uterine cavities along with two cervixes. The right sided cervical canal was patent. However left sided cervical canal was distended with fluid appearing hypointense on T1W1 and hyperintense on T2W1 measuring 4x2.1cm suggesting hydrocolpos. There was suspicion of left sided imperforate hymen. Both ovaries were normal. Limited slices through lower abdomen revealed non visualization of left kidney. No ascites was seen. So the diagnosis of HWW syndrome was made by didelphys uterus with left sided hydrocolpos suggested obstructed hemivagina and unilateral renal agenesis.

IVU showed absent left kidney with mild compensatory hypertrophy of right kidney.

The patient was planned for examination under general anaesthesia (EUA). All haematological investigations were normal. Small cystic bulge was present on left side of vagina. Right side cervix was visualized and right sided vaginal walls were normal looking with normal rugosities and absence of any bulge. The bulge on the left side of vagina was firm

extending up to vault, its margins could not be made out, upper limit could not be reached. Rugosity was present on the vaginal mucosa. Left cervix was not visualized as there was oblique vaginal septum. With wide bore needle 16G bulge was punctured at the point of maximum bulge on left side and approximately 30-50cc of thick mucous was aspirated followed by a resection of septa at the same time. Marsupialization of margins of septum was done. Left sided normal looking cervix was visualized after resection of septum.

Patient had uneventful post operative period. She was discharged and was called for regular follow up until puberty.

**DISCUSSION:**

The exact etiopathogenesis of HWW syndrome is still not known.

Mesonephric (Wolffian) and para-mesonephric (Mullerian) ducts are two paired urogenital structures from which internal genital organs and lower urinary tract are derived. Wolffian ducts play an important role in the development of internal genital organs and give rise to kidneys.<sup>7</sup> They are inductor elements for adequate fusion of the Mullerian ducts. If one of the Wolffian duct is absent, the ipsilateral kidney and ureter will fail to fuse in the midline. This process can be complete or incomplete. Uterus didelphys is formed if failure of fusion is complete. The Mullerian duct on the side lacking the Wolffian duct displaces itself laterally and cannot come into direct contact with the urogenital sinus in the centre with the resultant formation of a blind sac, imperforate or obstructed vagina.

A didelphic uterus results due to embryologic arrest during the 8th to 10th week of gestation. This ultimately affects the Mullerian and metanephric duct.<sup>8</sup> About 75% of patients with didelphys uterus have a partial or complete vaginal septum which is commonly longitudinal in the Herlyn-Werner-Wunderlich syndrome. Occasionally one hemivagina is obstructed by an oblique vaginal septum and asymmetry of vagina may result in complete

closure of one half with subsequent cryptomenorrhoea and haematometra.<sup>7</sup> The distal third of a vagina developing from the urogenital sinus is not affected.

Others associated anomalies include duplication of the kidneys and ureters, ectopic ureter, IVC duplication; renal dysplasia.<sup>9</sup> Renal agenesis is ipsilateral to the dilated uterine cavity. The right side is affected twice more frequently than the left side.<sup>4,5</sup>

In patients with uterine and vaginal abnormalities, work up for associated renal anomalies should be performed. USG has advantage of low cost and real time imaging.

MRI is considered gold standard for diagnosis. It evaluates uterine, cervical and vaginal morphology, also detects level of obstruction, characteristics fluid contents, no radiation hazard, can detect associated renal agenesis and can diagnose complications like endometriosis.

Early detection and treatment is very important and result in good prognosis with preservation of fertility. As much as 80% patients with uterus didelphys conceive but there is associated increase risk of premature delivery (22%) and abortion (74%). Caesarean section is needed in over 80% of patients.<sup>9</sup> Rare complications of adenocarcinoma of the obstructed side of the uterine cervix and clear cell carcinoma of the obstructed portion of the vagina have been described.<sup>9</sup>

## CONCLUSION:

The diagnosis is often difficult due to infrequency of the syndrome. A high index of suspicion is needed in patients with renal and uterine anomalies to detect the HWW syndrome for timely diagnosis and to prevent complications. Delay in diagnosis increases the risk of complications such as endometriosis and infertility.<sup>9,10</sup> If this syndrome is suspected, the diagnosis is simple and can be made by ultrasound, computed tomography and MRI of abdomen and pelvis. Optimal treatment is full excision and marsupialization of obstructing vaginal septum so both uteri can drain through the patent

vagina. Uterine surgery is usually not recommended.

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## IMPACT OF E-LEARNING ON MEDICAL EDUCATION AMONG MEDICAL STUDENTS OF LAHORE

Mahmood Danishwar, Raesham Bukhari, Jawaria Tariq, Jamshed Siddique, Maheen Anwar, Tahir Ismail

### ABSTRACT

**BACKGROUND:** E-learning refers to the use of internet technologies to deliver a broad array of learning modes that enhances learner's knowledge, skills and performance.

**OBJECTIVE:** The aim of our study was to note the impact of E-learning techniques on medical education and student performance and to compare the use of E-learning with traditional learning.

**METHOD:** Using cross-sectional study design we evaluated the impact of E-learning on medical education of 200 medical students (sample size) in three months. We analyzed data through SPSS 21.0.

**RESULTS:** There is evidence for the effectiveness and acceptance of E-learning within medical education community. Among the various means of E-learning, video lectures are the most popular among medical students. Our study has revealed that E-learning offers learners control over content, pace of learning and time thus it is more preferable than the traditional learning.

**CONCLUSION:** There is positive association between usage of E-learning techniques and better academic performance among medical students. In a nutshell, E-learning may be termed as 'right knowledge at the right time in the right place'.

E-learning also known as web-based-learning, distributed-learning, online-learning, computer-assisted-instruction, or internet-based-learning describes the use of information and internet technology to enhance knowledge and education<sup>[1]</sup>. E-learning is simply the marriage between education and technology<sup>[2]</sup>. Termed as 'digital-natives', the new generation of students is held to be experiential-learner, dependent on internet technology for accessing information and interacting with others<sup>[3]</sup>. Koohang and Paliszkievicz(2013) proposed that e-learning enhances active learning, which in turn enhances knowledge construction<sup>[4]</sup>.

Two modes of electronic-learning unfolds are:

1. Distance learning; providing information to students in remote areas
2. Computer-based-learning; providing stand alone multi-media packages<sup>[5]</sup>.

The vantages of e-learning include enhanced learning, time conservation, cost preservation, eco-friendly-system and self-empowerment<sup>[6,2]</sup>. Moreover, a survey of 400 students in University of Taiwan showed that e-learning is equally beneficial for instructors as for students, equipping them with modern teaching techniques thus improving their teaching efficiency<sup>[7]</sup>.

Lack of contact, isolation, concerns about quality and dependance on technology are among the few cons of E-learning<sup>[6,8]</sup>.

In Pakistan, mostly conventional method of study is being used. Allama Iqbal Open University, CIIT and Virtual University are among the few prominent universities stepping ahead and adopting the modern learning methodology i.e E-learning. The future demands enhancement of this technique for better knowledge base<sup>[9]</sup>.

E-learning is widely used in medical education globally. Medical students consider it a supplement to conventional learning techniques. One estimate suggested that by 2010 more than 30% of a physician's time will be spent obtaining information from internet and utilizing technology tools<sup>[2]</sup>.

### MATERIAL AND METHODS:

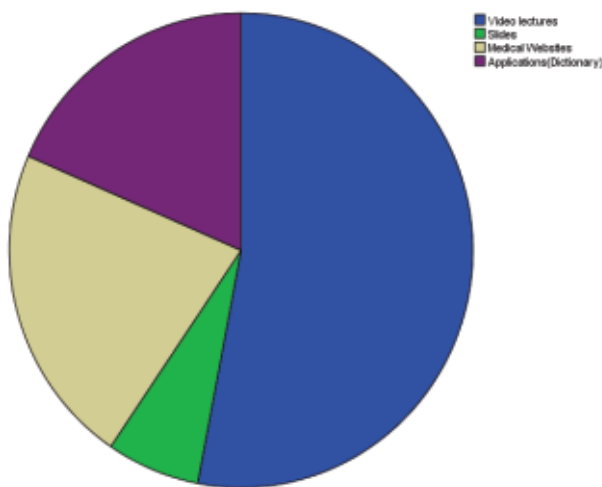
It was a Cross sectional study, conducted in Allama Iqbal Medical College Lahore, King Edward Medical University, CMH-Lahore Medical College and Institute of Dentistry, Akhtar Saeed Medical and Dental College and Ameer-ud-din Medical College over a period of three months. Sample size was 200 students. Non probability purposive sampling was done. MBBS students (of both genders from First year-Final year) of above mentioned colleges were included in the study. Students who had done Web Designing and Management Courses (as they would be already convinced) were excluded. Informed consent and demographic profile was taken from each student

and then they were inquired about the impact of E-Learning techniques on medical education. All the information was collected in a structured questionnaire.

The data was analyzed by SPSS version 21.0. Mean and standard deviations were calculated for numerical variables like age, duration of coping strategies used during dissection. Frequency tabulation and percentages were generated for nominal variables like dissecting room experience and coping strategies. Cross tabulation was done for variables of interest like gender and impact on performance.

**RESULTS:**

A total of 200 subjects fulfilling the inclusion criteria were included in our study. 75% from Allama Iqbal Medical College, 7.5% from King Edward Medical University, 7.5% from Combined Military Hospital, 5% from Ameer-ul-din Medical College and 5% from Akhtar Saeed Medical College. Among 200 subjects 52.5% were males and 47.5% were females. Out of 200 subjects 97.5% knew about E-learning and 2.5% did not know. 53% students used video lectures, 6.5% used slides, 22% used medical websites and 18.5% used medical applications (eg. dictionary) as E-learning techniques. (figure no 1). 52.5% were in favour of E-learning while 47.5% support traditional learning. According to 83.5%, their academic performance was improved by using E-learning while 16.5% thought it had no effect. The p-value shows that there is a positive association between the use of E-learning and performance of the medical students of medical colleges of Lahore.



**Figure No.1:** Pie Chart of techniques used for E-learning

chi-square,16.471,df,4,p-value,0.002 i.e significant

**DISCUSSION:**

A cross-sectional study was conducted by using a questionnaire for gathering information about E-learning and 200 students (52.5% were males and 47.5% were females) volunteered. Male students filled the questionnaire better than females and were more interested and more responsive. This result disagrees with the result of study done among undergraduate male and female students of Taibah University, KSA according to which the female students were more interested ( 67.2% were females and 32.7% were males).<sup>[12]</sup>

With the advancement of knowledge and technology E-Learning (Internet based learning) has become popular among different fields and is

**Table 3:** Frequency of Positive effects of E-learning techniques on Academic Performance

Positive Effect of E-learning	Frequency	Percent
Yes	167	83.5
No	33	16.5
Total	200	100.0

gaining equal popularity among the Medical students. It has become an essential part of their learning. It was observed that out of 200 students from different medical colleges of Lahore 195 students knew about E-learning while only 5 were unaware. While according to a study targeted on



**Table 4:** Crosstabulation

Usage	Better Performance		Total
	Yes	No	
Yes	144	19	163
No	23	14	37
Total	167	33	200

higher education institute in Sri Lanka concluded that among 174 students 58 were having high awareness about E-learning 44 had moderate knowledge and 72 knew only how to operate. The drastic increase in the use of E-learning techniques is due to easy access to the internet.

There are various means of E-learning i.e Video Lectures, Slides, Websites and Medical Applications. When the students were asked about their favourite means they were more inclined towards the video lectures as compared to all other means (53% students used video lectures, 6.5% used slides, 22% used medical websites and 18.5% used medical applications). The work of Kearney and colleagues shows the benefits of using video to produce authentic learning opportunities for students (Kearney and Campbell 2010; Kearney and Schuck 2006) and how 'ivideos' encourage academic rigour from an advocacy, research based perspective. Study done in Taibah university also showed that their students value online lectures to supplement their reading.<sup>[12]</sup>

E-learning has positive effects on the academic results of the medical students as 83.5% of the students involved said that their academic performance was improved by using E-learning while 16.5% thought it had no effect, Another study was conducted among students studying in medical sciences and dentistry (Entry of 2009) from Guilan University. 75 medical students were held as the intervention group (using virtual medical teaching) and 37 dentistry students were held as control group (using traditional education). The scores of both groups at final homogenized practical exam (out of 20) were compared. The average score for medical students were 15.45 while those for dentistry students were 12.06 which were significantly different from each other (value 0.0001).<sup>[5]</sup> The p-value shows that there is a positive association between the use of E-learning and performance of

the medical students. So E-learning techniques should be incorporated in traditional teaching system to improve the understanding and academic performance of the students.

### CONCLUSION:

- Majority of the students were aware of the E-learning techniques.
- E-learning has been proved to be better than the traditional learning.
- E-learning has improved the academic performance of the students.

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## COMPARATIVE STUDY OF TRANS HAEMORRHOIDAL DE ARTERIALIZATION VERSUS SUCTION BANDING OF HEMORRHOIDS

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Hemorrhoids are engorged, displaced and cushions. There can be 1st, 2nd, 3rd and 4th degree. They bleed on defecation. They are in relation to anus. There can be internal, external and intro external.

There are various modalities of treatment for these. In this study we have compared 1st, 2nd and 3rd degree hemorrhoids treated by THD and banding.

THD is a safe and effective treatment option. This same day procedure offers low morbidity with huge potential for immediate return to normal activity<sup>(1)</sup> among several office based procedure, RB ligation appeared to have the lowest incidence of recurrent symptoms and the need for re-treatment<sup>(2)</sup>.

### MATERIAL & METHODS:

100 cases of hemorrhoids were treated by THD, and 100 cases by banding.

There were of 1st, 2nd and 3rd degree hemorrhoids. 1st and 2nd degree were 70/70 THD banding while 3rd degree were 30/30 THD/banding. M:F ratio was 1:3, including 50 males and 150 females all aged 30-50 years.

Both male and female 30-50 years with 1st, 2nd and 3rd degree were included in the study. All comorbid or other associated problems were excluded by investigations.

### DISCUSSION:

The prevalence of hemorrhoid disease is reported to be 4-10% making it the most common disorder of the anal canal<sup>(3)</sup>. The treatment of hemorrhoid

depends on the type and severity of hemorrhoids, patient's preference and the expertise of Surgeons.

Cases	
THD 100	Banding 100
1 & 2nd Degree Hemorrhoids	
THD 70	Banding 70
3rd Degree	
THD 30	Banding 30
M	F
50	150
M : F 1 : 3	

Post procedural pain and disease recurrence remain the most challenging problems in the treatment of hemorrhoids<sup>(4)</sup>.

THD appears to be a very effective minimally invasive option to treat hemorrhoid and can be performed in a day surgery setting<sup>(5)</sup>.

THD also appears to be potential treatment option for 1st, 2nd, 3rd degree hemorrhoids<sup>(6)</sup>.

Low graded, 1st hemorrhoids can be treated with office based procedure such as rubber band ligation<sup>(7)</sup>.

In our study for THD Doppler probe, the set with needle and knot pusher was used.

All cases were done in spinal anesthesia. For banding a hand-held suction banding gun under no anesthesia with self illuminating proctoscope was used.

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In both group the hemorrhoids were targeted at pedicle above the dentate line.

**RESULTS:**

1st and 2nd degree 70/70 THD/banding and 3rd degree hemorrhoids 30/30 THD/banding were carried out. 50 male, 150 female M:F 1:3, 30-50 years of age both genders with no other associated disease process.

None of the patients in THD or banding group had post operative pain.

7 cases in THD had post OP bleeding as spots on 1st, 2nd day where as none in banding had post OP bleed.

After a follow up of 1 year 10 of THD had recurrence of 1st and 2nd degree hemorrhoids where as only 1 had a 1st degree hemorrhoids in banding group. With THD there is a greater likelihood of recurrence.

For an average following of one year the recurrence rate was high<sup>(8)</sup>.

Vacuum suction ligator may offer clear visualization of hemorrhoid and more precise placement of banding<sup>(9)</sup>.

Rubber band ligation is a good treatment option for hemorrhoid<sup>(10)</sup>.

**Conclusion:**

In our study we have found that THD needs spinal/GA anesthesia and has more rates of post OP

bleeding and recurrence rate where as banding can be done without any anesthesia and has less rate of post op bleeding and recurrence.

We recommend banding with suction ligator as procedure of choice for early and 3rd degree hemorrhoid.

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Post OP. Pain	
THD	Banding
0	0
Post OP Bleeding	
THD	Banding
7	0
Recurrence > 1 Year	
THD	Banding
10	1
Anesthesia	
THD	Banding
GA / Spinal	Nil
100	100

## CONTROL OF PAIN, IN NASAL SURGICAL AFTER CARE, AFTER SEPTOPLASTY. A COMPARATIVE STUDY BETWEEN XYLOMETAZOLINE AND NORMAL SALINE DROPS.

Shahbaz Mujtaba Ghauri<sup>1</sup>, Muhammad Nadeem<sup>2</sup>, Zafer Iqbal<sup>3</sup>

### ABSTRACT

**OBJECTIVE:** The objective of this study was to Compare mean pain scores of patients given Xylometazoline hydrochloride 0.1 per cent with that of physiological saline in nasal surgical aftercare who underwent septoplasty for deflected nasal septum.

**Methods:** A randomized comparative study was conducted at department of ENT, King Edward Medical University/Mayo Hospital, Lahore, from April \10th, 2010 to October 9th, 2010. One hundred & fifty indoor patients, who underwent septoplasty, were included. They were randomized to receive either xylometazoline hydrochloride 0.1 per cent nasal spray or a physiological saline aerosol. On the 10th post-operative day, mean pain scores were compared between the two groups by using a 100mm visual analogue scale (VAS) scoring sheet.

**Result:** Overall, mean pain scores were significantly higher in the xylometazoline group ( $p=0.001$ , t- test) than physiological saline group.

**Conclusion:** Physiological saline is better than Xylometazoline for relieving pain in nasal surgical aftercare after septoplasty.

**Key Words:** Deviated nasal septum, Septoplasty, Xylometazoline, Physiological Saline.

A deviated nasal septum (DNS) is labeled when the septum is not in the midline<sup>1,2</sup> and causing symptoms like nasal obstruction, chronic nasal congestion, sinusitis, repeated ear infections, headache or nose bleed.<sup>3,4</sup>

Septoplasty is the corrective surgery for these symptomatic septal deviations<sup>5</sup>. Patients undergoing septoplasty commonly experience a variety of symptoms like, pain, nasal blockage, rhinorrhea and bleeding in the post-operative period.<sup>6,7</sup> These symptoms, particularly pain, are related to post-operative inflammation, crusting and mucociliary dysfunction as a result of the surgery<sup>8</sup>.

Physiological saline and decongestants like Xylometazoline hydrochloride are commonly used preparations intended to combat such pain by promoting mucosal healing<sup>9</sup> and reducing nasal swelling and crusting<sup>10</sup> in nasal surgical aftercare<sup>11</sup>. Physiological Saline may serve to improve mucociliary clearance by increasing the ciliary beat frequency<sup>12,13</sup> and is useful in softening crusts after

nasal surgery<sup>14</sup>.

Xylometazoline hydrochloride may provide benefit for those symptoms that are supposed to be related to inflammatory vasodilatation, i.e. pain and bleeding.<sup>15</sup> It is not clear whether decongestants, with their potential side effects, confer any benefit on patients' symptoms, compared with simple physiological saline solutions which are relatively cheaper and potentially free of side effects.<sup>16</sup>

There is hardly any study conducted in Pakistan on this topic. Results of our study will promote the evidence based medical practice and will help provide an evidence for preference to any of these treatment modalities keeping in view the cost-effectiveness.

### PATIENTS AND METHODS

At department of ENT, King Edward Medical University/Mayo Hospital, Lahore, from April \10th, 2010 to October 9th, 2010. One hundred & fifty indoor patients, who underwent septoplasty,

## CONTROL OF PAIN, IN NASAL SURGICAL AFTER CARE, AFTER SEPTOPLASTY.

were included in the study. They were randomized to receive either xylometazoline hydrochloride 0.1 per cent nasal spray or a physiological saline aerosol. Oralparacetamol 1gram thrice daily was also given both groups as standard analgesia. On the 10th post-operative day, mean pain scores were compared between the two groups by using a 100mm visual analogue scale (VAS) scoring sheet.

### RESULTS

Out of 150 patients 90 (60%) patients were male & 60 (40%) patients were female. Patients who presented with deviated nasal septum were selected from 18-50 years of age group. Mean age of the patients was 26.51 years with a standard deviation of + 5.812. Most common presenting symptom, nasal obstruction was present in 60 (40 %) out of 150 patients. The second most common presenting complaint was persistent rhinorrhea in 36 (24 %) of patients. Headache / facial pain was present in 12 (8 %) patients. Only 6 (4 %) patients presented for cosmetic reasons. A total of 36 (24 %) patients presented with mixed symptoms.

The mean pain score with xylometazoline was 28.15 with standard deviation of +12.031 while mean pain score with physiological saline was 12.79 with standard deviation of + 6.57. Overall median pain scores were statistically significantly higher with xylometazoline

**Table 1:** Age distribution of patients (n=150)

Age(years)	No of patients	Percentage
18---25	50	33%
25----35	50	33%
35-----40	30	20%
40---42	20	13%

**Table 2:** Presenting symptoms

Symptoms	No of patients	Percentage
Nasal obstruction	60	40%
Rhinorrhea	36	24%
Head ache and facial pain	12	8%
Cosmetic reason	6	4%
Mixed symptom	36	24%

**Table 3:** Mean pain scores

Analgesic name	Xylometazoline Hydrochloride	Physiological Saline
N	75	75
Mean	28.15	12.79
Median	28.00	11.00
Mode	37	8
Std. Deviation	12.03	6.57

P value = < 0.001

Statistical test = t test

### DISCUSSION

Results of our study showed a significantly higher mean pain score associated with the use of xylometazoline, than physiological saline. M R HUMPHREYS, D GRANT, S AMCKEAN, C Y ENG, J TOWNEND, A S EVANS did a randomised, single-blinded, comparative clinical trial to compare the effect of these two commonly used products on patient symptom scores following nasal surgery<sup>17</sup>. One hundred and twenty patients undergoing septoplasty or functional endoscopic sinus surgery as an isolated procedure were included in the study while our study included 150 patients all undergoing septoplasty. Main outcome measures, in this study, were Visual analogue scale symptom scores for nasal obstruction, rhinorrhoea, pain, loss of sense of smell and bleeding assessed at day 10 post-operatively while Visual analogue scale score only for pain at day 10 post-operatively was main outcome measure in our study. In above mentioned study, overall, median pain scores were statistically significantly higher with xylometazoline compared with physiological saline (p = 0.030, chi-square test). For pain, median (interquartile range, median test) of xylometazoline and physiological saline group were 22 (5–35) and 10 (5–22) while number of patients in each group were 63 and 57 respectively. These results are comparable to our study.

A clinical trial has been going on since January, 2008 by a series of The U.S. National Institutes of Health comparing saline sprays vsSterimar, a commercially available aerosolised isotonic saline solution, comparing patients' symptom scores

following septal surgery<sup>18,19,20</sup>. The trial will help to establish efficacy and symptom control and advantages of one solution and delivery device over the other.

## CONCLUSION

Mean pain score of patients given Xylometazoline hydrochloride 0.1 per cent were significantly higher than mean pain score of patients given physiological saline in nasal surgical after care who underwent septoplasty for deflected nasal septum.

Hence according to our study there is no evidence to support the use of xylometazoline hydrochloride 0.1 per cent over physiological aerosolised saline alone for pain relief following nasal surgery.

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## ALPHA FETO PROTEINS(AFP)LEVEL IN DIFFERENT KINDS OF LIVER DISEASES AT MINAR, MULTAN.

Madiha Rehman, Saif ur Rasool, Saad Rehman

### ABSTRACT

**Background:** Alphafetoprotein (AFP) is an important tumour marker. It's role in diagnosis and monitoring the therapy of cancer of liver is well established. It's serum concentration in patients with hepatocellular carcinoma (HCC) is above 400 ng/ml. AFP levels are not evaluated in HCC only raised levels are also observed in other liver diseases. However they are not studied in detail.

**Objectives:** To evaluate serum AFP levels in patients with malignant and non-malignant diseases of liver and to assess whether these levels are related to the liver function parameters.

### Subjects and Methods:

**Study Design:** Cross sectional study

**Study Setting:** MINAR, Multan

**Study Duration:** From January to December

**Data Collection and Analysis:** A total of 92 patients, 52 males, 40 females, with age ranging from 10 to 95 years (47.2 SD<sup>^</sup>IS.8) were studied. The patients belonged mostly to southern Punjab with poor economic status. Chemiluminescent immunoassay technique was used to estimate serum AFP levels. An automatic analyzer, Immulite -2000 was used for this purpose.

**Results:** There was a wide variation of AFP levels in all liver diseases. However high mean levels were observed in Chronic Hepatitis B, Chronic Hepatitis-C, Ascites with Hepatitis-C, Chronic Hepatitis (B+C), Acute Hepatitis (B+C) and Liver Malignancies. In liver malignancies the highest mean levels were observed i.e., above 1000 ng/ml. Highest mean Bilirubin levels were observed in patients with Acute Hepatitis-C (9.45±11.66 mg/dl) and Acute Hepatitis (B+C) i.e., 10.45±8.7 mg/dl. In all liver diseases high Bilirubin levels were seen except Hepatitis-A and B.

**Conclusion:** It is concluded that in all liver diseases the increased AFP levels are observed and that retarded liver function cause abnormal AFP levels which may also indicate the severity of the disease. Thus serum AFP levels and liver function are closely related.

**Key words:** Serum Alpha Feto proteins, Liver disease, Malignancy.

Liver diseases are very common in the world. Liver cancer represents about 2% of all new cancers. Males are affected slightly more commonly than females, and the average patient is 50 years old.<sup>3,4</sup> Estimation of AFP in sera of patients of hepatocellular carcinoma is a very common investigation. The clinical significance of AFP lies in the detection and monitoring of primary liver cell carcinomas, which often develop secondary to liver cirrhosis or chronic hepatitis. In these risk groups, AFP determination is suitable for early detection of liver cell carcinoma and thus may be used as a screening method. Elevated AFP levels are found in more than 90 % of all patients with primary liver cell carcinoma. AFP serum concentration of >1,000 ng / ml and sometimes > 10,000 ng/ ml up to 1,000,000

ng/ ml has been reported. A direct relationship between AFP serum levels and the disease stage has been determined primary liver cell carcinoma. High AFP levels indicate a large tumour mass and a poor prognosis. The postoperative increase in AFP and often indicates progression several months before other diagnostic procedures can be approached, enabling an early change in therapy to be considered. Other tumors where high AFP levels occur are gastric carcinomas, colorectal carcinomas, biliary and pancreatic carcinomas and liver metastasis. High preoperative AFP and / or hCG levels indicate a poor prognosis. Differentiation between primary liver carcinoma, liver metastases and other carcinomas can be made by combined AFP and CEA determination. Low AFP levels in the presence of

high CEA levels indicate liver metastasis (positive predictive value > 90%). In primary liver cell carcinoma, CEA can be elevated in 20-60 % of cases, the values then lying mostly between 3 and 10 ng/ml, and rarely over 20 ng/ml. There is a definite link between AFP level and liver malignancy. A constant rise in, and persistent level of, AFP is observed in certain other malignancies, namely GCT<sup>66,67</sup>, pediatric hepatoblastoma (Hb), hepatocellular carcinoma (HCC)<sup>68,69,70</sup> and, in rare cases, tumors of the gastrointestinal tract.<sup>71</sup> An AFP test is routinely used for differential diagnosis, as well as for monitoring of surgery and chemotherapy, in GCT, Hb, and HCC.

### OBJECTIVES:

To evaluate serum AFP levels in patients with malignant and non-malignant diseases of liver and to assess whether these levels are related to the liver function parameters.

### SUBJECTS AND METHODS:

A Cross sectional study was carried out at MINAR, Multan from January to December. A total of 92 patients, 52 males, 40 females, with age ranging from 10 to 95 years (47.2 SD<sup>^</sup>IS.8) were studied. The patients belonged mostly to southern Punjab with poor economic status. Chemiluminescent immunoassay technique was used to estimate serum AFP levels. 5 CC blood was taken from each sample which was allowed to clot followed by centrifugation to get serum. Serum was then used in immunoassays to find the AFP level. The serum samples were stored at 4 C° in a fridge for use in future. An automatic analyzer, Immulite -2000 was used for this purpose.

### RESULTS

The mean AFP levels observed in different diseases were following: Hepatitis-A, 0.97 ng/ml (n=1), Hepatitis-B (Non symptomatic carrier), 4.2 ng/ml (n=1), Chronic Hepatitis B, 120 ng/ml (n=1), Chronic Hepatitis-C, 12.0±14.3 ng/ml, Ascites with Hepatitis- C, 370 ng/ml (n=1), Acute Hepatitis-C, 8.15±8, Chronic Hepatitis (B+C), 18.91±63.79 ng/ml, Cirrhosis of liver (B+C), 2.4±0.707 ng/ml, Acute Hepatitis (B+C), 81.05±103.2 ng/ml, Hepatic encephalopathy (B+C), 4.882±4.43 ng/ml, Cirrhosis of liver e diabetes mellitus (No viral tests done), 4.1±4.10 ng/ml n=2, Liver Malignancies, 1020.3±805.1 ng/ml, Healthy Control 1.5 ng/ml (n=1). There was a wide variation of AFP levels in all liver diseases. However high mean levels were observed in Chronic Hepatitis B, Chronic Hepatitis-C, Ascites with Hepatitis-C, Chronic Hepatitis (B+C), Acute

Hepatitis (B+C) and Liver Malignancies. In liver malignancies the highest mean levels were observed i.e., above 1000 ng/ml.

Results of liver function tests (LFT) showed the mean levels of bilirubin, SGOT, SGPT and alkaline phosphatase in patients with liver diseases. Their relative distribution is displayed figures 9 to 12. Analysis of serum samples for Bilirubin levels and liver enzymes produced highly varying results. Highest mean Bilirubin levels were observed in patients with Acute Hepatitis-C (9.45±11.66 mg/dl) and Acute Hepatitis (B+C) i.e., 10.45±8.7 mg/dl. In all liver diseases high Bilirubin levels were seen except Hepatitis-A and Hepatitis-B (The patient was non-symptomatic carrier) where only one sample was available. Highest mean SGOT levels were observed in patients with Acute Hepatitis-C (429±496.4) and Acute Hepatitis (B+C) i.e., 546±649.1 mg/dl. In all liver diseases high SGOT levels were seen except Hepatitis-B (The patient was non-symptomatic carrier) where only one sample was available. Highest mean SGPT levels were observed in patients with Acute Hepatitis-C (773.5±235.5) and Acute Hepatitis (B+C) i.e., 617.5±611.5 mg/dl. Normal AP values were observed in Acute Hepatitis (B+C), Cirrhosis of lever B + C, Chronic hepatitis B + C, Ascites with hepatitis-C and Hepatitis-B. In other patients high values were observed. Highest mean AP levels were observed in patients with Hepatitis-A.

### DISCUSSION:

Alphafetoprotein (AFP) is composed of a single polypeptide chain with a relative molecular mass of 69,000. It consists of 590 amino acids and 39% of the amino-acid sequence corresponds to that of albumin. Unlike albumin it is a glycoprotein with 4% of carbohydrate residues. There are low levels of AFP in normal subjects. There is no information on mechanisms that may control the synthesis of AFP by the fetus and thus determine the concentrations in maternal and fetal fluids. The functions of AFP are also unknown. Probably it serves a function similar to that of albumin. In the fetus, AFP is synthesized by the liver, the gastrointestinal tract and the yolk sac<sup>87</sup>. AFP has two clinical applications: firstly for detecting and monitoring primary hepatocellular carcinomas, which arise mostly in cirrhotic livers; and secondly for monitoring the therapeutic response of and to some extent also for diagnosing, germ cell tumours. Literature shows that elevated serum AFP levels are also found in around 9% of patients with liver metastases of other malignancies such as breast, bronchial, and colorectal carcinomas, though

the values found in such patients are rarely above 100 ng/ml and scarcely ever above 500 ng/ml<sup>88</sup>. Because of its high sensitivity, AFP assay is also

**Table 1:** Serum AFP among subjects

Variables n= 92	Serum AFP lever Mean + SD (ng / ml)
Hepatitis A (n=1)	0.97
Chronic Hepatitis B (n=1)	120
Chronic Hepatitis B non-symptomatic Carrier (n=1)	4.2
Chronic Hepatitis C	12.0±14.3
Acute Hepatitis C	8.15±8.0
Hepatitis C with ascites (n=1)	370
Acute Hepatitis B and C	81.05±103.2
Cirrhosis of liver with Hepatitis B & C	2.4±0.707
Hepatic encephlopathy B & C	4.882±4.43
Cirrhosis of liver e diabetes mellitus	4.1±4.10
Liver Malignancies	1020.3±805.1
Healthy Control (n=1)	1.5

suitable for the early detection of hepatocellular carcinoma in high-risk groups, i.e. patients with Hepatitis-A, Hepatitis-B (Non symptomatic carrier), Chronic Hepatitis B, Chronic Hepatitis-C with complications such a septicemia and pregnancy problems, Ascites with Hepatitis- C, Acute Hepatitis -C, Chronic Hepatitis (B+C), Cirrhosis of liver (B+C), Acute Hepatitis (B+C), Hepatic encephlopathy (B+C), Cirrhosis of liver e diabetes mellitus (No viral tests done),... Patients in these categories should therefore have their serum AFP assayed twice yearly. There was a wide variation of AFP levels in all liver diseases in our study. Highest mean levels were observed in patients with liver malignancies (1020.3±805.1 ng/ml) where the values only in some patients were above 1000 ng/ml. In patients suffering from ascites with HCV infection, the level was above 300 ng/ml. Similarly in patient who was diagnosed to have Chronic Hepatitis B (pathogenin), the observed level was above 100 ng/ml. Owing to the fact that we have only one patient in each case of hepatitis B and ascites with HCV infection, we are cautious to make any comment on the AFP level in relation to the disease. The group of patients having acute hepatitis-B, the observed mean level was above 50 ng/ml (81.05±103.2 ng/ml). Overall view of the results shows that high mean levels were observed in Chronic Hepatitis B, Chronic Hepatitis-C, Ascites with Hepatitis-C, Chronic Hepatitis (B+C), Acute Hepatitis (B+C) and Liver Malignan-

cies. In liver malignancies however the levels observed showed an increased trend. Some of them have above 1000 ng/ml (n=19). In diseases other than liver malignancies the mean levels were mostly below 100 ng/ml. The high levels of AFP observed i.e in benign diseases may be a warning of incidence of cancer in future. Although the elevated AFP levels found in benign liver diseases in our study such as hepatitis are within the lower limit of the pathologic range (very rarely 500 ng/ml) but may be critical for future threat of cancer. Such AFP-positive patients may have an increased incidence of hepatocellular carcinoma and a poorer five-year prognosis. The AFP levels can also categorized in three different liver diseases. In the diseases such as hepatitis A, B, acute hepatitis C, chronic hepatitis B & C, cirrhosis of liver, hepatic encephalopathy B & C, cirrhosis of liver with diabetes mellitus. the value of AFP levels ranges from 0.97 to 12.0 ng/ml. All these values were taken against standard control sample in which AFP level 1.5 ng/ml. In the second category three diseases have shown similar ranges of AFP level. These diseases are acute hepatitis B & C in which AFP level is 81.0 ng/ml, chronic hepatitis B 120 ng/ml and ascites C value is 370 ng/ml. The maximum value of AFP level is observed in patients of liver malignancies, which is upto 1020. 38 patients suffering from both chronic hepatitis B and C. While 19 and 18 patients suffering from chronic hepatitis C and liver malignancies were selected respectively. The number of patients suffering from in rest of the diseases such as hepatitis A, B, C, ascites C, hepatic encephalopathy B & C, acute hepatitis and cirrhosis of liver etc. The number of patients ranged from 1-5. The lowest values of SGPT were found in the patients of hepatitis A, cirrhosis of liver infected with B & C, which is 52 IU/l and 60 IU/l respectively. In one patient who was non symptomatic and HB positive, the value of both AFP and SGPT was normal. The highest value of SGPT were observed in acute hepatitis B & C and acute hepatitis C, where the levels were 617 IU/L and 773 IU/L respectively. The lowest values of SGOT were in the patients of hepatitis A which was of 48 IU/L, and cirrhosis of liver with diabetes milletus which was of 57.5 IU/L. While the maximum values were observed in patients of acute hepatitis B & C and acute hepatitis C i.e., 429 IU/L and 546 IU/L respectively. The highest value of bilirubin was observed in patients of hepatitis A while the lowest was observed in acute hepatitis B & C. The lowest value patients of hepatitis A was 0.5 mg/dl and highest values observed in acute hepatitis B & C and acute hepatitis C, were 10.45mg/dl and 9.45mg/dl respectively.

In one non-symptomatic carrier with chronic hepatitis B for the last 21 years all biochemical tests were normal which shows that the patients with hepatitis B can live very long without any complaints of liver disease. Comparison of liver function test results and AFP levels shows that liver function is consistently retarded in all liver patients and maximum levels of enzymes are observed with elevated levels of AFP in patients suffering from acute hepatitis C & acute hepatitis B & C, while alkaline phosphatase values are normal in all patients.

### CONCLUSION

It is concluded that in all liver diseases the increased AFP levels are observed and that retarded liver function causes abnormal AFP levels which may also indicate the severity of the disease. Therefore it is suggested that detailed clinical evaluation to find a correlation, if exists between liver enzymes and AFP levels is urgently required.

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## PREVALENCE OF HEPATITIS-B AND HEPATITIS-C IN BLOOD DONORS OF SOUTHERN PUNJAB AND THE LEVEL OF THEIR LIVER FUNCTION

Madiha Rehman, Saad Rehman, Saif ur Rasool

### ABSTRACT

**Objectives:** The main objectives of this study were to assess the incidence of hepatic infection (HBS and HCV) in blood donor of Nishtar Hospital, Multan, to evaluate the effectiveness of techniques for the detection of HBs and HCV and to find the level of liver function in persons found positive and negative for Hepatitis-B and C.

### Subjects and Methods:

**Study Design:** Cross sectional study

**Study Setting:** Blood bank of Nishtar Hospital, Multan

**Study Duration:** From January to December 2009.

**Data Collection and Analysis:** A total of 6865 blood donors (males: 6528 Females: 337) who visited the blood bank of Nishtar Hospital, Multan for blood donations during the year 2009 were included in the study. The data on blood donors referred from various wards of Nishtar Hospital to blood bank was collected.. Record of Hepatitis-B antigen (HBsAg), Hepatitis-C antibodies and levels of LFT markers was also maintained for comparison between different groups of the study. The blood donors referred to blood bank were divided into three groups depending on the presence or absence of hepatitis markers.

**Results:** A total of 6865 blood donors (,males: 6528 Females: 337) who visited the blood bank of Nishtar Hospital, Multan for blood donations during last one year were included in the study. The mean age of these persons was  $44.4 \pm 7.6$  years (range: 18-55). The average anti-HCV positive rate was 0.62% (29/4562), which was 1.07% in the rural population, compared with 0.22% in the urban population. The anti-HCV positive rate in the 40–59-year age group was higher than in those aged <40 years. History of blood transfusion and transmission in families were the main risk factors for HCV infection in this area. The analysis of the records of blood donors showed that most of them belonged to B+(45.8%) and then A+ (27.2%). Out of 6865 blood donors, 323 (4.7%) were found positive for HBsAg. whereas 327 (4.8%) were found positive for HCV infection. The incidence of HBV and HCV in males and females was approximately equal.

**Conclusion:** We conclude that the incidence of HBs and HCV is very high in general population of southern Punjab. This shows that the screening procedure for HBS and HCV adapted by blood bank is not very efficient and gives many false negative results.

**Key words:** Hepatitis B, Hepatits C, Screening.

Viral infections are at the main cause of mortality. The most common viral infection is hepatitis which is the most frequent cause of death in Pakistani population. According to a news report, even though one out of 10 Pakistani suffers from the virus of either Hepatitis B or C, the hepatitis-infected population of 15 million awaits the proper implementation of a National Programme for Prevention and Control of Hepatitis in Pakistan to control the

deadly disease. Unsafe drinking water, unscreened blood transfusion and the rampant use of used syringes have spread hepatitis, making it one of the biggest concerns for the country's health managers. Health professionals and government officials give conflicting statements about the prevalence rate of Hepatitis B in the country. Going by their statements the prevalence rate may vary from 4.8 to 5.8 percent. Millions of Pakistanis have been infected with the

deadly virus, but no public department or agency has accurate information about the number of positive cases. Going by the figure of 5.8 percent prevalence rate, there may be around 8 million Hepatitis B patients in the country. Hepatitis B and C are global health problems as worldwide 350 million people are carriers of the Hepatitis B virus. The virus causes a deadly liver disease having same mode of transmission as AIDS. Medical experts believe that the Hepatitis B virus was spreading fast because of ignorance among the patients and a lack of proper preventive measures. There are five types of hepatitis- A, B, C, D and E - of which A and E are caused through oral infection, contaminated water and unhygienic food. Hepatitis B, C and D are caused through un-sterilised syringes, sexual relation, and blood transfusion and from mother to newborn baby. The disease is transmitted by body fluids such as blood, semen, saliva and vaginal secretions. It is claimed that the Hepatitis B virus is 100 times more concentrated in the blood than the HIV virus making it much easier to spread. Hepatitis C is often called a 'silent epidemic' and it can live in the body for decades, often with no symptoms, while attacking the liver. The long-term consequences of Hepatitis C can include liver disease, liver cancer and death. There is also no cure for Hepatitis C. Prevalence of hepatitis may be higher than reported. In another work on hepatitis, Khalida Kazmi<sup>[1]</sup> writes, "Pakistan is endemic area for viral hepatitis B. It is more aggressive due to co-infection and super-infection with delta virus. Intra-familial spread of hepatitis B is quite high.

The highest reported incidence in spouses is 23.5 percent. Pakistan has a high carrier rate of hepatitis B. It is between 10 to 14 percent with ELISA and RIA techniques respectively. Hepatitis B is more prevalent in males as compared to females (8.13%/6.7% respectively). Transplacental transmission from mother to infant is not the major route of transmission for HBV, as none of the infants of HBV positive mothers had HBsAg in cord blood. The route of transmission of hepatitis B in infants is

horizontal from mother to infants as they are close to mothers during infancy. Hence infants of hepatitis B positive mothers must be vaccinated against hepatitis B. Sub types of hepatitis B have different geographical distribution. The four major sub types of HBsAg are ayw, adw, adr, and ayr. In our country, the most prevalent sub type is ayw (78-95%), adw prevalence is (2.4-14%), adr (1.0-7.7%) and ayr (2.4%). Delta hepatitis poses a common community health problem in Pakistan.

In a medical and public health literature over a 13-year period (January 1994-September 2007) to estimate the prevalence of active hepatitis B and chronic hepatitis C in Pakistan, analyzing data separately for the general and high-risk populations and for each of the four provinces and included 84 publications with 139 studies (42 studies had two or more sub-studies) in their review. They estimated the likely range of prevalence in different population sub-groups. A weighted average of hepatitis B antigen prevalence in pediatric populations was 2.4% (range 1.7-5.5%) and for hepatitis C antibody was 2.1% (range 0.4-5.4%). A weighted average of hepatitis B antigen prevalence among healthy adults (blood donors and non-donors) was 2.4% (range 1.4-11.0%) and for hepatitis C antibody was 3.0% (range 0.3-31.9%). Rates in the high-risk subgroups were far higher<sup>[2]</sup>.

#### OBJECTIVES:

The main objectives of this study were to assess the incidence of hepatic infection (HBS and HCV) in blood donor of Nishtar Hospital, Multan, to evaluate the effectiveness of techniques for the detection of HBs and HCV and to find the level of liver function in persons found positive and negative for Hepatitis-B and C.

#### SUBJECTS AND METHODS:

This retrospective study was conducted under collaboration between Department of Chemistry, Bahauddin Zakariya University, Multan and Institute of Nuclear Medicine and Radiotherapy (MINAR). The experimental work was performed at

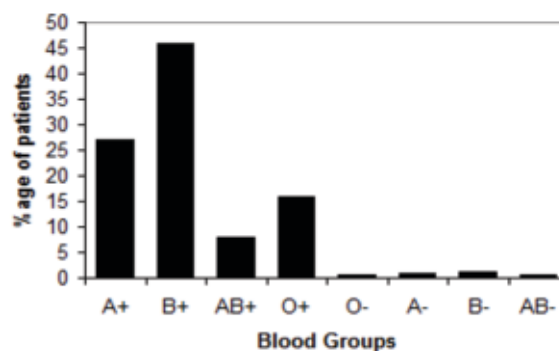
Biochemistry Laboratory of MINAR. All the volunteer blood donors of Nishtar Hospital, Multan who donated blood during the study period were included in the study. The inclusion criteria followed was age 18-60 years, weight more than 50 kg and a haemoglobin concentration above 13 g/dL. The data on blood donors referred from various wards of Nishtar Hospital to blood bank was collected. Age, sex and addresses of these donors were noted in a record register. Record of Hepatitis-B antigen (HBsAg), Hepatitis-C antibodies was also maintained. A thorough medical history was taken by a medical officer to ensure that the donor is free of all communicable diseases. The exclusion criteria used was history of jaundice, malaria, drug addiction, anemia, history of repeated transfusions and any evidence of cardiac, renal, or pulmonary disease.

## RESULTS:

The distribution of blood donors bled at Blood bank of Nishtar Hospital during last one year according to their blood groups is Fig-1. The analysis of the records of blood donors showed that most of the blood donors belonged to A+ (27.2%), B+(45.8%), AB(7.7%)+ and O+ (15.8%) blood groups. Table-1 shows the percentages of HBsAg and HCV observed in this population. Out of 6865 blood donors, 323 (4.7%) were found positive for HBsAg, whereas 327 (4.8%) were found positive for HCV infection. Comparison of the incidence of HBV infection between males and females shows that the prevalence of these infections in blood donors is not statistically different ( $p=0.8722$ ). The incidence of HCV infection in females (5.3%) is also not significantly higher ( $p=0.1225$ ) than the incidence of HBsAg (3%).

**Table 1:** Distribution of HBsAg positive and HCV positive rate among subjects and its gender distribution

	Total	HBsAg positive	HCV positive
Total	6865	323 (4.7%)	327 (4.8%)
Males	6528	313 (4.8%)	309 (4.7%)
Females	337	10 (3%)	18 (5.3%)
P value		$p=0.1225$	$p=0.8722$



**Graph no 1:** Distribution of Blood groups in all blood donors

## DISCUSSION:

The main cause of chronic hepatitis in Pakistan is said to be HBV and HCV. Pakistan carries one of the world's highest burdens of chronic hepatitis and mortality due to liver failure and hepatocellular carcinomas is very high in our population. However, national level estimates of the prevalence of hepatitis B and hepatitis C are currently not available<sup>[14],[11],[15],[12],96,[13],98</sup> some studies have been conducted in different institutes of the country as show below:

Author & Year	Place of Study	Anti-HCV	HBsAg
Mumtaz S et al 2002[4]	Islamic International Medical College Rawalpindi	6.21%	5.86%
Khattak MF et al 2002[5]	AFIT, Rawalpindi	4.0%	3.3%
Fayyaz KM et al 2002[6]	Quaid-e-Azam Medical College, Bahawalpur	--	7.53%
Ali et al 2003[7]	CMH, Quetta	1.87%	--
Zaidi A et al 2004[8]	Hayatabad Medical Complex, Peshawar	1.34%	1.46%
Sirhindi GA et al 2005[9]	Shaikh Zayed Postgraduate Medical Institute Lahore	4.16%	3.36%
Mehmood MA et al 2004[10]	Nishtar Medical College/Hospital Multan	0.27%	3.37%
Asif N et al 2004[11]	Shifa International Hospital Islamabad	5.14%	2.51%
Ahmed J et al 2004[12]	Rehman Medical Institute Peshawar	2.2%	1.9%
Ujjan ID et al 2006 <sup>96</sup>	Isra University Hospital, Hyderabad	8.68%	3.65%
Aziz MS 2006[13]	DHQ Hospital Skardu	1.1%	8.4%
Ijaz AU et al 2007 <sup>98</sup>	Ghurki Trust Teaching Hospital, Lahore	5.34	1.52



The prevalence of Hepatitis B and C Observed at various regions of the country

Various studies<sup>[5],[16],[17]</sup> in Pakistan estimate the prevalence of exposure to HBV to be between 2.28% and 3.3% and HCV to be at 6 %, 5-9. In the study of figures as high as 17% for HCV were reported<sup>[18]</sup>. Dual infection by both B and C were seen in 6% of cases. Overall there were more men with CLD than women (60% vs. 40%). In another study in Pakistan combined infection was seen in 8% of cases<sup>[19]</sup>.

In a study<sup>[19]</sup> on 18,202 blood donors using ELISA technique at Blood Transfusion Services, Pakistan Institute of Medical Sciences, Islamabad, 603 individuals (3.31%) were positive for anti HCV antibodies while 351 individuals (1.92%) showed positivity for HBsAg. In this study the prevalence rate of HBV was low as compared to HCV. The authors claim that the reason might be the vaccination programmes and increased public health awareness that lowered this rate. There is no screening method available to completely eradicate the risk of these Transfusion Transmitted Infections (TTIs) but proper screening and selection of donor before collection can minimize these TTIs. Majority of blood donations in our country are replacement or voluntary. Voluntary blood donors are safer source of blood supply and special emphasis must be given to increase this source to higher levels. Regarding modes of HBV and HCV transmission, awareness and education of donors is required. HBV and HCV positive donors should be permanently deferred for future donations and must be informed about their disease and referred to a physician.

Although CLD is commonly caused by viral hepatitis in Pakistan, it may have some other relatively less common and potentially treatable aetiology, including autoimmune liver disease, primary biliary cirrhosis, Wilson's disease and haemochromatosis. In rural Sind 17% of all patients tested had evidence of exposure to HCV<sup>[17]</sup>. However, patients with CLD, who do not have evidence of exposure to either of the two viruses, have not yet been studied in this region. The purpose of this study

was to find out the proportion of patients who had CLD but were negative for both hepatitis B and C viral markers and to compare the demographic features and mortality of this group of CLD, with those with a viral aetiology.

A Study shows that among 1,131 volunteer blood donors enrolled, 46 (4.1%) were positive for anti-HCV antibodies. Positive donors had a family history of jaundice and were more likely to have been shaved (facial and armpit) by barbers<sup>[20]</sup>. The transfusion of blood is a life saving procedure and benefits thousands of patients worldwide. Serological testing of HBV and HCV is compulsory in blood banks routinely. Blood donors include the adult population in the 18-60 year age group, so the prevalence in other age groups is missed in such studies. But it is generally accepted that the evaluation of donor's blood for seropositivity of HBV and HCV gives an idea for the epidemiology of these infections in the general population<sup>[15]</sup>.

Seroprevalence rate of HBsAg and anti HCV antibodies varies in different regions of Pakistan as shown in Table II. The seroprevalence of HBV in healthy donors varies from 1.46% (HMC, Peshawar) to 8.4% (DHQ Hospital Skardu) in different parts of our country<sup>[13],[8]</sup>. The prevalence rate for HBS in our blood donors is 4.7%. In a study conducted Mehmd MA the prevalence rate was found to be 3.37%. Our finding shows that the prevalence of HBV in our population is higher than already reported incidence. The reason should be improvement in the method of detection. Similarly, the infection rate of HCV in various studies varies from 0.27% (Nishtar Medical College, Multan)<sup>[10]</sup> to 8.68% (Isra University Hospital, Hyderabad) 96 to 8.68%. The incidence reported from Multan was the lowest compared to various regions of Pakistan. We observed an incidence of 4.8% for HCV.

## CONCLUSION:

The findings of this work show that the incidence of HBs and HCV is very high in general population of southern Punjab. Our finding shows



prevalence much higher than already reported. We believe that methodology adapted previously might not be very accurate. So our data gives more reliable positivity rate for this region of the country.

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## RISK FACTORS FOR ECTOPIC PREGNANCY IN INTRA-CYTOPLASMIC SPERM INJECTION CYCLES WITH GONADOTROPIN RELEASING HORMONE ANTAGONIST PROTOCOL

Shazia Ashraf, Aliya Zainab Asad, Nudrat Sohail

### ABSTRACT

**BACKGROUND:** Assisted reproductive technology (ART) results in higher number of ectopic pregnancies than spontaneous cycles, the reasons maybe underlying pathologies in ART patients. However, the process of assisted technique may in itself carry some risks for an ectopic pregnancy. Risk of ectopic pregnancy is considered less in Intra-cytoplasmic sperm injection cycles (ICSI) cycles as compared to IVF cycles as male has a dominant role in infertility here. This study was carried out in a cohort of patients undergoing ICSI to see the frequency and possible risk factors of ectopic pregnancy.

**OBJECTIVES:** To determine Risk factors for ectopic pregnancy in Intra-cytoplasmic sperm injection cycles with Gonadotropin Releasing Hormone Antagonist protocol

### SUBJECTS AND METHODS:

**Study design:** Retrospective cohort study

**Study duration:** Jan, 2013 to Dec 2015

**Sample size:** 104 subjects undergoing Intra-cytoplasmic sperm injection cycles with Gonadotropin Releasing Hormone Antagonist protocol.

**Sample Selection:** All patients had who had undergone antagonist protocol and fresh embryo transfers in the ICSI cycles were included and those with frozen thawed embryo transfers and long protocol were excluded.

**Data Collection and analysis:** Risk factors were evaluated including age, type of infertility, reason for infertility, number of eggs retrieved, number of embryos transferred, estrogen levels and transfer difficulty. Data was analyzed on SPSSver: 21.0. Nominal data was presented as frequency and percentages. Chi-square test was used to assess significance with  $p < .05$  as statistical significant.

**RESULTS:** Frequency of ectopic pregnancy was 4.8%. Greater number of embryos transferred, cleavage stage and higher E2 levels were seen as prominent factors in ectopic pregnancies. Although all had primary infertility, tubal factor still was 40%. Age and BMI did not seem to have any specific relationship in ectopic pregnancy

**CONCLUSION:** Three embryo transfer and high estrogen levels were some prominent parameters seen in patients ending in ectopic pregnancies. Tubal factor also was prominent considering that all those patients ending in ectopic had primary infertility and 4 out of 5 had male factor infertility.

**KEY WORDS:** ART, ICSI Cycle, Ectopic pregnancy, cleavage stage transfers, GnRh antagonit.

Ectopic pregnancy is a life threatening problem Hemorrhage from ectopic pregnancy is still the leading cause of pregnancy-related maternal mortality in the first trimester and accounts for 4 percent of all pregnancy-related deaths, despite improved diagnostic methods leading to earlier detection and treatment. <sup>(1)</sup>

ART increases the risk of ectopic pregnancy<sup>(2,3)</sup>.

This risk has been reported from about one to 5.4%<sup>(4,5,6,7)</sup>. Recently however, there is a trend towards decreasing rate. It is now being quoted as 1.2 to 2%<sup>(8)</sup>, almost same as in a natural conception. The reason may be avoidance of practices thought to be a possible risk factor for ectopic pregnancy in ART, like multiple embryo transfer.

The pathogenesis is different in a spontaneous

versus ICSI ectopic pregnancy. In a natural conception cycle an embryo travels through the tube and factors delaying its passage through the tube to the endometrium are responsible for its abnormal implantation, whereas in an ART cycle the embryo travels retrograde to embed in the tube or other ectopic sites. Therefore, endometrial receptivity has been studied in this respect. Decreased endometrial receptivity is being considered as a possible reason for this retrograde travel. It has been noted that conditions leading to high estrogen levels can decrease endometrial receptivity<sup>(9)</sup>, such as higher number of follicles produced, GnRh agonist trigger etc.<sup>(10)</sup> Fresh embryo transfers, due possibly to its associated hyperestrogenemia have also been noted to end up in higher incidence of ectopic pregnancies<sup>(11)</sup>.

Among other risk factors it was noted that tubal pathology had a major role, be it due to endometriosis or corrective surgery or infectious disease<sup>(12)</sup>. Cleavage stage transfers have been shown to be risk for ectopic pregnancies<sup>(13,14)</sup>. However, some studies give unequivocal results when comparing blastocyst with cleavage stage embryos.<sup>(15)</sup>

This study was carried out to check variables associated with risks of ectopic pregnancy in a group of patients who got pregnant as a result of ICSI and fresh embryo transfers. ICSI patients are considered at a lesser risk of ectopic as compared to couples undergoing IVF.

### METHODOLOGY:

Retrospective cohort study was carried out at a private facility in Lahore between 2013 to 2015. After taking permission from ethical committee of the facility all patients had who had undergone antagonist protocol and fresh embryo transfer in the ICSI cycles were included and those with frozen thawed embryo transfers and long protocol were excluded. Risk factors were evaluated including age, type of infertility, reason for infertility, number of eggs retrieved, number of embryos transferred, estrogen levels and transfer difficulty. Data was

analyzed on SPSSver: 21.0. Nominal data was presented as frequency and percentages. Chi-square test was used to assess significance with  $p < .05$  as statistical significant.

### RESULTS:

The study group comprised of 104 patients who had clinical pregnancies as a result of ICSI cycles. Mean age was  $31.03 \pm 5.12$  with age range from 20 to 40 years. 80.0% of ectopics resulted in women between the age of 26 to 35. All patients who ended in an ectopic pregnancy had primary infertility. Male factor was present in 80% of patients. Semen parameters were normal for only one couple. 40% had tubal pathology. (Table 1). Four out of five ectopics had had cleavage stage embryos transferred. Only one had a blastocyst stage embryo. Estrogen levels were divided into three groups. First group of 4000 to 6000pmol/l, did not have any ectopic. Beyond 6000 the frequency of ectopic pregnancy steadily increased. Maximum number was seen in 9000 to 12000pmol/l group that is 60%. Maximum no of ectopic pregnancies, 60%, occurred where three embryos were transferred. Two embryos were still a risk for ectopic, 40% occurring in this group. No ectopic pregnancy was seen in single embryo transfer. All ectopic pregnancies had easy transfers. No technical difficulty or catheter staining with blood was noted. Same method was followed in all patients. Most of the ectopics occurred in patients with normal BMI. No relationship was noted in overweight patients.

### DISCUSSION:

Incidence of ectopic pregnancy in this study was 4.8%. the incidence of ectopic pregnancies has been quoted as high as 8% before 1996. Over time it has decreased to about 2% in fresh cycles<sup>(4)</sup>. The reason can be adoption of certain protocols like transfer on day 5 instead of 3 as it has been shown to decrease the risk of ectopic pregnancies in ART<sup>(13,14)</sup>. Transfer of frozen thawed embryos are also favorable for intrauterine pregnancies, as discussed

**Table 1:** Risk factors for Ectopic pregnancy (n=104):

Variables		Ectopic pregnancy n =5		Intrauterine pregnancy n =99		Chi-square P value
		Frequency	Percentages	Frequency	Percentages	
Age of subjects	20 - 25 years	1	20.0%	9	9.1%	X <sup>2</sup> =1.473 P =.479
	26 - 35 years	4	80.0%	73	73.7%	
	36 - 40 years	0	0.0%	17	17.2%	
Type of infertility	Primary	5	100.0%	61	61.6%	X <sup>2</sup> =3.024 P =.082
	Secondary	0	0.0%	38	38.4%	
Stage of Transfer	Cleavage	4	80%	83	83.8%	X <sup>2</sup> =.051 P =.821,
	blastocyst	1	20.0%	16	16.2%	
No of Embryo Transfer	One	0	0.0%	7	7.1%	X <sup>2</sup> =1.197 P =.550
	Two	2	40.0%	55	55.6%	
	Three	3	60.0%	37	37.4%	
E2 Levels	4000 - 6000	0	0.0%	40	40.4%	X <sup>2</sup> =3.526 P =.172
	6001 - 9000	2	40.0%	29	29.3%	
	9001 - 12000	3	60.0%	30	30.3%	
Male factor	Yes	4	80.0%	42	42.4%	X <sup>2</sup> =2.724 P =.099
	No	1	20.0%	57	57.6%	
Transfer difficulty	No	5	100.0%	95	96.0%	X <sup>2</sup> =.210 P =.648
	Yes	0	0.0%	4	4.0%	
Tubal factor	Yes	2	40.0%	32	32.3%	X <sup>2</sup> =.127 P =.721
	No	3	60.0%	67	67.7	
BMI	Normal (BMI (18.5 - 24.9)	3	60.0%	41	41.4%	X <sup>2</sup> =.688 P =.709
	Overweight (BMI 25 - 30)	1	20.0%	26	26.0%	
	Obese (BMI > 30)	1	20.0%	32	32.0%	

below.

The age bracket of 26 to 35 was the one in which most of the ectopics were encountered, probably because this was the age with maximum number of patients. Maybe larger sample size in higher age bracket can clarify whether older age is associated with ectopic pregnancy in ART cycles or not.

All patients had primary infertility, with 80% of the couples having male factor infertility. That may point towards some genetic element affecting endometrial implantation. However, there is paucity of evidence in this regard.

Various studies have pointed out tubal factor to be an important variable<sup>(12)</sup>. In our study it was present in 40 % of ectopic pregnancies. Endomet-

riosis and tubal surgeries have been seen to have a major role in tubal pathology in ART patients<sup>(16)</sup>. In this subset of patients PID and endometriosis would stand prominent but data in this regard was not collected.

Endometrial thickness was in a range of 0.8 to 1.2cm. No ectopic pregnancy was seen beyond 1.2 cm. This is in accordance with other researchers also. Endometrial thickness below 9 mm increases the risk of ectopic pregnancy by four fold, as compared to an endometrial thickness over 1.2 cm<sup>(17)</sup>. All the inseminations were easy and no technical difficulty was encountered.

The number of embryos transferred is directly proportional to rate of ectopic pregnancies<sup>(18,19)</sup>. This



was reflected in the current study also. Maximum number of ectopics were seen when three embryo transfer was done. No ectopic pregnancy occurred after single embryo transfer.

High estradiol levels were seen to be associated with higher ectopic pregnancy rate. In our study most ectopics had high estrogen level, no ectopic was noted below 6000pmol/l and majority occurred in the group with minimum E2 levels of 9000pmol/l. Decler et al., in their research, noted that half of the ectopics during their study period occurred when they were transferring embryos in fresh cycles as opposed to frozen thawed cycles<sup>(8)</sup>. The possible reason suggested in literature is an altered endometrial receptivity with high estrogen levels.<sup>(20,21)</sup> and increased uterine contractions, which may again be a factor facilitating ectopic pregnancy<sup>(22)</sup>. High estrogen levels also increase the ciliary motion of tubal endothelium<sup>(23)</sup>. Another suggestion in literature is of vascular endothelial factor A (VEGFA) and prostaglandin E2 (PGE2)<sup>(24)</sup>. Both increase during LH surge but their amount has been noted to be more in ectopics rather than normal pregnancies<sup>(25,26)</sup>. However, these parameters were not checked in our pregnancies. The group of patients in this study were those with fresh embryo transfers which therefore was a constant variable.

The number of follicles aspirated, in this study, did not have a prominent association with ectopic pregnancy, although greater number of follicles aspirated would mean raised estrogen levels. Embryo transfer technique was the same for all. It was done under ultrasound guidance and aim was to deposit it in mid uterus<sup>(26)</sup>.

### CONCLUSION:

Three embryo transfer and high estrogen levels were some prominent parameters seen in patients ending in ectopic pregnancies. Tubal factor also was prominent considering that all those patients ending in ectopic had primary infertility and 4 out of 5 had male factor infertility. All ectopic pregnancies had cleavage stage embryos transferred except one.

Number of oocytes aspirated did not stand prominent as independent variable. The main drawback of the present study is its retrospective nature resulting in collection of limited data. However, it does guide for further research.

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## PREVALENCE OF HIV IN PATIENTS PRESENTING TO DOTS PROGRAM IN A TERTIARY CARE HOSPITAL

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### ABSTRACT

Tuberculosis is one of most documented ancient disease yet it still in top ten deadly disease. Pakistan ranks fifth in high TB burden area. Pakistan has an estimated 510000 new TB cases each year and about 15000 are developing drug resistant TB cases each year. 19000 were new case detection and 5500 deaths were attributed to AIDS in 2016 in Pakistan. There are multiple factors for failure of treatment. Among them, HIV positivity is main factor. There are many studies both locally and internationally that address this issue. Our study is one small step to high and improve this scenario.

**Objective:** To determine the frequency of HIV among patients presenting to Jinnah Hospital Lahore DOTS program.

**Study Design, Sample size and Data collection procedure:** It is cross sectional study, involving 1319 patients conducted over three years from January 2015 to December 2017 at DOTS center Jinnah Hospital Lahore. Both genders with age more than fourteen years are involved in study.

**Results:** 1426 patients were presented and counselled for screening in the above period time and majority of patients agreed for screening. Total of 1319 patients were enrolled in the study. 52% (n=687) patients were male and 48% (n=632) were female (Figure 1 and 2). Among age distribution 62% (n= 819) ranged in age between 15 to 30 years (Figure 3). Majority of patients were of pulmonary tuberculosis about 66%(n=878). 98% (n=1298) patients are negative for HIV upon screening.

**Conclusion:** Although HIV is less prevalent in our country, but it is more prevalent in tuberculosis patients when they are compared to nontuberculous population. When a patient presents for tuberculosis treatment it provides good opportunity to screen for HIV. Last but not the least, patients who are diagnosed with HIV should be thoroughly screen for tuberculosis, as these diseases has close relationship.

**Abbreviations:** Human Immune Deficiency Virus(HIV), Pulmonary Tuberculosis(PTB), Extra-pulmonary tuberculosis(EPTB), Directly Observed Treatment Short course(DOTS). Acquired immune deficiency syndrome(AIDS)

**Key Words:** Tuberculosis, HIV, DOTS.

Tuberculosis is one of most documented ancient disease and yet despite all the resources we are still unable to control the disease. TB is one of the top 10 causes of death worldwide<sup>1</sup>. Seven countries account for 64% of the total, with India leading the count, followed by Indonesia, China, Philippines, Pakistan, Nigeria, and South Africa<sup>2</sup>.

Pakistan has an estimated 510000 new TB cases each year and about 15000 are developing drug resistant TB cases each year<sup>1</sup>. Pakistan ranks fifth among TB high-burden countries worldwide and it

accounts for 61% of the TB case in the WHO Eastern Mediterranean Region<sup>1</sup>. According to UNAIDS program, there were about 130000 peoples living with AIDs. Among them 19000 were new case detection and 5500 deaths were attributed to AIDS in 2016 in Pakistan<sup>2</sup>. Although from this data Pakistan is although a low risk country for AIDs, but geographical location put her in high risk for such a deadly disease.

Without proper treatment, 45% of HIV-negative people with TB on average and nearly all

HIV-positive people with TB will die<sup>2</sup>. TB is a leading killer of HIV-positive people: in 2016, 40% of HIV deaths were due to TB. There are multiple factors for failure of treatment. Among them, HIV positivity is main factor. The presentation, diagnosis and treatment in peoples suffering from HIV and TB require altogether different strategy. For instance, the people with AIDs have more severe and aggressive form of tuberculosis. Radiological picture is also very different. So, it is imperative to diagnose the AIDs simultaneously with TB.

**OBJECTIVE:**

To determine the frequency of HIV among patients presenting to Jinnah Hospital Lahore DOTS program.

**Material and Methods:**

This was cross sectional study that was carried out from January 2015 to December 2017.

**Samples and Data collection procedure:**

Both genders, male and female were included in study. Patients were adults with age more than 14 years. The patients enrolled were either diagnosed at DOTS facility or they were referred for treatment. Diagnosis of tuberculosis was physician based. Written permission was taken from all enrolled participants/patients that their clinical and laboratory findings may be published scientifically without disclosing their identity.

**Procedure:**

Three milliliter venous blood was collected in Ethylene Diamine Tetra-Acetic Acid (EDTA) tubes and send to lab, where all blood samples were analyzed by rapid screen method for HIV. Patients who diagnosed with HIV were then referred to HIV treatment facility located in same hospital.

**Statistical Analysis:**

Descriptive statistics of all continuous variables were calculated as means and standard deviation, whereas categoric data were expressed as percentages. All analyses were done with SPSS version 20.0 for Windows.

**RESULTS:**

1426 patients were presented and counselled for screening in the above period time and majority of patients agreed for screening. Total of 1319 patients were enrolled in the study.

52% (n=687) patients were male and 48% (n=632) were female (Figure 1 and 2). Among age distribution 62% (n= 819) ranged in age between 15 to 30 years (Figure 3). Majority of patients were of pulmonary tuberculosis about 66%(n=878). 98% (n=1298) patients are negative for HIV upon screening.

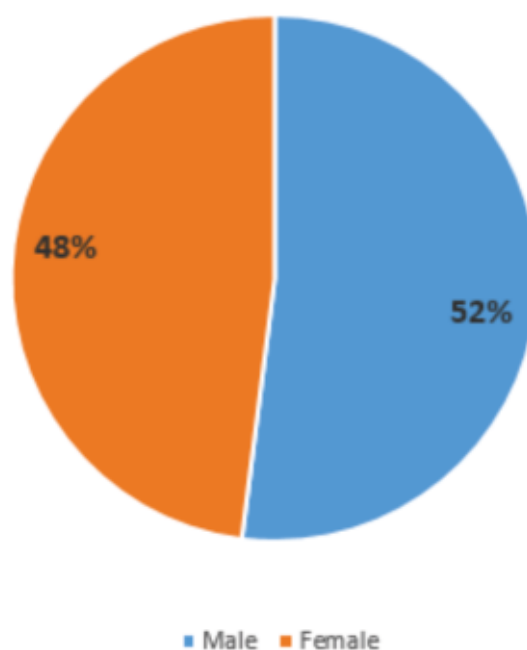


Figure 1: Sex distribution

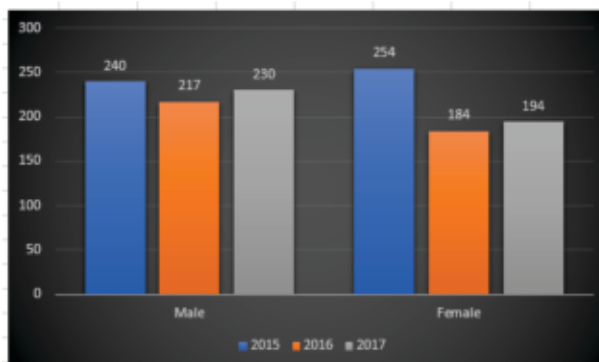
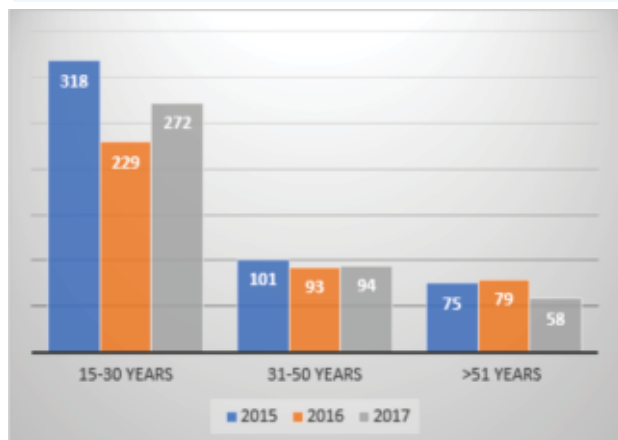


Figure 2: Detail of sex distribution yearly

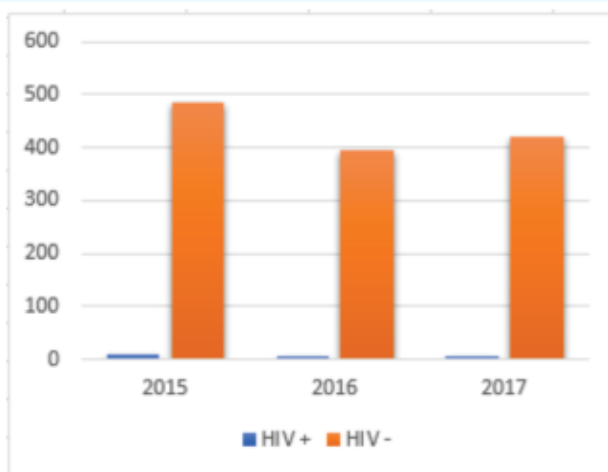


**Table 1:** Characteristics and prevalence of patients presenting in study

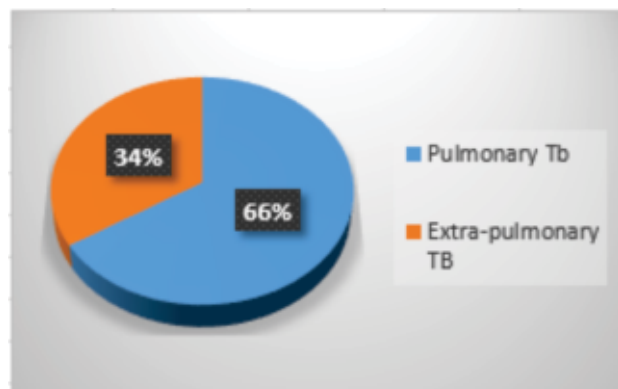
Year	Total Patients	Male	Female	15-30 years	31-50 years	>51 years	PTB	EPTB	HIV+	HIV-
2015	494	240	254	318	101	75	330	164	10	484
2016	401	217	184	229	93	79	266	135	6	395
2017	424	230	194	272	94	58	282	142	5	419



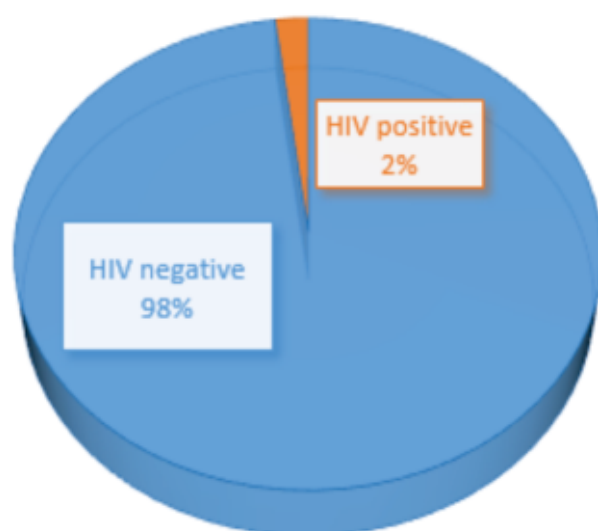
**Figure 3:** Age distribution yearly wise



**Figure 5 & 6:** Distribution of HIV in tuberculous patients over all and yearly



**Figure 4:** Frequency of PTB and EPTB



**DISCUSSION:**

This study high lights the importance of screening of patients with tuberculosis in our set up. Although the number patients diagnosed in our study are quite less (total 21 patients), but this high- lights that if these patients were missed their treatment may be complicated and the response may be not up to the mark. Moreover, screening at DOTs provides the excellent opportunity for HIV positive patients to be counselled for treatment.

The prevalence of HIV positivity in TB patients is only two percent. This is in line with study by Hussain et al, who showed prevalence of HIV among TB patients 0.38%<sup>3</sup>. But this figure is relatively low when compared to WHO. According to WHO the estimates is 6.9 per 100000 population<sup>5</sup>. This is because HIV clustered in some areas. According to Health Services academy Islamabad, data study conducted in 2016 showed more HIV positivity in Faisalabad<sup>6</sup>.

In our study male to female ratio presenting to DOTs is almost equal. This is because our DOTs center is in a city and there is good awareness among the peoples to present for prompt treatment. In Pakistan the male-to-female ratio in the reported HIV cases is about 10:17. In a study conducted by Hussain et al, prevalence of HIV was 22 times higher among male TB patients (0.67%) as compared to

female TB patients (0.03%)<sup>3</sup>. The reason may that sexual promiscuity is reported less common among female population as compared with male population<sup>8,9</sup>. Considerable number of reported HIV/AIDS cases in Pakistan have been male overseas Pakistani workers<sup>10</sup>. Extramarital sexual activities of these male workers play a key role for HIV infection<sup>11</sup>. Rise in HIV in Pakistan is partially driven by injection drug users, clear majority of which are men<sup>12</sup>. Prevalence of HIV among IV drug user in Karachi in Pakistan is up to 42.2%<sup>13</sup>. However, there is limitation in study, that we do not consider the distribution of HIV positivity relative to gender distribution.

There is no specific data from our country regarding the age distribution and HIV positivity. According to Safdar et al, 38% of total Pakistani population in 2007 is aged between 0 and 14 years old and among these groups, 3460 cases (4%) were noted to have a TB infection<sup>4</sup>. The majority in our study were young patients. This is because as social contact increases there is more chance of getting tuberculosis. Limitation in our study as we do not consider the age distribution and HIV positivity.

Majority of our patients have pulmonary tuberculosis. Again, we do not consider the relation of pulmonary and extra-pulmonary tuberculosis to HIV positivity. Study conducted by Hussain et al, showed that extra-pulmonary tuberculosis is more common among HIV positive patients. In their study, HIV infection was 1.65 times higher among extrapulmonary TB cases as compared with pulmonary TB cases in their study<sup>3</sup>. A similar study conducted in India which showed that HIV infection is 1.3 times more likely in extrapulmonary patients<sup>14</sup>. Comparable results have been observed in other studies conducted in developed countries<sup>15</sup>.

Apart for limitations discussed in each section, there are other limitations as well. This is small study conducted in only one center. We did not check all the patients with ELISA, which has better efficacy in detecting HIV. Similarly, pediatric population is missing in our study. Last but not the least, we did not probe into the cause of HIV positivity.

### CONCLUSION:

Our study highlights the fact although HIV is still less prevalent in our country, but we should take specific measure to curtail this disease. Measures should include education of masses regarding the cause and management of disease through all sort of media. Similarly, when a patient presents for tuberculosis treatment it provides good opportunity to screen for HIV. Last but not the least, patients who

are diagnosed with HIV should be thoroughly screened for tuberculosis, as these diseases have close relationship.

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## APLASTIC ANEMIA: ASSESSMENT OF SEVERITY IN ADULTS PRESENTING TO A TERTIARY CARE HOSPITAL IN LAHORE

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### ABSTRACT

Aplastic anemia is relatively rare disorder. Its incidence is 2-3 million per year in Europe However, In Pakistan idiopathic severe aplastic anemia is more common.

**Objective:** To determine the grades of severity in newly diagnosed cases of Aplastic Anemia in adults presenting to a tertiary care hospital.

**Study Design:** A retrospective cross-sectional study.

**Sample technique:** Non Probability / consecutive Sampling technique

**Place and Duration of study:** The Hematology Department of Allama Iqbal Medical College/Jinnah Hospital Lahore, from December 2015 to December 2016

**Methodology:** Medical records of Adults aged 15 -60 years diagnosed with Aplastic anemia were reviewed. Camitta's criteria applied to assess the severity of aplastic anemia. Data included frequencies of different grades of severity in both gender. The data was analyzed through SPSS (Statistical Packages for Social Sciences) version 20 and documented as percentages.

**Results:** Among 60 diagnosed cases of Aplastic anemia, there were 42 males (70%) and 18 females (30%). Mean age of presentation was 35±18. In all 28 cases (46%) had Very-severe Aplastic Anemia, 14 cases (23%) had Severe Aplastic Anemia and 18 cases (30%) had Non-Severe Aplastic Anemia.

**Conclusion:** Aplastic anemia is more frequent in young males and most common type is Very-Severe Aplastic anemia at presentation.

**Key Words:** aplastic anemia, pancytopenia, cammita's criteria

Aplastic Anemia is a relatively rare and heterogeneous disorder. It is defined as “pancytopenia with a hypo-cellular bone marrow in the absence of an abnormal infiltrate and with no increase in reticulin”<sup>2</sup>. To diagnose Aplastic Anemia, there must be at least two of following: Hb<10 g/dl, platelet count <50× 10<sup>9</sup>/l, Absolute Neutrophil counts (ANC)<1.5 × 10<sup>9</sup>/l<sup>1</sup>.

Its incidence is 2-3 per million per year in Europe, but higher in East Asia. There is a biphasic distribution, with peaks at 10-25 years and over 60 years<sup>2</sup>. In Pakistan, Aplastic Anemia is found mostly in young males and the most common type is Idiopathic Severe Aplastic Anemia<sup>7</sup>.

Patients are commonly diagnosed with symptoms of Anemia and Thrombocytopenia. Majority of cases are idiopathic in Acquired Aplastic anemia in which Haemopoietic tissue is the target of an autoimmune process dominated by Oligoclonal expression of cytotoxic CD8+ T cells<sup>1</sup>. Camitta's criteria is used to assess severity as: Severe AA (SAA), Very-severe AA (VSAA) and Non-severe AA (NSAA). The assessment of disease severity is also important in treatment decisions and prognosis<sup>2</sup>.

### OBJECTIVE:

- 1) To assess the severity in newly diagnosed cases of Aplastic Anemia presenting to tertiary care hospital.

### OPERATIONAL DEFINITION:

Camitta's criteria was used to assess severity, which is as follows:

- **Severe AA (SAA):** Marrow cellularity <25% or 25-50% with <30% residual haemopoietic cells plus at least 2 of following: Absolute Neutrophil Count (ANC)<0.5 × 10<sup>9</sup>/l, Platelets <20 × 10<sup>9</sup>/l, Reticulocyte count <20 × 10<sup>9</sup>/l.

- **Very Severe AA (VSAA):** As for SAA, Absolute Neutrophil Count (ANC)<0.2 × 10<sup>9</sup>/l

**Non-severe AA (NSAA):** AA not fulfilling the criteria for SAA or VSAA.

### METHODOLOGY:

#### INCLUSION CRITERIA:

Sixty diagnosed cases of acquired Aplastic anemia were included in the study presenting at Hematology department of Allama Iqbal Medical College Lahore from December 2015 to December

2016. The selection of patients was based on the diagnosis of Aplastic anemia confirmed by bone marrow trephine biopsy in adults aged 15 -60 years in both gender.

**EXCLUSION CRITERIA:**

Following cases were excluded; Aplastic Anemia with paroxysmal nocturnal hemoglobinuria clones diagnosed by flow cytometry, post-chemotherapy and radio-therapy induced marrow Aplasia , i.e., within 6 months of remission induction therapy in leukemia, lymphomas and solid tumors; constitutional anemia such as Fanconi's Anemia by physical examination for skeletal deformities and confirmation by cytogenetic studies.

**DATA ANALYSIS:**

Effect modifiers like age, gender etc were addressed through stratification of data. All the information was entered in a structured Proforma. Statistical analysis was carried out using Statistical Package for Social Sciences (SPSS) version 20. Descriptive statistical analysis was performed by calculating frequency and percentages for qualitative variables. Quantitative variables were expressed as the mean ± standard deviation.

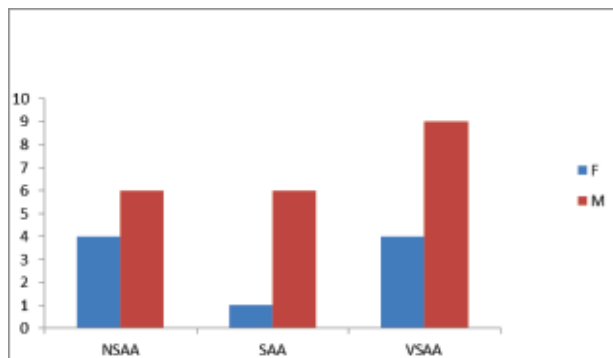
**RESULTS:**

Among 60 diagnosed cases of Aplastic anemia, there were 42 males (70%) and 18 females (30%). Mean age of presentation was 35± 18. In all, 28 Cases(46%) had Very-severe Aplastic Anemia, 14 cases (23%) had Severe Aplastic Anemia and 18 cases (30%) had Non-Severe Aplastic Anemia. Mean age of male was 18 in VSAA at presentation and mean age of female was 21.1. Table I summarizes values of both qualitative and quantitative variables in both genders. In SAA, mean bone marrow cellularity 10%±1, mean value of platelets 6x10<sup>9</sup>/l±8 and mean value of ANC was 0.5x10<sup>9</sup>/l±0.79 in both genders. In VSAA ,mean value of bone marrow cellularity was 8%±1 ,mean value of platelets 4x10<sup>9</sup>/l±8 and mean value of ANC was 0.09x10<sup>9</sup>/l±0.79 in both genders. In NSAA ,mean value of bone marrow cellularity was 23%±1,mean value of platelets 14x10<sup>9</sup>/l±8 and mean value of ANC was 1.6x10<sup>9</sup>/l±0.79 in both genders. Whereas,Table II and III summarizes values of different variables in female and male patients respectively. In females frequency of severity was as follows :VSAA 44%, SAA 22% and NSAA 33%.In VSAA, mean value of bone marrow cellularity 8%±1,mean value of platelets 4x10<sup>9</sup>/l±8, mean value of ANC was 0.09x10<sup>9</sup>/l±0.79 in females. In SAA ,mean value of bone marrow cellularity was 15%±1,mean value of platelets

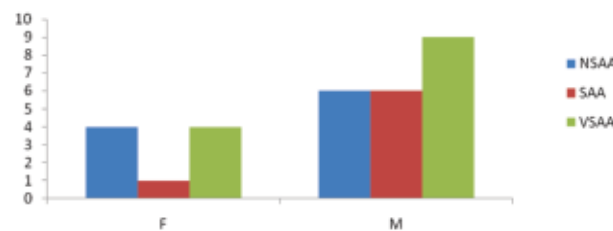
15x10<sup>9</sup>/l±8 and mean value of ANC was 0.5x10<sup>9</sup>/l±0.79 in females .In NSAA ,mean value of bone marrow cellularity 33%±1,mean value of platelets 21x10<sup>9</sup>/l±8 and mean values of ANC was 1.9x10<sup>9</sup>/ l±0.79 in females. In males frequency of severity was as follows: VSAA 52%, SAA 23% and NSAA 23%. Chart II shows male/female proportion comparison in different grade of severity. Chart III clearly shows than VSAA is more frequent type in both genders .

*Table 1: Statistical Analysis overall ,both genders*

Frequency of severity	Mean BM cellularity% ±SD	Mean value of Platelet ±SD	Mean value of ANC±SD
VSAA (46%)	8%±1	4x 10 <sup>9</sup> /l±8	0.09 x 10 <sup>9</sup> /l±0.79
SAA (23%)	10%±1	6x 10 <sup>9</sup> /l±8	0.50 x 10 <sup>9</sup> /l±0.79
NSAA(30%)	23%±01	14x10 <sup>9</sup> /l±8	1.6 x 10 <sup>9</sup> /l±0.79



*Chart II: Male / Female proportion comparison in different grades of severity*



*Chart III: Male / Female Wise No. of Cases in each Grade of Severity*

**DISCUSSION:**

In my Study percentages of male and female were 70% and 30% respectively with mean age of presentation for male was 18 years and for female it was 35 years. It was more frequent in adult males than female ones. As was in international study conducted at India showed similar male predo-



minance with mean age of presentation at 16 years<sup>3</sup>. Frequency of different grades of severity was as follows in my study: VSAA 46%, SAA 23% and NSAA 23% with predominance of VSAA in both male and female patient. While study from India showed NSAA was more predominant type with frequency of 55% in adults followed by SAA and VSAA with frequencies of 35% and 10% respectively<sup>4</sup>. Another international study from North Bengal showed similar male predominance with NSAA 44% more frequent than SAA 34% and VSAA 21% type<sup>5</sup>. Another study by Mahapatra Met al revealed SAA: 75% as more frequent followed by VSAA: 15% and NSAA:10% .it also showed male predominance with median age of presentation of 25 years<sup>5</sup>.

Study conducted at NIBD Karachi showed similar male predominance with percentage of 74%, however, the mean age of presentation in male was

**Table 2: Statistical analysis female**

Frequency of severity	Mean BM cellularity% ±SD	Mean value of Platelet ±SD	Mean value of ANC±SD
VSAA (44%)	8%±1	4x10 <sup>9</sup> /l±8	0.09x10 <sup>9</sup> /l±0.79
SAA(22%)	15%±1	15x10 <sup>9</sup> /l±8	0.5x10 <sup>9</sup> /l±0.79
NSAA(33%)	21%±1	12x10 <sup>9</sup> /l±8	1.9x10 <sup>9</sup> /l±0.79

**Table 2: Statistical Analysis Male**

Frequency of severity	Mean BM cellularity% ±SD	Mean value of Platelet ±SD	Mean value of ANC±SD
VSAA (52%)	6%±1	4x10 <sup>9</sup> /l ± 8	0.09x10 <sup>9</sup> /l±0.79
SAA (23%)	10%±1	8x10 <sup>9</sup> /l ± 8	0.55x10 <sup>9</sup> /l±0.79
NSAA (23%)	24%±1	15.0x10 <sup>9</sup> /l ±8	1.39x10 <sup>9</sup> /l±0.79

21 year 6 in my study it was 18. SAA was more frequent 61% followed by VSAA 22% and NSAA 15 % which is inconsistent with results of my study in which VSAA is more frequent type followed by NSAA. Another study conducted at Sheikh Zayed Hospital Lahore showed similar inconsistency in frequency of severity with SAA more frequent type<sup>7</sup>. The study conducted at Aga Khan University Hospital on pediatric patients also showed VSAA more frequent followed by SAA and NSAA respec-

tively with male predominance<sup>8</sup>. Young male predominance was a consistent feature revealed by both local and international studies. The limitations of study are that data was collected retrospectively for a period of time, and that the medical record was the source of information.

## CONCLUSION:

Acquired Aplastic anemia shows young male predominance. Very Severe Aplastic anemia was more frequent clinical stage at presentation in both genders followed by Non-severe and Severe Aplastic anemia. So, we recommend that further local studies need to be done in order to obtain better information with regards to prognosis, treatment selection and outcome.

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## AN EVALUATION OF COAGULATION PARAMETERS IN LIVER CIRRHOSIS

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### ABSTRACT

**Background:** Cirrhosis is the late stage liver disease in which irreversible scarring of liver tissue is present. Coagulation abnormalities in cirrhotic patients are assessed by measuring prothrombin time (PT), activated partial thromboplastin time (APTT) and platelet count.

**Methods:** A retrospective study was conducted from November 2016 to April 2017. Fifty patients and fifty healthy controls were included in the study. Age, gender, clinical features, PT, APTT and platelet counts were noted on a proforma.

**Results:** Out of 50 patients, 17 (34%) males and 33 (66%) females were present in the study. 28 (56%) patients had mildly prolonged PT (15-20 sec), 33 (66%) patients had moderately prolonged APTT (51-100 sec) and 23 (46%) patients had mildly decreased platelet count (100000-149000 cells/ul). The difference of mean values of PT and APTT in the patient and control group was statistically extremely significant ( $p < 0.0001$ ). Comparison of mean values of platelet count in the patient and control group was statistically highly significant ( $p=0.002$ ). Conclusion: Prolongation of PT, APTT and decreased platelet counts are usually present in patients of liver cirrhosis.

**Key words:** cirrhosis, prothrombin time, activated partial thromboplastin time, platelet count.

Cirrhosis is defined as the late stage liver disease in which scar tissue replaces the normal healthy tissue of the liver<sup>1</sup>. Parenchymal necrosis, regeneration and scarring is mostly present in cirrhosis. Liver cirrhosis is the thirteenth leading cause of death globally, with worldwide mortality rate increased by 45.6 % from 1990 to 2013<sup>2</sup>. Patients with liver cirrhosis have coagulation abnormalities that result from derangements in the clotting and fibrinolytic systems, as well as from reduced number and function of platelets<sup>3</sup>.

PT and APTT are considered as the first-line global screening tests for measuring coagulation abnormalities in patients of liver cirrhosis. Prothrombin time checks for the presence of vitamin K dependent extrinsic factors VII, X, II, and fibrinogen. The activated partial thromboplastin time determines the activities of intrinsic clotting factors such as factor VIII, IX, XI, XII and common pathways of coagulation cascade<sup>4</sup>. The PT and APTT are prolonged in patients of advanced chronic liver disease.

Thrombocytopenia (platelets below 150000

cells/ul) frequently complicates chronic liver disease and leads to delayed medical management<sup>5,6</sup>.

### Aims and Objectives

In this study PT, APTT and platelet counts were used to assess the hemostatic defects in patients with liver cirrhosis. It will help the haematologists and the gastroenterologists to cope with the severity of coagulation defects and their complications such as bleeding and thrombosis, leading to better management and treatment of cirrhotic patients<sup>7</sup>.

### SUBJECTS AND METHODS

A retrospective study was conducted from November 2016 to April 2017 in Pathology Department of Allama Iqbal Medical College/Jinnah Hospital, Lahore. Fifty patients and fifty healthy controls were included in the study. In both groups age, gender, PT, APTT and platelet counts were noted on a proforma. In the patient group, clinical features were also noted.

PT and APTT noted in the study conducted were performed by manual-tilt method. PT and

APTT kits manufactured by Singapore Biosciences PTE Ltd and controls manufactured by HUMAN GmbH, Wiesbaden, Germany were used.

After due consent, 5ml blood was drawn with 5cc disposable syringe under aseptic measures. 3 ml blood was added into the evacuated anticoagulant (sodium citrate) vial in a ratio of 1:9 for performing PT and APTT. 2ml blood was transferred into the EDTA vacutainer for determining platelet count.

Within one hour of sample collection, PT and APTT were performed. The blood was centrifuged for 15 minutes and platelet poor plasma was transferred into the clean glass test tubes.

For PT, plasma was incubated at 37°C and then thromboplastin was added. Timer was started and stopped on formation of a coagulum. The time was noted in seconds.

For APTT, plasma was also incubated at 37°C. After incubation, phospholipid and a contact activator such as ellagic acid were added followed by addition of calcium which was also pre-warmed to 37°C. On addition of calcium, clotting initiated and timer was started. Timer was stopped on formation of a fibrin clot and the time was noted in seconds.

The platelet count was determined by automated haematology analyzer (Sysmex KX-21). It determined the platelet count automatically with other haematology parameters within few minutes after whole blood sample (50 µL) was sucked through suction inlet.

PT and APTT results were classified into normal, mildly prolonged, moderately prolonged and severely prolonged PT and APTT. Platelet count results were classified into normal platelet count, mild, moderate and severe thrombocytopenia<sup>8</sup>.

#### Statistical analysis

Statistical package for social sciences (SPSS) version 20 software was used to analyze the study results. Simple frequencies and percentages were determined. Comparison of mean PT, APTT and platelet count of patients was done with that of controls by applying student 't' test and the p-value was obtained. The results were expressed as mean ±

standard deviation. The p-value less than 0.05 was considered to be statistically significant.

#### Inclusion criteria

Primarily, patients with presence of liver cirrhosis were included in the study, irrespective of etiology. Diagnosis of liver cirrhosis was based on:

- (i) clinical features (ascities and neurological disorder)
- (ii) biochemical investigations (raised serum bilirubin and reduced serum albumin)
- (iii) abdominal ultrasound

All patients of cirrhosis of liver irrespective of gender and socioeconomic status were included in the study.

#### Exclusion Criteria

1. Age above 80 years.
2. The patients of liver cirrhosis with a previous history of coagulation disorders.
3. Patients taking drugs such as aspirin, oral contraceptives, heparin and warfarin that lead to changes in the coagulation parameters.
4. Patients with liver damage due to causes other than cirrhosis.
5. Pregnant females.

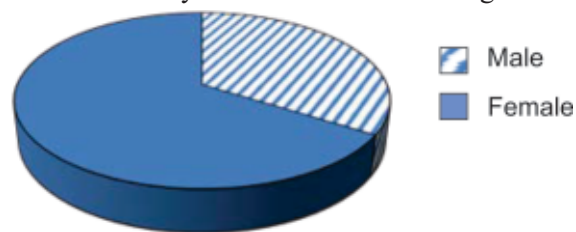
## RESULTS

### Age Distribution of Patients

The mean age of patients with cirrhosis was 54.04 ± 11.76 with range of 28- 80 years.

### Gender Distribution of Patients

17 (34%) were males and 33 (66%) were females in the study conducted as shown in figure 1



**Figure 1:** Gender Distribution of Patients

### Clinical Findings

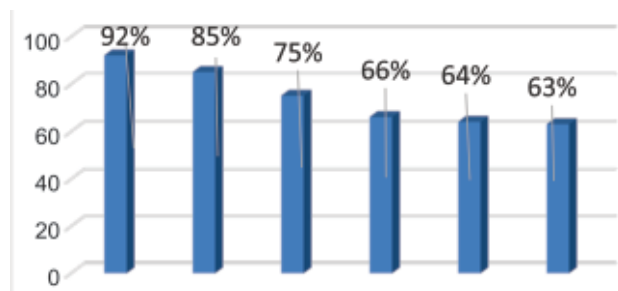
The frequency of clinical findings in patients with cirrhosis is shown in the figure 2. Pallor was present in 46(92%) patients, fever in 42(85%) patients, as cities in 37(75%) patients, jaundice in 33 (66 %) patients, splenomegaly in 32 (64 %) patients and edema in 31 (63 %) patients.

### Laboratory Investigations

#### 1. Prothrombin Time and Activated Partial Thromboplastin Time

PT and APTT were noted in the patient group. Both PT and APTT were categorized into normal, mildly, moderately and severely prolonged PT and

APTT. Frequencies and percentages were calculated.



**Figure 2:** Clinical Findings in Cirrhotic Patients

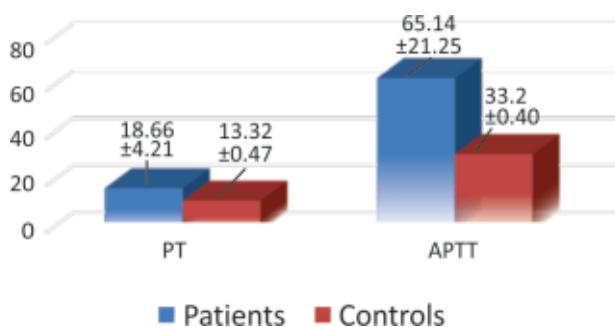
Out of 50 patients, 8 (16%) patients had PT value in the range of 13-14sec (normal PT), 28 (56%) patients had PT value in the range of 15-20 sec (mildly prolonged PT) and 14 (28%) patients had PT

**Table 1:** PT in the Patient Group

Patients	Normal PT (13-14 sec)	Mildly Prolonged PT (15-20 sec)	Moderately Prolonged PT (21-50 sec)	Severely Prolonged PT (> 50 sec)
Number	8	28	14	0
Percentage (%)	16	56	28	0

value in the range of 21-50sec (moderately prolonged PT) as shown in the table 1. No patient had PT value above 50 sec (severely prolonged PT) in the study conducted.

Out of 50 patients, 2 (4%) patients had APTT value in the range of 33-35sec (normal APTT), 11 (22%) patients had APTT value in the range of 36-50sec (mildly prolonged APTT), 33 (66%) patients had APTT value in the range of 51-100sec (moderately prolonged APTT) and 4 (8%) patients had APTT value greater than 100sec (severely prolonged APTT) as shown in the table 2.



**Figure 3:** Comparison of Mean Values of PT and APTT in the Patient and Control Group

Comparison of mean values of PT and APTT for patients and controls is shown in the table 3 and figure 3. The mean value of PT was 18.66±4.21 as compared to control mean value of 13.32±0.47. The

mean value of APTT was 65.14±21.25 as compared to control mean value of 33.2±0.40. The difference of mean values of PT and APTT in both patients and controls is statistically extremely significant (p-

**Table 2:** APTT in the Patient Group

Patients	Normal APTT (33-35 sec)	Mildly Prolonged PT (36-50 sec)	Moderately Prolonged PT (51-100 sec)	Severely Prolonged PT (> 100 sec)
Number	2	11	33	4
Percentage (%)	4	22	66	8

**Table 3:** Comparison of Mean Values of PT and APTT in the Patient and Control Group

Parameter	Patients (Mean ± SD)	Controls (Mean ± SD)	p-value
PT (sec)	18.66 ± 4.21	13.32 ± 0.47	* < 0.0001
APTT (sec)	65.14 ± 21.25	33.2 ± 0.40	* < 0.0001

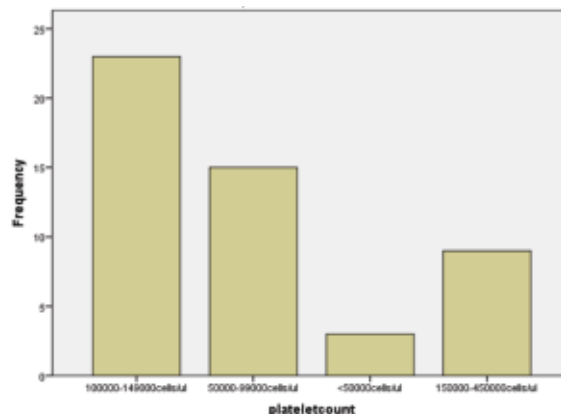
\* Statistically extremely significant p-value

value < 0.0001).

## 2. Platelet Count

Platelet count in the patient group was classified into normal platelet count, mild, moderate and severe thrombocytopenia. Frequencies and percentages were calculated.

Out of 50 patients, 9 (18%) patients had platelet count in the range of 150000-450000 cells/ul (normal platelet count), 23 (46%) patients had platelet count in the range of 100000-149000 cells/ul (mild thrombocytopenia), 15 (30%) patients had platelet count in the range of 50000- 99000 cells/ul (moderate thrombocytopenia), and 3 (6%) patients had platelet count less than 50000 cells/ul (severe thrombocytopenia) as shown in the table 4 and figure 4.



**Figure 4:** Platelet Count in the Patient Group



**Table 4:** Platelet Count in the Patient Group

Patients	Normal Platelet Count (150000-450000 cells/ul)	Mild Thrombocytopenia (100000-1490000 cells/ul)	Moderate Thrombocytopenia (50000-99000 cells/ul)	Severe Thrombocytopenia (< 50000 cells/ul)
Number	9	23	15	3
Percentage (%)	18	46	30	6

The mean value of platelet count in patients with cirrhosis was  $115280 \pm 44504$  cells/ul, which is significantly lower than the normal range of 150,000 – 450,000 cells/ul ( $p=0.002$ ).

## DISCUSSION

The degree of disturbed hepatic function determines the extent of coagulation abnormalities<sup>9</sup>. In our study there was significant prolongation of prothrombin time and activated partial thromboplastin time in cirrhotic patients. This finding is the same as reported in previous studies<sup>10,11</sup>. In the present study, 28 (56%) patients had mildly prolonged PT and 33 (66%) patients had moderately prolonged APTT.

Prothrombin time is prolonged in liver diseases because liver is not able to manufacture sufficient amount of clotting factors including those involved in extrinsic pathway. The APTT is also increased in liver diseases, the reason being that factors IX, XI and XII and fibrin stabilizing factors are also synthesized by the liver<sup>12</sup>.

In the present study blood platelet count was significantly decreased in patients with liver cirrhosis. This finding is compatible with the previous studies<sup>13,14,15</sup>. In the present study, 23 (46%) patients had mild thrombocytopenia.

Thrombocytopenia is a common finding in diagnosed liver disease patients<sup>16</sup>. Thrombocyto-

**Table 5:** Comparison of Mean Values of Platelet Count in the Patient and Control Group

Parameter	Patients (Mean $\pm$ SD)	Controls (Mean $\pm$ SD)	p-value
Platelet Count (cells/ul)	$115280 \pm 44504$	$248940 \pm 306086$	* 0.002

\* Statistically highly significant p-value

penia is usually mild to moderate in patients with uncomplicated cirrhosis and is not associated with severe bleeding<sup>17</sup>. Hypersplenism secondary to portal hypertension and decreased levels of hepatic thrombopoietin are the common reasons leading to thrombocytopenia in patients of liver cirrhosis<sup>18</sup>.

## CONCLUSION

We conclude that significant prolongation of PT and APTT can be used as a reliable marker of coagulopathy in patients of liver cirrhosis. Thrombocytopenia is usually encountered in patients of liver cirrhosis.

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## FREQUENCY OF HYPERTENSION AND MICROALBUMINURIA IN DIABETIC PATIENTS WITH RETINOPATHY

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### ABSTRACT

**Introduction:** Diabetes Mellitus (DM) is a major health problem in the developed world. It has also been increasingly recognized as a serious health problem in Pakistan. Currently there are about 7 million diabetic patients in Pakistan and this number is increasing day by day.

**Objective:** The objective of this study was to determine the frequency of hypertension and microalbuminuria in diabetic patients with retinopathy.

**Methods:** This cross-sectional study was conducted at District Head Quarters HOSPITAL MIANWALI from 1st June, 2015 to 30 November 2017 and enrolled 131 diabetic patients. Their fasting blood sugar, random blood sugar and 24-hour urine for protein analysis were measured in addition to recording their blood pressure for the purpose of identification of hypertensive patients. All patients were screened for diabetic retinopathy using a WelchAllyn Fundoscope.

**Results:** Hypertension and microalbuminuria were present in 51.9% and 47.3% patients respectively. Diabetic retinopathy was found in 39.7% study participants. Both hypertension and microalbuminuria were found to be significantly associated with diabetic retinopathy ( $p < 0.05$ ). Microalbuminuria was associated with age of the study participants ( $p=0.05$ ).

**Conclusion:** This study showed that hypertension and microalbuminuria were significantly associated with the development of diabetic retinopathy.

**Key words:** diabetes mellitus, diabetic retinopathy, microalbuminuria, hypertension, GFR

The burden of diabetes mellitus on healthcare systems is increasing throughout the world and it is a major chronic health-related problem worldwide. With more than 7 million diabetic patients, diabetes has become a serious health issue in Pakistan.<sup>1</sup> According to estimates by the World Health Organization (WHO), Pakistan will rank 4th in the world according to the population burden of diabetes mellitus by year 2030.<sup>1</sup>

Diabetic patients are commonly classified as having type 1 diabetes mellitus or IDDM (insulin dependent diabetes mellitus; characterized by complete lack of insulin secretion by the pancreas) and type 2 diabetes mellitus or NIDDM (Non-insulin dependent diabetes mellitus; characterized by insulin resistance and an inadequate release of insulin in response to hyperglycemia).<sup>2</sup> However, development of diabetes is also seen in other conditions such as pregnancy (gestational diabetes mellitus), pancreatic disease (chronic pancreatitis), drugs (corticosteroids etc) and endocrinopathies e.g., Cushing syndrome.<sup>3</sup>

Uncontrolled hyperglycemia leads to a number of microvascular and / or macrovascular complications in the body and diabetic retinopathy is one of the most severe complications of diabetes mellitus

affecting the ocular apparatus. In adults aged 20 and above diabetic retinopathy is the most common preventable cause of blindness.<sup>4</sup> Diabetic retinopathy usually develops after 20 years of diagnosis of diabetes mellitus in nearly all patients with IDDM and about 50% of patients with NIDDM.<sup>5</sup> However, it has also been noted earlier in the course of disease. For example, the prevalence of diabetic retinopathy was reported to vary between 21% in patients whose duration of diabetes was less than five years.<sup>3</sup> The same study reported an increase in the prevalence of diabetic retinopathy with the increase in duration of disease i.e., 60% with a disease duration of at least 15 years.<sup>3</sup> Similarly, the prevalence of proliferative retinopathy was 1.2% with a duration of diabetes less than 10 years and as much as 67% for a duration of diabetes more than 35 years.<sup>3</sup> Background diabetic retinopathy has been reported in up to 25% of newly diagnosed type 2 diabetic patients.<sup>1</sup>

Development of diabetic retinopathy is associated with a number of factors such as the duration of diabetes mellitus, presence of diabetic nephropathy, chronic hyperglycemic state, dyslipidemias, pregnancy and hypertension.<sup>4</sup> It has been suggested that micro-albuminuria is particularly found associated with proliferative retinopathy in diabetics with onset

of diabetes at younger age and patients who have diabetic retinopathy irrespective of the onset of disease and the association is so strong such that individuals with microalbuminuria are more likely to have diabetic retinopathy.<sup>6</sup>

These observations suggest that microalbuminuria can be regarded as a predictive marker for the risk of proliferative diabetic retinopathy in diabetic patients. In addition to microalbuminuria, hypertension has also been described to independently affect the development of diabetic retinopathy.<sup>7,8</sup> In fact, effective reduction in blood pressure has been linked to a reduced incidence and progression of diabetic retinopathy.<sup>4</sup> In a study by Abdelghaffar W et al, prevalence of microalbuminuria in patients with DR was found to be 31.98%<sup>9</sup> while another study by Nabais C et al showed that prevalence of hypertension in DR patients was 79.6%.<sup>10</sup>

In addition to microalbuminuria and hypertension increasing age male gender, poor glycemic control and duration of diabetes have also been identified as being independently associated with the development of diabetic retinopathy.<sup>11</sup>

Since the prevalence of diabetes mellitus in Pakistan is very high (7%-11%) depending on a number of factors such as age, region, gender etc<sup>12</sup>, and as much as 64% of diabetics in Pakistan also have cocomitant hypertension<sup>4</sup>, this study was conducted with an aim to determine the association of microalbuminuria and hypertension with diabetic retinopathy in our region. We hoped to get a picture of current trends in the pathogenesis of diabetic retinopathy and its association with the aforementioned risk factors. We hoped to draw attention towards early recognition of microalbuminuria and management of hypertension as well as microalbuminuria in diabetic patients to reduce or delay the precipitation of diabetic retinopathy.

## MATERIAL AND METHODS

The study was conducted with an objective to determine the frequency of hypertension and microalbuminuria in diabetic patients with retinopathy at DHQ hospital, Mianwali, Punjab. For the purpose of this study, diabetic retinopathy was defined as the presence of a minimum of one micro aneurysm in any field, or presence of hemorrhages (dot & blot, or flame shaped), or maculopathy (with or without clinically significant edema) on fundoscopy.<sup>13</sup> Similarly, hypertension and microalbuminuria were defined as systolic blood pressure  $\geq 140$  mmHg and diastolic Blood pressure  $\geq 90$  mmHg.<sup>14</sup> and presence of urine albumin level between 30-300 mg/24 hours.<sup>15</sup>

It was a descriptive cross-sectional study conducted at DHQ hospital from 1st June, 2015 to 30 November, 2017 with a sample size of 131. The number was arrived at using the WHO Sample Size Determination in Health Studies software keeping the prevalence of microalbumin-uria in diabetic retinopathy as 31.98%<sup>9</sup>, with a confidence interval of 95% to achieve a precision level of 9%. Non-probability purposive sampling was used to complete the population sample for this study. Male and female diabetic patients (both IDDM and NIDDM) with an age of 20-60 years and who had been diagnosed with diabetes for at least five years were enrolled in the study. Patients with renal disease due to any other cause, established hypertensive and / or diabetic nephropathy and patients with retinopathy due to any other cause were excluded from the study to make sure these conditions do not introduce bias into the results of this study.

Patients who had consented to participate in this study were advised fasting blood sugar, random blood sugar and 24-hour urine for protein analysis. Blood pressure was recorded after resting the patient in supine position for five minutes using a mercury sphygmomanometer. The study participants were screened for the presence of diabetic retinopathy using a WelchAllyn Fundoscope with fully dilated pupils and these findings were later confirmed by slit-lamp examination with a 90D lens. The patients were later grouped into two groups based on the presence or absence of diabetic retinopathy for the purpose of statistical analysis. The data collected was entered into and analyzed via SPSS v 20. Mean $\pm$ SD were calculated for numerical variables and frequencies and percentages were calculated for categorical variables. The data was stratified by age, gender and duration of diabetes mellitus with respect to outcome variables i.e. presence of hypertension and micro-albuminuria. Post stratification chi-square test was used to determine association between diabetic retinopathy; and hypertension and micro-albuminuria and a p value  $\leq 0.05$  was taken as significant.

## RESULTS

Diabetic retinopathy was diagnosed in 43 (41.35%) patients. The frequency of microalbuminuria and hypertension was 56.7% (n=59) and 48.07% (n=50) respectively. Table-1 shows the descriptive statistics of the study population.

Diabetic retinopathy was diagnosed in 43 (41.35%) patients and when cross-tabulated against age, sex, presence of hypertension and microalbu-



minuria, it was found to be significantly associated with hypertension ( $p = 0.012$ ) and microalbuminuria ( $p = 0.045$ ). When the outcome variables such as hypertension and microalbuminuria were stratified by age, gender and duration of diabetes, only microalbuminuria was found to be associated with age of the patients and duration of diabetes mellitus ( $p < 0.05$ ).

## DISCUSSION

Diabetic retinopathy is a well known microvascular complication of diabetes mellitus. Other micro- and macrovascular complications of diabetes mellitus include diabetic nephropathy, diabetic neuropathy, coronary artery disease, peripheral vascular disease and peripheral autonomic complications. The reported prevalence of diabetic retinopathy in Pakistan is 27% while the prevalence of type 2 diabetes mellitus is around 10%.<sup>16,17</sup> However, limited data about risk factors associated with diabetic retinopathy is available from Pakistan.

In our study, which focused on microalbuminuria and hypertension only, we found that both these variables were significantly associated with the development of diabetic retinopathy ( $p < 0.05$ ). More over, development of microalbuminuria was significantly associated with the duration of diabetes mellitus and age of patients ( $p < 0.05$ ). No statistically significant association was found between diabetic retinopathy and age and sex of study participants.

In a study, Stratton and colleagues reported that there was a significant association of male sex, increased age, chronic hyperglycemia (characterized by persistently increased HbA1c), tobacco smoking and hypertension with the development and progression of diabetic retinopathy in type 2 diabetic patients.<sup>18</sup> Another study identified duration of diabetes mellitus, poor control of blood glucose levels, male gender and hypertension as independent risk factors strongly associated with the development of diabetic retinopathy.<sup>11</sup> Similar observations have been reported elsewhere. For example duration of diabetes mellitus, persistent hyperglycemia and sustained hypertension were reported to be strongly associated with the development of diabetic retinopathy.<sup>19</sup>

This study was designed to determine the common risk factors for the development of diabetic retinopathy in this population and the results of this study indicate that presence of microalbuminuria and hypertension are associated with the development of diabetic retinopathy in diabetic patients. This study did not compare type-1 diabetes with

**Table 1:** Descriptive statistics of study participants

Variable	Mean	Standard Deviation	Minimum	Maximum
Age (yrs)	46.09	8.61	31.00	59.00
Duration of diabetes (yrs)	13.27	3.47	7.00	18.00
Systolic BP	146.97	15.15	121.00	170.00
Diastolic BP	84.71	5.87	75.00	95.00

type-2 diabetes with regards to the prevalence of risk factors for diabetic retinopathy.

Interestingly, a French study reported that diastolic arterial hypertension, and not microalbuminuria was associated with a risk of developing diabetic retinopathy.<sup>20</sup> The researchers prospectively followed 104 diabetic patients who had developed diabetes at a younger age over a decade and reported that diabetic retinopathy developed in 39 (37.5%) patients. They noted that the duration of diabetes mellitus, poor glycemic control as depicted by increased HbA1c readings, diastolic arterial hypertension and male gender were significantly associated with diabetic retinopathy. Microalbuminuria was diagnosed in only 21 patients (20.2%).<sup>20</sup>

Another study reported that there was a statistically significant association between microalbuminuria and diabetic retinopathy was found only in type 1 diabetes mellitus.<sup>21</sup> The prevalence of microalbuminuria was more in type 1 diabetic patients compared to patients with type 2 diabetes mellitus (25.61% vs 17.78%). The study identified high levels of glycosylated hemoglobin, longer duration of diabetes mellitus, treatment with insulin in type 2 diabetes mellitus and hypertension as factors affecting the development of diabetic retinopathy.

Our study population, on the other hand, consisted only of patients with type 2 diabetes mellitus. The results of a study from Iran appear to be in conformity with our results which reported that microalbuminuria was associated with diabetic retinopathy in patients with type 2 diabetes mellitus and that microalbuminuria could reliably serve as a marker for diagnosis of diabetic retinopathy.<sup>22</sup> Similar results have been reported from India where a longer duration of disease was also found to be associated with diabetic retinopathy, albeit insignificantly.<sup>23</sup> This association between microalbuminuria and diabetic retinopathy is so strong that it has been recently been recommended that diabetic patients with microalbuminuria should be screened for the presence of diabetic retinopathy.<sup>24</sup>

**CONCLUSION**

Presence of microalbuminuria and hypertension are significantly associated with the development of diabetic retinopathy. Patients diagnosed with diabetes should regularly be screened for the development of microalbuminuria and /or hypertension and these conditions be aggressively managed to reduced the precipitation of diabetic retinopathy.

**Study limitations:**

This was a small hospital based study with a small sample size therefore these results do not reflect the population patterns of these problems. Association of microalbuminuria and hypertension with diabetic retinopathy was not stratified by type of diabetes mellitus as well by treatment modality i.e., use of insulin or oral hypoglycemic drugs. Assessment of glycemic control in study population was also not done in this study.

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## SPECTRUM OF COMPLICATIONS AND THEIR OUTCOME IN PATIENTS OF LIVER CIRRHOSIS HOSPITALIZED TO TERTIARY CARE HOSPITAL, GUJRANWALA, PAKISTAN

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### ABSTRACT

**Objective:** To determine the spectrum of different complication and their outcome in patients of liver cirrhosis hospitalized to tertiary care hospital, Gujranwala, Pakistan.

**Study Design:** Cross-sectional study

**Methodology:** After written informed consent, the data of all the hospitalized liver cirrhosis patients was collected prospectively by purposive sampling using a structured proforma from June 2016 to May 2017. Age of the patients was the only quantitative variable, while gender, complications of liver cirrhosis, and outcome of the hospitalization were the qualitative variables. Statistical analysis was performed using SPSS version number 25. During descriptive interpretation of data, means and standard deviation were calculated for continuous variables, and frequencies and percentages were computed for different categorical variables.

**Results:** Out of total of 1304 hospitalized liver cirrhosis patients, 48.1% were male and 51.9% were female. Their mean age was 54.51 + 14.32. 509 (39%) patients had upper GI bleed (UGIB), 294 (22.5%) had hepatic encephalopathy, 157 (12%) had Spontaneous bacterial peritonitis (SBP), 100 (7.7%) had infections other than SBP, 89 (6.8%) had tense ascites, 66 (5.1%) had hepatocellular carcinoma (HCC), 54 (4.1%) had renal impairment, 23 (1.8%) had hepatic hydrothorax, and 12 (0.9%) patients had hepatopulmonary syndrome (HPS). 20.2% (n = 264) liver cirrhosis patients were hospitalized with multiple infections. Amongst these patients, 59.5% (n = 157) patients had SBP, 17.4% (n = 46) had respiratory tract infection, 12.5% (n = 33) had gastroenteritis, 7.2% (n = 19) had leg cellulitis, and 3.4% (n = 9) had abdominal wall cellulitis. The outcome of the hospitalization of these cirrhotic patients was not so good. Amongst 1304 patients, 1099 (84.3%) recovered and 205 (15.7%) died.

**Conclusion:** Upper GI bleed is the commonest complication with which liver cirrhosis patients are hospitalized in our population, followed by hepatic encephalopathy, spontaneous bacterial peritonitis, infections other than SBP, tense ascites, refractory ascites, hepatocellular carcinoma, hepatic hydrothorax, renal impairment, and hepatopulmonary syndrome. The outcome of the hospitalization in liver cirrhosis patients is very poor. There is an acute necessity for alternative approaches to achieve the care of these end stage liver disease patients.

**Keywords:** Liver cirrhosis, Complications of cirrhosis, in-hospital mortality, Statistical analysis, SPSS

Liver cirrhosis has a huge burden on health system of Pakistan<sup>1</sup>. Worldwide prevalence of liver cirrhosis ranges from 4.5% to 9.5% of the overall population<sup>2,3,4</sup>. The hepatitis C virus infection is the most common etiology of liver cirrhosis in Pakistani people<sup>5</sup>. Different complications among

CLD patients include upper gastrointestinal bleed (UGIB), hepatic encephalopathy ((HE), spontaneous bacterial peritonitis (SBP), infections other than SBP, tense ascites, refractory ascites, hepatocellular carcinoma (HCC), hepatic hydrothorax, renal impairment, and hepatopulmonary syndrome

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(HPS). UGIB<sup>6</sup> presents with hematemesis or melena or both. Hematochezia is usually symbolic of a lower GI source, it may be seen in brisk UGIB.<sup>6</sup> Hepatic encephalopathy<sup>7</sup> is defined by neuropsychiatric manifestations due to liver dysfunction, including behavior changes, reverse sleep pattern, tremors, asterixis, unilateral or bilateral Babinski sign, increased deep tendon reflexes, and coma. Hepatic myelopathy<sup>8</sup> is a special pattern of HE characterized by severe motor abnormalities. Cases with spastic paraplegia have been reported. They do not respond to ammonia lowering, rather to liver transplantation. SBP is suspected if CLD patients presents with abdominal pain or tenderness. The diagnosis is made if ascitic fluid absolute polymorpho nuclear leukocyte count is  $> 250$  cells/mm<sup>3</sup> without any evident intrabdominal, surgically treatable source of infection.<sup>9</sup> Infections other than SBP include secondary bacterial peritonitis, respiratory tract infection, gastroenteritis, leg cellulitis, abdominal wall cellulitis. HCC complicates approximately 1.3 out of 100 cirrhotic patients each year.<sup>10</sup> Tense ascites requires large volume paracentesis followed by medical management,<sup>11</sup> while refractory ascites is defined by unresponsiveness to low sodium diet and high dose diuretics and recurs rapidly after therapeutic paracentesis.<sup>12</sup> Hepatic hydrothorax complicates approximately 5% of cirrhotic patients.<sup>13</sup> Serum creatinine  $> 1.5$  mg/dl in cirrhotic patients defines renal impairment, where diagnosis of hepatorenal syndrome (HRS) has to be made by exclusion of all pre-renal, renal and post-renal diseases.<sup>14</sup> Oxygen saturation  $< 80\%$  suspect HPS, while alveolar-arterial gradient  $> 15$  mm Hg confirm it.<sup>15</sup> The outcome of the admitted cirrhotic patients is disappointing with a high in-hospital mortality world-wide, ranging from 13.5% to 35%.<sup>16,17</sup> The objective of our study was to determine the spectrum of different complication and their outcome in patients of liver cirrhosis hospitalized to tertiary care hospital, Gujranwala, Pakistan.

## METHODOLOGY

This cross-sectional study was conducted in the

Department of Medicine unit 1, GMC Teaching hospital, Gujranwala from June 2016 to May 2017. After written informed consent, the data was collected prospectively by purposive sampling using a structured proforma. All the diagnosed liver cirrhosis patients with age greater than 12 years who were hospitalized for different complications of liver cirrhosis were included in this study. Patients who presented with hematemesis or melena were included in a group with a label of upper GI bleed. Other presentations include hepatic encephalopathy, SBP, HCC, tense ascites, renal impairment, respiratory tract infection, gastroenteritis, leg cellulitis, abdominal wall cellulitis, and HPS. The outcome of the hospitalization of all the patients in term of recovery or death was also noted. Age of the patients was the only quantitative variable, while gender, complications of liver cirrhosis, and outcome of the hospitalization were the qualitative variables. Statistical analysis was carried out using the Statistical Package for Social Science (SPSS), version 25. During descriptive analysis of data, mean and standard deviation were calculated for continuous variables, and frequencies and percentages were computed for different categorical variables

## RESULTS

Out of total of 1304 hospitalized liver cirrhosis patients, 627 (48.1%) were male and 677 (51.9%) were female. Their age ranged from 13-110 years, with a mean value of  $54.51 \pm 14.32$ . Amongst total 1304 patients, 509 (39%) had upper GI bleed in term of hematemesis or melena, and 294 (22.5%) had hepatic encephalopathy. Amongst patients who presented with hepatic encephalopathy, 2 patients had hepatic myelopathy as well. 157 (12%) patients had Spontaneous bacterial peritonitis (SBP), 100 (7.7%) had infections other than SBP, 89 (6.8%) had tense ascites, 66 (5.1%) had HCC, 54 (4.1%) had renal impairment, 23 (1.8%) had hepatic hydrothorax, and 12 (0.9%) had HPS (Table 1).

20.2% (n = 264) liver cirrhosis patients were hospitalized with multiple infections. Amongst these



patients, 59.5% (n = 157) patients had SBP, 17.4% (n = 46) had respiratory tract infection, 12.5% (n = 33) had gastroenteritis, 7.2% (n = 19) had leg cellulitis, and 3.4% (n = 9) had abdominal wall cellulitis (Picture 1). The outcome of the hospitalization of these cirrhotic patients was not so good. Amongst 1304 patients, 1099 (84.3%) recovered and 205 (15.7%) died (Picture 2).

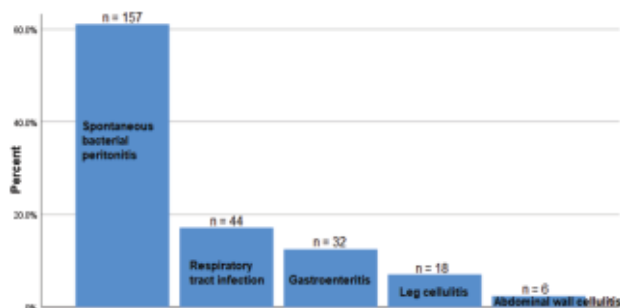
**DISCUSSION**

Liver cirrhosis has a broad spectrum of compli-

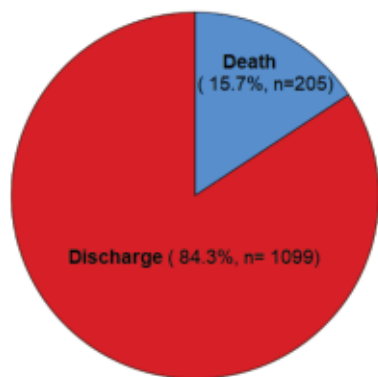
**Table 1:** Complications with which Liver cirrhosis patients were hospitalized to tertiary care hospital Gujranwala (n = 1304).

Complications of Liver cirrhosis	Frequency (Percent)
Upper GI bleed	509 (39%)
Hepatic encephalopathy	294 (22.5%)
SBP	157 (12%)
Infections other than SBP	100 (7.7%)
Tense ascites	89 (6.8%)
Hepatocellular carcinoma	66 (5.1%)
Renal impairment	54 (4.1%)
Hepatic hydrothorax	23 (1.8%)
HPS	12 (0.9%)

GI = Gastrointestinal; SBP= Spontaneous bacterial peritonitis; HPS = Hepatopulmonary syndrome;



Picture 1: Infections in hospitalized liver cirrhosis patients (n = 1304)



Picture 2: Outcome of hospitalization in liver cirrhosis patients (n=1304)

cations with which these patients present at hospitals on different occasions. Without considering liver transplantation, these complications have a bad sequela overall. If once these patients got recovered, they present with another complication later. Hence, decompensated liver cirrhosis has a high morbidity and mortality. In our study, UGIB was the commonest reason of hospitalization among cirrhotic patients. International research suggests that UGIB is self-limited without any definite therapy in approximately 80% of the patients.<sup>18,19</sup> Similarly, in our patients, 22.5% presented with hepatic encephalopathy (HE). In 2007, Poordad<sup>20</sup> estimated the burden of HE of 30-45% among CLD patients. Like all previous estimates,<sup>21</sup> SBP was found in 12% of our group of cirrhotic patients. In 1999 Navasa and colleagues<sup>22</sup> reported multiple bacterial infections other than SBP in cirrhotic patients. They found urinary tract infections, pneumonia, and bacteremia in 20%, 15%, and 12% patients respectively. However, in our data, respiratory tract infection was the commonest finding followed by gastroenteritis, leg cellulitis, and abdominal wall cellulitis. 6.8% cirrhotic patients were hospitalized for tense ascites, where LVP<sup>11</sup> was the chief purpose of admission. This group also included the patients with refractory ascites as well. In our study, 5.1% CLD patients had HCC, while existing reports point 3-5% annual incidence of HCC in patients with cirrhosis.<sup>23</sup> Other known complications of liver cirrhosis like hepatic hydrothorax, renal impairment, and hepatopulmonary syndrome were also seen in our patients. The death rate in our cirrhotic patients during studied one year was 15.7%. Similarly, Brown and his colleagues<sup>16</sup> found 13.5% mortality in 2016, while in 2011, Alsultan<sup>17</sup> reported in-hospital mortality of 35% among cirrhotic patients. Hence, without definitive treatment of liver cirrhosis with liver transplantation, these all above complications will occur and lead to a very high mortality among liver cirrhosis patients.

**CONCLUSION**

This study concluded that upper GI bleed is the

commonest complication with which liver cirrhosis patients are hospitalized in our population, followed by hepatic encephalopathy, spontaneous bacterial peritonitis, infections other than SBP, tense ascites, refractory ascites, hepatocellular carcinoma, hepatic hydrothorax, renal impairment, and hepatopulmonary syndrome. The outcome of the hospitalization in liver cirrhosis patients is very poor. There is an acute necessity for alternative approaches to achieve the care of these end stage liver disease patients.

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## CLINICAL OUTCOME WITH ABVD CHEMOTHERAPY IN PATIENTS OF HODGKIN LYMPHOMA

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### ABSTRACT

**Background:** Hodgkin lymphoma is most common tumor in the world and predominant histologic subtypes also differs by geographic location and economic advancement, whereas in Pakistan like other economically disadvantaged areas, mixed cellularity HL (MCHL) is predominately present. There are also different treatment options are used for HL, chemotherapy, radiotherapy or both combined and hematopoietics stem cell transplantation depending upon stage of tumor. However different successful outcomes were observed in developed countries but little bit in developing countries.

**Objective:** To assess the response of ABVD chemotherapy regimen in Hodgkin lymphoma patients of any subtype.

**Methodology:** Patients of Hodgkin lymphoma were registered from the Department of Oncology, Mayo Hospital Lahore, Pakistan, from January 2015 to July 2017, using non probability purposive sampling. One hundred out of 107 patients of either sex having Hodgkin lymphoma were given ABVD chemotherapy to assess the response after minimum of four up to maximum of eight cycles of ABVD chemotherapy depending upon their stage, prognostic factors and interim response evaluation. Data were entered and analyzed in SPSS-22 version.

**Results:** Out of 107 patients only 100 (93.45%) patients completed the planned therapy and rest of the 7(6.5%) patients either lost to follow up. The mean age of the patients was  $34.46 \pm 16.60$  years with 32% patients were twenty years or below and 61% presented in advanced stage while 39.0% were in early stage disease. Poor prognostic factors including bulky disease, B symptoms and extra nodal disease was present in 19%, 55% and 37% patients respectively. On completion of planned therapy overall 77 % ( $p= 0.01$ ) patients achieved complete remission (CR). More than 90% patients of age 20 years or less achieved CR compared to 70% who were above 20 years. CR rates were 100%, 94% and 61% ( $p= 0.01$ ) in early stage (favorable risk), early stage (unfavorable risk) and in advanced stage disease groups respectively. Almost 85% ( $p<0.001$ ) patients with mixed cellularity subtype were disease free after completion of planned therapy. High international prognostic score was also associated with poor response to therapy as best response rates were dropped from 100% with IPS of two or less, to only 33% ( $p<0.001$ ) if it was five or more.

**Conclusion:** It is concluded from this analysis that ABVD chemotherapy has excellent response in Hodgkin lymphoma patients with early stage especially of favorable risk group, in patients younger than twenty years age, with less number of poor prognostic factors and in mixed cellularity subtype.

**Keywords:** Hodgkin lymphoma, Classic Hodgkin lymphoma, Mixed Cellularity Hodgkin lymphoma, ABVD chemotherapy.

Hodgkin lymphoma (HL) is a tumor involving lymph nodes (LN) and lymphatic system. HL is the most common tumor in adults and first described by the pathologist and reformer of British, Thomas Hodgkin<sup>1</sup>. The WHO classification divides HL into 2 main types: Lymphocytes-Predominant Hodgkin Lymphoma (LPHL) and Classical Hodgkin Lymphoma (CHL). CHL is further divided in 4

subtypes: Nodular Sclerosis CHL (NSHL), mixed cellularity CHL (MCHL), Lymphocyte-Depleted CHL (LDHL) and Lymphocyte-Rich CHL (LRHL)<sup>2</sup>. The predominant histologic subtype also differs by geographic location and economic advancement. In developed countries such as in US and Europe, nodular sclerosis HL (NSHL) is the predominant histologic subtype and accounts for most of the peak

in young adults<sup>1,3</sup>. In economically disadvantaged areas, mixed cellularity HL (MCHL) is more frequent in children and older adults. In various studies conducted in Pakistan, mixed cellularity was the commonest histopathological type which is reported in 60.78 percent of patients<sup>4</sup>. The frequency of other subtypes that is Nodular sclerosis in about 34.17% and Lymphocyte Depleted HL (LDHL) the least common<sup>4</sup>.

In all over world different treatment options are used for HL, chemotherapy, radiotherapy or both combined and hematopoietics stem cell transplantation depending upon stage of tumor. Some studies show successful cure rate 80-90% in the patients of HL by using chemotherapy and radiotherapy<sup>5-6</sup>. A number of trials have shown that ABVD is the preferred chemotherapy for most patients with classic Hodgkin lymphoma<sup>7</sup>. In final analysis of GHSG HD 11 trial published in 2010, 1,395 patients were randomized in a two-by-two factorial design to receive either four cycles of ABVD or BEACOPP, the overall complete response (CR) rate was 94.1%, but in the ABVD arms at least 92.8% went into complete remission, 2.0% had partial remission, 2.6% had no change in their disease status, 1.4% experienced progressive disease. Consequently, ABVD remained the standard regimen in early stage disease with unfavorable prognosis since toxicity with BEACOPP protocol was increased as compared to ABVD (73.8% vs. 51.5 grade 3 or 4 toxicity;  $P < .001$ )<sup>8</sup>.

Through this study we are able to assess the response to ABVD among the patients with HL in all age groups and find the outcome of this disease in our population where the prevalent subtype of the disease is mixed cellularity which is different from the developed world where nodular sclerosis is the most common subtype of Hodgkin lymphoma and use this data to improve the treatment outcome in our patients.

## SUBJECTS AND METHODS:

Using non probability purposive sampling

technique, all Patients of Hodgkin lymphoma (HL) were registered from the Department of Oncology, Mayo Hospital Lahore, Pakistan, from January 2015 to July 2017 and included in this study. All participating patients were explained about the study and informed written consent was also taken before start of treatment. Ethical clearance was taken from Institutional Ethical Review Committee, Mayo Hospital Lahore, Pakistan. All demographic information, diagnosis of HL, physical examination, staging and ABVD chemotherapy cycles were recorded on pre-designed performa.

Repeat blood tests were done before each cycle of chemotherapy to ensure safety of the patients. Planned treatment was continued without any dose reduction if WBC count is more than  $2.5 \times 10^3$  /microliter and platelets count is more than  $80 \times 10^3$  /microliter on day-1 of the next intended cycle. In case these threshold values are not exceeded, then it is advised either wait or give growth factors support depending upon the clinical status, till the WBCs count and platelets rise to the desired safe level maximum within period of one week and then give full dose treatment as soon as the criteria is met. Response for the purpose of this study was assessed after completion of four cycles of chemotherapy.

Data were entered and analyzed through SPSS-22 version. Quantitative variable like age is presented as mean and standard deviation. Data was stratified for the histopathological type (Nodular Sclerosis (NS), mixed cellularity (MC), Lymphocyte-Depleted (MC) and Lymphocyte-Rich (LR), age (20 years old or below, 21 years or above) Stage I, II, III, IV, early stage (favorable, unfavorable) and advanced stage., and IPS to address the effect modifiers. Response rates in the form of complete remission (CR), partial remission (PR), stable disease (SD) and progressive disease (PD) was presented in the form of frequency and percentages.

## RESULTS:

Out of 107 patients only 100 (93.45%) patients



completed the planned therapy and rest of the 7(6.5%) patients either lost to follow up or died and could not complete the therapy, therefore they were excluded from the final data analysis.

The mean age of the patients was  $34.46 \pm 16.60$  years and the age range was 12-70 years. In the distribution of patients by sex, there were 58% male and 42% female patients.

These 100 (100%) patients were distributed in stages (I-IV) at the time of presentation and from them only one percent of patients in Stage I, 38.0% were in Stage II, 20.0% were in Stage III and 41.0% were presented in the Stage IV disease. Further classifying the staging into early and advanced stage disease, there were 61.0% patients presented in advanced stage, while 39.0% patients presented in early stage disease. Amongst early stage 23.0% were in favorable group and 16.0% were from unfavorable group at presentation.

Histologically, there were 24.0% patients of Nodular Sclerosis, 72.0% of Mixed Cellularity, 1.0% of Lymphocyte Depleted and 3.0% patients were Lymphocyte Rich subtype.

Bulky disease (X), B symptoms (B) and Extranodal disease (E) are the three parameters which are considered as part of staging process and are must for treatment planning of the patients. In this regard, 19.0% patients were having bulky disease, B symptoms were present in 55.0% patients and as far as Extranodal disease is concerned 37.0% were having Extranodal disease at the time of presentation.

International prognostic Score in advance stage disease (61 patients), there were 3(4.9%) were having international prognostic score (IPS) of one or less than one, 10(16.4%) were having score of two, 16(26.2%) were having three, 17 (27.9%) were having four, and only 15 (24.6%) were having score of 5 or more. Amongst factors in IPS, Albumin less than 4.0 grams/dl and anemia ( Hemoglobin less than 10.5g/dl) were the most common with frequency of 46 (75.4%) and 43 (70.5%) respectively.

High white blood cell count (above 15000/ micro-liter) was found in 20 (20.0%) patients and the least commonly found factor was lymphopenia found in only 8 (13.1%) patients.

Overall response rate after four cycles of chemotherapy out of 100 patients was 83%, with 46 % patients went into complete remission, 37% had partial remission, 10% patients had no change in their disease status and progressive disease was seen in 7% patients ( $p < 0.001$ ). The response of ABVD therapy was better in females, with almost 60% achieving complete remission compared to only 36% in males ( $P=0.004$ ). All 23 (100%) patients in early disease with favorable risk factors showed complete remission and only half of the patients (8 patients) showed complete remission in early stage disease with unfavorable risk factors while rest of the half showed partial remission (Table-1). In advanced disease group, Only 44 patients out of 61 (72.1%) benefitted from the therapy in terms of both complete remission (24.6%) and partial remission (47.5%). Also 16.4% in advanced disease had no response and 11.5% had progressive disease compared to none in the early stage disease ( $p < 0.001$ ). With unfavorable risk factors, Extranodal disease and B symptoms have significant impact on complete remission rates with ABVD chemotherapy, with only 19% and 25.5% patients going into CR if these factors were present compared to almost 62% and 71% respectively, if these factors were absent ( $p < 0.001$ ).

Mixed cellularity, the prevalent disease subtype, showed overall response rate of both complete remission and partial remission of 88.9% (CR 54.2%, PR 34.7%) in total of 72 patients compared to 70.9% (CR 29.2%, PR 41.7%) in nodular sclerosis ( $p < 0.002$ ). Also rates of stable disease and progressive disease were 16.7% and 12.5% patients in Nodular sclerosis as compared to 8.3% and 2.8% patients of mixed cellularity subtype. (Table-2)

Complete remission rates were inversely related to international prognostic score. Two third of patients went in to CR with IPS of one or less

third in with IPS of three and virtually none if the IPS was 5 or more ( $P<0.001$ ). On the contrary, the patients not responding to the therapy and those with progressive disease were increasing parallel with the increasing number of international prognostic score. Amongst these, especially lymphopenia, leukocytosis and low albumin had the highest relative risk, with almost 50% ( $p=0.06$ ), 40% ( $p=0.01$ ) and 38% ( $p=0.007$ ) patients not responding to therapy if any of these factor was present respectively.

compared to only one half with IPS of 2, about one

Younger patients of age 20 years or less had the overall response of 93.7% (CR=78.1% and PR= 15.6%), compared to the patients older than 20 years who had overall response of 78.0% (CR=30.9% and PR= 47.1%). On the other hand 3.1% versus 13.2% patients had stable disease and 3.1% and 8.8% ( $P<0.001$ ) had progressive disease in the favor of younger age group.

#### **DISCUSSION:**

Hodgkin lymphoma is a rare Hodgkin lymphoma (HL) accounts for approximately 10 percent of all lymphomas and approximately 0.6 percent of all cancers diagnosed in the developed world annually<sup>9</sup>. HL has a bimodal age distribution curve. The pattern of age-specific incidence differs by geographic location and appears to parallel the level of industrial development. Pakistan, listed as lower-middle income country by the World Bank, and like other early industrialized or transitional economies intermediate pattern with both a childhood and a second decade peak has been described<sup>7-8</sup>. In our study, although it does not represent the population based registry, we have an initial peak at around 18 years 32.0% patients were between 12 to 20 years, 19% patients came from the age group of 21 to 30 years. Another peak with 17% of patients has been seen in

the patients who are in fifth decade of their life. As reported in international literature, instead of slight male predominance, especially in children and in middle and older adulthood<sup>10</sup>, majority of patients in our study were males accounting for total of 58% in our study. Being male is also one of the prognostic factor when we calculate the risk using international prognostic score system, therefore along with other factors males can be at higher risk of poor response to therapy or relapse after treatment, which is validated in our study as almost 60% women achieved complete remission compared to only 36% men.

Regarding response of the therapy, overall 83 (83%) patients responded to the therapy, which is certainly lower than what is reported in international literature. Out of these, only 46 percent compared to 80% achieved complete response. Compared to the trial done in our neighboring country's Tata Memorial Hospital, complete response was seen in 71 % patients but this was after completion of the six cycles of chemotherapy<sup>11</sup>. It is to be remembered that our study included patients with all subtypes and mostly had advanced disease, and our results only show the interim results for advanced stage patients in which more cycles of chemotherapy are recommended with respect to their stage and other characteristics of the disease, and hopefully if two third of our patients out of those who responded partially (37%) will go into CR, we will have fairly equal response rates in the region. Out of 100 patients, 10 percent patients had no change in their disease status and progressive disease was experienced by seven percent patients. Younger patients had better results with the ABVD regimen as compared to the older adults. When the data stratified to young versus older, patients of age 20 years or less have the overall response of 93.7% with majority going into complete remission (78.1%) compared to the patients older than 20 years, with only 78% overall response and less than one third had complete remission after four cycles of ABVD chemotherapy. The Children's Cancer Group (CCG)

in its trial obtained an overall complete response to in 83% patients in whom the ABVD like regimen was used<sup>12</sup>. Although our response rates are slightly inferior to some international randomized trials, but still encouraging as our sample size is smaller and other poor prognostic factors are in higher frequency than the trials conducted in western world. The excellent response rate in children may translate into better survival as shown by international studies that most children and adolescents with HL have an excellent prognosis with current therapy. The overall five-year survival rate for early stage disease exceeds 90 percent, regardless of the therapeutic regimen chosen.

Classical HL is a heterogeneous group of tumors characterized by the presence of a minority of neoplastic cells (Reed-Sternberg cells and their variants) in an inflammatory background. The morphology of the neoplastic cells and the composition of the inflammatory background differ depending upon the subtype of HL. The predominant histologic subtype also differs by geographic location and economic advancement. In developed countries such as the US, nodular sclerosis HL (NSHL) is the predominant histologic subtype accounting for almost 70% of total Hodgkin Lymphoma Patients. Pakistan following the pattern of economically disadvantaged areas, about 60.78 percent of the patients have mixed cellularity subtype<sup>4, 7, 13-15</sup>. In our study prevalent subtype is mixed cellularity (72.0%), with nodular sclerosis being the 2nd most common (24% patient). The reason for the increased prevalence of mixed cellularity classic Hodgkin lymphoma is not clearly known, but often in the mixed cellularity type, is associated with Epstein-Barr virus (EBV) infection. EBV is found infrequently in nodular sclerosis HL, whereas it is detected in about 40 percent of lymphocyte rich HL, 70 percent of mixed cellularity HL, and close to 100 percent of lymphocyte depleted HL (LDHL). In a study conducted in Aga Khan, EBV-LMP1 staining was demonstrated in 71% of the mixed cellularity and 54.2% of nodular sclerosis

subtypes<sup>16</sup>. This can be another area of work in our population to find the incidence of EBV in our population, which is not only linked to the HL, but it has been associated with variety of other diseases like infectious mononucleosis, Burkett's lymphoma, nasopharyngeal carcinoma and multiple sclerosis<sup>17</sup>.

When compared the disease response in different subtypes of classic Hodgkin's lymphoma, Mixed cellularity showed overall response (both complete remission and partial remission) 88.9% versus 70.9% in nodular sclerosis. In the sub analysis, nodular sclerosis complete remission rates were almost one half of the mixed cellularity subtype type (29.2% versus 54.2%). Most studies in western world have shown better response rates nodular sclerosis with ABVD, but it seems that this regimen works as effectively in mixed cellularity patients bringing the overall response close to the 90 percent. Of note, the rare subtypes, out of three patients with Lymphocyte Rich (LRHL),<sup>2</sup> had partial response and one patient showed progressive disease, while only one patient of lymphocyte depleted HL (LDHL) experienced progressive disease even after completion of planned chemotherapy.

In our study, majority of patients (61%) presented in advance stage disease, compared to 39% in early stage. Amongst early stage disease only about 60% patients were in favorable risk group. The percentage of poor prognostic factors like B symptoms were higher (55.0%) in our study population as compared to the international data in which B symptoms are present in less than 20 percent of patients with stage I/II and up to 50 percent of patients with advanced disease. 19.0% of the patients in our study were having bulky disease and extranodal disease was present in 37.0% of the patients.

Comparing the response amongst various subsets of early disease, All 23 (100%) patients in early disease with favorable risk factors showed complete response which is even better than many international studies (EORTC H8F trial and GHSG

HD<sup>10</sup> Trials with CR rates of 93 % and 92% respectively), ABVD remains the "gold standard" chemotherapy for early disease with unfavorable risk factors. Four to six monthly cycles of ABVD are usually required for patients with bulky disease<sup>219</sup>. But in our study response rates dropped deep down with only half of the patients (8 patients) showed complete remission in this group compared to 82% patients EORTC H8F study, close to 90% in GHSG HD11 and 95% in GHSG follow-up trial, HD<sup>14</sup> trial. The wide variation in the results may be looked upon to find factors which can be improved to bring the response rates close to the international trials. This might be due to improper staging, as we rarely use PET scan in our patients due to lack of resources, or difference in disease and population characteristics.

In advanced disease group, 72.1% benefitted from the therapy in terms of both complete remission (24.6%) and partial remission (47.5%). Moreover 16.4% in advanced disease showed no response and 11.5% had progressive disease. In short, rates of complete remission behave inversely with advancing stages of the disease and addition of poor prognostic factors whereas rates of progressive disease rise parallel with these factors. According to different studies approximately 80 percent of patients with advanced stage HL will attain a complete response after treatment with ABVD but the recommended approach is to give atleast 6 to 8 cycles of chemotherapy. Again our point of analysis in this specific study is not beyond four cycles, therefore the optimistic view would be that most partial responder will attain complete response after recommended treatment bringing our rates approximately around 70% which is not much lower than the rates stated in literature varies widely between 68 to 86%<sup>20-23</sup>.

International prognosis score system, one point is given for each of Serum albumin <4 g/dl, Hemoglobin <10.5 g/dl, Male gender, Age >45 years, Stage IV disease, White blood cell count  $\geq 15,000$ /microliter, and Absolute lymphocyte count



<600/microliter and/or <8 percent of the total white blood cell count, for a total score ranging from zero to seven, representing increasing degrees of risk.

Most of the international studies address the survival and relapse rates with number of prognostic factors, but it is also associated with response rates. In our study, it has been noticed that in our patients of Hodgkin lymphoma, higher percentages of patients present with three, four, and five or more factors (28%, 17%, and 15%) compared to international data in which lower rates (23%, 12%, and 7%) were present, putting large number of our patients population at increased risk of poor response to therapy, recurrence and poor overall survival 24.

### CONCLUSION:

It is concluded from this study that four cycles of ABVD chemotherapy has excellent response in early stage disease patients especially with favorable risk factors, in patients younger than 20 years old, with less number of poor prognostic factors and in mixed cellularity subtype of classic Hodgkin lymphoma. It is recommended that clinical research is needed to find poor risk factors specific for our population and to develop other cost effective, less toxic regimens for our high risk patients particularly who present with advanced disease.

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## EFFICACY OF STEROID INJECTION IN TENNIS ELBOW

Muhammad Zafar Iqbal, Tayyab Mahmood Khan, Sajid Mumtaz Khan

### ABSTRACT

**Background:** Lateral epicondylitis is a common condition for which an effective treatment options remains unknown. Crystalline suspension of injectable steroids has been used to treat joint and soft tissue disorders for many years; they reduce the inflammation by decreasing local infiltration of inflammatory cell and mediators. Purpose of this study was to evaluate the clinical outcomes of corticosteroid injections in tennis elbow in terms of pain relief, improvement in hand grip and elbow movements.

### Subjects and Methods:

**Study Design:** Clinical trial

**Study Duration:** Dec 1st, 2017 to Mar 31st, 2018

**Study Setting:** Department of orthopedic surgery, Unit II, Services hospital Lahore.

**Sample Selection:** All patients having symptoms of tennis elbow for 3 or more than three months were included in this study. Patients having age less than 18 years, patients with inflammatory conditions causing chronic pain were excluded from study.

**Data Collection and Analysis:** 65 randomly selected patients of tennis elbow were admitted through Outpatient department of orthopedic surgery. Data was entered and analyzed in SPSS. Patient outcome was assessed using pain, tenderness and Cozens criteria and physical function was assessed by DASH Score for disability of elbow.

**Results:** A total number 65 patients were studied with 23 males (35.4%) and 42 Females (64.6%). This result shows excellent results in 60 (93.3%) patients; in 03(4.6%) patients it was good, while 2 (3.1%) patients had poor results. Mean Vas score was compared with independent t test for base line  $7.8 + 2.24$  and at 6 weeks  $3.7 + 1.12$ . ( $t = 13.20, p < 0.000$ ) and for DASH score of  $77 + 12.12$  at baseline and  $25 + 8.12$  at 6 weeks. ( $t = 28.79 P < 0.000$ ). (Table no:2).

**Conclusion:** This procedure is associated with high rate of patient satisfaction regarding pain relief, extensors strength and elbow movements with low complication rate. Therefore we suggest this conservative option of management for tennis elbow on short term basis.

**Keywords:** Tennis elbow, steroid injection, lateral epicondylitis, conservative management.

Tennis elbow is one of the most common syndromes of upper extremity encountered in orthopedic practice.<sup>1</sup> It was Rung<sup>2</sup> in 1873 who described lateral humeral epicondylitis in German Medical literature. In 1883 Morris related its association with lawn tennis<sup>3</sup>. The incidence of this condition is 1.3% in general population<sup>4</sup> while in tennis players it is 9.1%. Mostly the patients suffer from this condition at 30 to 60 years of age with equal male and female distribution.

The origin of extensor carpi radialis brevis is the most commonly affected structure while in 50% of the patients there is degeneration of extensor digitorum communis. Although the pathology was initially thought to be inflammatory but now it is thought it is tendinosis with degenerative characteristics as there is angiofibroblastic hyperplasia.<sup>5,6</sup>

More than 40 different treatment modalities have been described to treat tennis elbow with corticosteroid injections being the most commonly

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## EFFICACY OF STEROID INJECTION IN TENNIS ELBOW

used. The treatment of tennis elbow is essentially conservative, with 80% of the patients having symptomatic improvement<sup>7</sup>. In this study we used steroid injections for tennis elbow<sup>8</sup>. Several non-surgical treatment modalities with preliminary research have provided some relief in treatment of tennis elbow like non-steroidal anti-inflammatory drugs<sup>9</sup>, physiotherapy<sup>10</sup>, autologous blood injections<sup>11</sup>, platelet rich plasma<sup>12</sup>, botulinum A toxin injection<sup>13</sup>, shock wave therapy<sup>14</sup>, Topical nitrates<sup>15</sup>, epicondylar elbow straps<sup>16</sup> and Laser treatment<sup>17</sup>. Also numerous surgical techniques have been described as a treatment of tennis elbow including open<sup>18</sup> and arthroscopic release<sup>19</sup>.

Our study shows better results regarding pain relief, extensor strength and elbow movements. The aim of study was to assess the efficacy of treatment of lateral epicondylitis with steroid injections in terms of pain relief, elbow movements and extensors strength

### MATERIAL AND METHODS

This study was conducted at Orthopedics Department of Services Hospital Lahore from Dec 1st, 2017 to Mar 31st, 2018. A total number of 65 patients with diagnosed case of tennis elbow were given local steroid injection on OPD basis. Each Patient was given 40mg of Inj. Triamcinolone mixed with 2% lidocaine injection. The injection was administered in outpatient department after observing all aseptic measures. The needle was introduced just proximal to lateral epicondyle and the contents were injected on the under surface of extensor carpi radialis brevis muscle. Gentle passive stretching exercises of extensor group of muscles were started as soon as the pain permitted.

### Follow Up

All patients were followed at 2nd week and 6th week. Pain intensity was assessed by visual analogue score (VAS Score) with range of 0-10 in which 0 was the best situation and 10 the worst. Physical function was assessed by DASH Score (disability score of shoulder and hand) with 1 being no

disability and 100 severe disability. Outcome was defined as excellent, good or poor at the end of 2nd and 6th week by using the following criteria.

Results	Pain	Tenderness	Cozen's score
Excellent	No	No	-ve
Good	No	Deep	-ve
Poor	+ve/-ve	Superficial	+ve

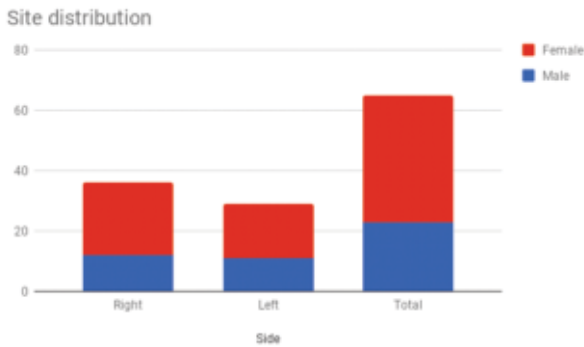
All data was analyzed by using SPSS software.

### RESULTS:

A total number 65 patients were studied with 23 males (35.4%) and 42 Females (64.6%). This condition was found to be more common (53.9%) among 41-55 years of age. Right side was affected (55.4%). This result shows excellent results in 60 (93.3%) patients; in 03(4.6%) patients it was good, while 2 (3.1%) patients had poor results. Mean Vas score was compared with independent t test for base line  $7.8 + 2.24$  and at 6 weeks  $3.7 + 1.12$ . ( $t = 13.20$ ,  $p < 0.000$ ) and for DASH score of  $77 + 12.12$  at baseline and  $25 + 8.12$  at 6 weeks. ( $t = 28.79$   $P < 0.000$ ). (Table no:2). No statistical significance was found between outcome among gender and age. (Table no:3)

**Table 1:** Demographic and clinical profile of patients

Variables n= 65	Frequency	Percent
Age : Mean= SD = Minimum age= Maximum age		
25 – 40 years	30	46.1
41 - 55 years	35	53.9
<b>Gender</b>		
Male	23	35.4
Female	42	64.6
<b>Side involved</b>		
Right	36	55.4
Left	29	44.6
<b>Outcome</b>		
Excellent	60	92.3
Good	3	4.6
Poor	2	3.1

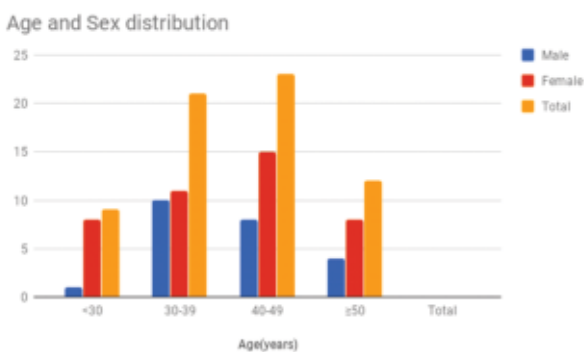


**Table 2:** Comparison of mean VAS and DASH score, baseline, and 6th week

	Baseline Mean ± SD	2 <sup>nd</sup> Week Mean ± SD	6 <sup>th</sup> Week Mean ± SD	t test P value
Vas Score	7.8 ± 2.24	6.2 ± 1.98	3.7 ± 1.12	t = 13.20 P = 0.000
DASH score	77 ± 12.12	55 ± 18.12	25 ± 8.12	t = 28.79 P = 0.000

**Table 3:** Outcome, age and gender Crosstabulation

Outcome n=65	Excellent n =60	Good n =3	Poor n =2	Chi-square P value
<b>Age</b>				<b>chi-sq = 0.552 P = 0.759</b>
< 40 year	27 (45.0%)	2 (66.0%)	1 (50.0%)	
> 40 years	33 (55.0%)	1 (34.0%)	1 (50.0%)	
<b>Gender</b>				<b>chi-sq = 2.383 P = .304</b>
Male	21 (32.3%)	2 (66.0%)	0 (50.0%)	
Female	39 (67.7%)	1 (34.0%)	2 (50.0%)	



**DISCUSSION:**

Tennis elbow is enthesopathy of common extensor origin. This minor self-limiting disease has got too much controversy with respect to pathophysiology and management. Although pathogenesis of tennis elbow has not been established with certainty. Its spectrum ranges from inflammation to necrosis of the tissue. The success of treatment is

likely to correlate with type and extent of disease process. Steroid injections for tennis elbow are very effective on short term basis but long term effects are lacking. Our study shows that corticosteroid injections have good results in terms of pain relief, elbow movements and grip strength<sup>16</sup>. Lot of studies have shown that steroids injection have good results in tennis elbow on short term basis.

Smidt et al reviewed 13 randomized controlled trials. He evaluated the effects of steroid injection with lignocaine compared with placebo injections. His study showed that short term effects of corticosteroid injection for tennis elbow are superior regarding pain relief, grip strength and elbow movements. Although treatment with steroids injections in our study is highly successful but still there remains a lack of information regarding long term efficacy of steroid injection.

A study conducted by Lebedzinski R et al shows that steroid injection for tennis elbow shows significantly better result upto 6 weeks. The mean DASH score was also better in steroid group .In another study conducted by Krogh TP et al also shows that Glucocorticoids was more effective in reducing the pain on short term basis.

In a study by Shiple BJ also favored glucocorticoid injections for tennis elbow. According to his opinion that glucocorticoids significantly reduces pain and disability caused by lateral epicondylitis.

Study of Nevelos AB suggests that triamcinolone acetonide injection is a useful preparation for relief of tennis elbow pain<sup>20</sup>.

Our study is consistent with these studies that corticosteroid are most effective to treat tennis elbow for short term basis and cause early resolution of symptoms.

**CONCLUSION:**

On the basis of results of this study the authors advocated that steroid injection in combination with lidocaine injection (2%) as treatment for patients presenting with tennis elbow demanding a quick



return of daily activities. Considering factors such as cost and time lost from work, a local steroid injection for Pain relief at acute presentation appears to be best method to treat tennis elbow.

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## ASSOCIATION OF BMI AND MUSCLE MASS AMONG DIABETIC PATIENTS IN DIABETIC CENTRE JINNAH HOSPITAL LAHORE

Sahar Majeed, Romessa Khan, Naheed Pirzada, Saira Aleem, Saira Khan, Saba Abid

### ABSTRACT

**Introduction:** Diabetes is defined as a disease in which the body's ability to produce a response to the hormone insulin is impaired resulting in abnormal metabolism of carbohydrates and elevated levels of glucose in the blood. Diabetes leads to decrease in muscle mass called sarcopenia and increase in obesity. BMI disturbance and decrease in muscle mass have a positive correlation. Former Studies reflect that Obesity and Sarcopenia in the elderly diabetics may potentiate each other maximizing their effects on disability, morbidity and mortality.

**Objective:** To determine the association of the muscle mass and BMI of diabetic patients.

**Methodology:** This study was conducted in the diabetes center of Jinnah Hospital Lahore, over a period of 2 weeks. Total of 150 diabetic patients were included in the study, through Non probability purposive sampling, and their demographic and anthropometric data was collected.

**Results:** About 34.7% patients were obese having a BMI greater than 30 kg/m<sup>2</sup>. About 5.33% patients were sarcopenic of which 2.0% were males and 3.33 % were females. BMI and muscle mass showed a positive correlation in diabetic patients.

**Conclusion:** Sarcopenia and obesity are co-existing illnesses that lead to metabolic and functional disabilities. BMI and muscle mass have a positive correlation with each other

**Key words:** Obesity, BMI, Muscle Mass, Sarcopenia.

In the world, due to an increasingly sedentary way of life, metabolic disorders like diabetes are now rampant. Diabetes is defined as a disease in which the body's ability to produce a response to the hormone insulin is impaired resulting in abnormal metabolism of carbohydrates and elevated levels of glucose in the blood<sup>1</sup>. Sarcopenia is a combination of inadequate muscle mass accumulation in young ones and reduced muscle mass in the elderly. Sarcopenia along with obesity has an additive effect on insulin resistance<sup>2</sup>. Body Mass Index is a person's weight in kilograms divided by his or her height in meters squared. Overweight are those that have a BMI of 27.3 or more for women and 27.8 or more for men. Obesity is a BMI of 30 or more for either sex. Increased BMI is deemed to be central to a rising incidence of diabetes in an early age<sup>9</sup>.

According to International Diabetic Federation (IDF) 215.2 million males and 199.5 million females from 20-79 years were diabetics in the year 2015<sup>3</sup>. 60% of diabetics live in Asia. 11.6 % adults have diabetes in China. According to IDF there were 6.9 million cases of diabetes in Pakistan in 2014 and prevalence of diabetes in adults of 20-79 years of age

was 6.8%.

Diabetes is linked with an increased loss of body mass and appendicular lean mass. It also causes generalized fat loss in men<sup>4</sup>. With loss of muscle mass, the loss of function and strength of muscle is also accompanied which has been positively linked to increased probability of falls which for the elderly might mean higher injury and death rates<sup>5</sup>.

Age has a negative association with lean body mass and appendicular skeletal muscle mass has a positive association with arm and calf circumference.<sup>6</sup> Sarcopenia has been linked to insulin resistance, diabetes and obesity with the latter most being a causative factor to the development of insulin resistance and thus diabetes and vice versa, insulin resistance has been thought to cause Sarcopenia<sup>7</sup>.

There is a positive association between muscle mass and body mass index in elderly diabetic patients. There is a prevalence of obesity that is 76.8% in females and 26.8% in males<sup>3</sup>.

Early identification of the signs of Sarcopenia and help in the nutritional and exercise categories might lead to healthier aging and thus lesser money

spent on morbidity due to Sarcopenia in the longer run<sup>8</sup>.

Due to such a high prevalence of diabetes and known associated morbidities with Sarcopenia we intend to investigate the link between the two. For this purpose we prefer anthropometry, as it is an easy and inexpensive method. Anthropometry involves the systematic measurement of physical properties of the human body, primarily dimensional descriptors of body size and shape.

### METHODOLOGY:

The study was conducted in Jinnah Hospital Lahore which is a tertiary care, 5000 bed government hospital located on Allama Shabbir Ahmed Usmani road Faisal town, Lahore.

The study lasted for 4 weeks from 20th April to 20th May 2017. Sample size taken was 150 and sampling technique was Non probability purposive sampling. Inclusion criteria was of 150 compliant patients in Jinnah Hospital Lahore presented during the time period of 20th April to 20th May 2017. Exclusion criteria included non-diabetic and non-compliant patients.

### DATA ANALYSIS:

Data was entered in SPSS 21 and frequency distribution of BMI and muscle mass was calculated. Later on its correlation was found.

### RESULTS:

Demographic and anthropometric data of one hundred and fifty diabetic patients presenting in Diabetic centre of Jinnah hospital Lahore was collected. About 60 (40%) were male and 90(60%) were female. Of all the patients 93(62%) patients had a family history of diabetes. The frequency distribution of duration of diabetes showed that most of the patients (42.8%) 65 were diabetics for less than 5 years. The diabetic patients presenting in JHL had 3 ways of managing their diabetes; 57(38%) took insulin, 62(41.3%) took medication while 19(12.7%) adopted both methods. But some people 12(8%) used lifestyle modification as a tool to control their diabetes. There were some perceptions regarding weight change in patients which included weight gain or loss after the development of diabetes. The data showed that 100 (66.7%) patients believed that they experienced a weight loss after diabetes while 18(12%) relayed to have gained weight after it. Some patients 32 (21.3%) had no

**Table 1:** The frequency distribution and percentage of BMI in diabetic patients.

Categories of BMI	BMI ranges	Frequency	Percentage %
underweight	<18.5	6	4.0
normal	18.5-25	33	22.0
overweight	25.1-30	59	39.3
obese	>30	52	34.7
<b>Total</b>		150	100.0

**Table 2:** The frequency and percentage of muscle mass in diabetics.

Muscle mass	Frequency	Percentage %
normal	11	7.33
abnormal	139	92.66
Total	150	100

**Table 3:** Showing correlation of BMI and Muscle mass in diabetics.

Correlations			
		in kg /meter sq.	muscle mass
in kg /meter sq.	Pearson Correlation	1	.238**
	Sig. (2-tailed)		.003
	N	150	150
muscle mass	Pearson Correlation	.238**	1
	Sig. (2-tailed)	.003	
	N	150	150

\*\* . Correlation is significant at the 0.01 level (2-tailed).

weight change complains. The patients were recorded for their food intake as well which showed that 15(10%) had high food intake, 34(22.7%) had low food intake and 101 (67%) had normal food intake even after the development of diabetes. About 34.7% patients were obese having a BMI greater than 30 kg/m<sup>2</sup>. About 5.33% patients were sarcopenic of which 2.0% were males and 3.33 % were females. BMI and muscle mass showed a positive correlation in diabetic patients as it is 0.003 greater than 0.001.

### DISCUSSION:

We studied the relationship of BMI and muscle mass in diabetic patients within the age ranges of 18-80 visiting JHL. In other researches it was found that an average association exists between obesity and Sarcopenia in diabetics<sup>3</sup>.

We used the following formula<sup>6</sup> to calculate the muscle mass of patients which comprises of age, weight and height;

**Male:** Lean mass = -15.605-(0.032x age) + (0.192x height) + (0.502x weight)

**Female:** Lean mass =  $-13.034 - (0.018 \times \text{age}) + (0.165 \times \text{height}) + (0.409 \times \text{weight})$

We calculated the BMI by using the formula which comprises of weight and height;

$\text{BMI} = \text{weight (in kg)} / \text{height (meters square)}$

In people with diabetes Sarcopenia, the cause of insulin resistance can be increased lipolytic activity of centrally located adipocytes leading to an increase in fatty acids in the portal venous circulation resulting in decreased total hepatic insulin output causing synthesis/formation of Apo lipoprotein B and lipoproteins. So obesity and Sarcopenia can be the cause of hyperinsulinemia<sup>5</sup>.

Present study indicated that 92.6% diabetic patients had abnormal muscle mass and only 7.34% showed normal muscle mass in case of BMI, 22% of patients were in the normal range while 34.7% were obese.

Moreover a previous study on the collective effects of obesity and lower muscle mass in older adults showed that those patients with sarcopenic obesity have twice the risk of functional disability in daily life activities than those without sarcopenic obesity<sup>11</sup>.

Anthropometric measurements have prognostic and therapeutic importance in approximating muscle mass. This can serve as a screening method to become a low cost diagnostic tool for evaluation of Sarcopenia initially in health care centers. After the screening, a confirmatory DEXA-scan helps to support early treatment of Dm<sup>12</sup>.

One drawback in the evaluation of muscle mass by anthropometry could be in cases of protein energy malnutrition. The increase of water content with muscle tissues hides the loss of functional muscle proteins<sup>2</sup>.

Our study provides baseline data of muscle mass of the diabetic patients visiting JHL. The accuracy of our findings is limited due to personal errors in anthropometric measurements. The individual variability may exist in the measurements, so the measurements should be taken more than once.

### CONCLUSION:

- BMI and muscle mass have a significantly linear relationship ( $p < 0.003$ )
- The direction of the relationship is positive i.e. BMI and muscle mass are positively correlated.

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## ANTIMICROBIAL SUSCEPTIBILITY PROFILE OF URINARY ISOLATES FROM A TERTIARY CARE HOSPITAL

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### ABSTRACT

**Introduction:** Urinary tract infections (UTIs) are among the most common human bacterial infections both in the community and as well as hospital settings. The objective of this study was to determine the antimicrobial susceptibility pattern of bacterial pathogens in the patients of urinary tract infection reporting at a tertiary care hospital.

**Materials and Methods:** This cross sectional study was carried out in the Microbiology section, Pathology Department, Allama Iqbal Medical College, Lahore from January 2017 to September 2017. Non-probability consecutive sampling was done. Bacterial concentration of 10<sup>5</sup> CFU/ml was considered as significant attained after inoculating 1 ul of urine on Cysteine Lactose Electrolyte deficient agar. The culture media was then incubated at 37°C for 24 to 48 hours. Identification of the microorganisms was done through Gram staining, biochemical tests and serology. The antimicrobial susceptibility of culture positive bacterial isolates was performed by modified kirby bauer disk diffusion method. Zone sizes were interpreted Clinical Laboratory Standard Institute guidelines (CLSI) 2017.

**Results:** Out of the 206 culture positive urine samples, gram negative bacteria accounted for 178 (86%) of the total isolates while rest of the 28 (14%) were Gram positive bacteria. The most prevalent bacterial isolate was Escherichia coli (E. coli) 92 (44.6%) followed by Klebsiella pneumoniae 36 (17.4%). Pseudomonas aeruginosa (P. aeruginosa) 20 (9.7%) and The susceptibility pattern of E. coli showed that 64% of the bacterial isolates were sensitive to imipenem, 70% to amikacin, 59% to piperacillin/tazobactam and 68 % to nitrofurantoin. In case of P. aeruginosa, 55% bacterial isolates were sensitive to tazobactam/piperacillin, 65% to imipenem. The antibiogram of K. pneumoniae revealed that 60 % of the bacterial isolates were sensitive to imipenem and 54% to piperacillin/tazobactam. Linezolid and vancomycin were the most effective antimicrobials amongst the Enterococcus spp. as 89% showed susceptibility to vancomycin and 100% to linezolid by this bacterial isolate.

**Conclusion:** Majority of the bacterial isolates were sensitive to nitrofurantoin and amikacin while susceptibility to most of the other commonly used oral antibiotics was very low. Among the beta lactam drugs, imipenem showed good susceptibility against Enterobacteriaceae family.

**Key Words:** Antimicrobial susceptibility. Urinary pathogens. Urinary tract infection. Escherichia coli

Urinary tract infections (UTIs) are among the most common human bacterial infections both in the community and as well as hospital settings.<sup>1-3</sup> This disease affects people of all age groups, being more common in women because of anatomy of female genitourinary tract.<sup>4</sup> Community acquired UTIs and Hospital acquired UTIs not differ very

much causative bacterial but in antimicrobial susceptibility pattern.<sup>5</sup> In most of the cases there is a need to start prophylactic therapy before culture and sensitivity results are available. Area-specific monitoring studies aimed at obtaining knowledge about the type of bacteria responsible for UTIs and their resistance patterns may help the clinician to choose

the right empirical treatment. *Escherichia coli* is the leading cause of UTI among hospitalized and Community acquired UTIs with prevalence as high as 71%.<sup>7</sup> Followed by other gram negative rods Like *Klebsiella* species, *Pseudomonas aeruginosa*, *Citrobacter* Species, *Proteus* species. Among gram positive *Enterococcus* species and *Staphylococcus* species are main cause of UTIs. Ampicillin, trimethoprim/ sulfamethoxazole, ciprofloxacin and nitrofurantoin are the most commonly used oral antibacterial drugs in the treatment of UTIs in community settings.<sup>6</sup> Hospital acquired UTIs are a serious threat especially for immunocompromised patients as it can cost a significant financial burden to the hospital management.<sup>4</sup> Members of the family Enterobacteriaceae is a well known cause of urinary tract infections.<sup>8</sup>

The injudicious use of antimicrobials has led to selective pressure on bacterial population with emergence of resistant mutants.<sup>9</sup> Extended Spectrum Beta-Lactamase (ESBL), Metallo Beta-Lactamase (MBL) and Amp-C mediated beta-lactamases are some of the enzymes produced by Enterobacteriaceae and other non-lactose fermenters causing UTIs.<sup>9</sup> In addition to cephalosporins, the uropathogens are also exhibiting increasing resistance to antibiotics like cotrimoxazole, quinolones and nitrofurantoin. The wide array of resistance mechanism has jeopardised the empirical use of quinolones and cephalosporins. The therapeutic options to treat UTIs caused by multidrug resistant bacteria have forced the clinicians to switch to carbapenems, colistin and fosfomycin.<sup>10,11</sup> The aim of this study was to determine the types of bacteria isolated from the urinary tract infections and their susceptibility pattern from patients reporting in tertiary care hospital in order to rationalize the use of antibiotics.

### Materials and Methods

This cross sectional study was carried out in the Microbiology section, Pathology Department, Allama Iqbal Medical College, Lahore. Non-probability consecutive sampling was done. All

culture positive urinary specimens from patients reporting at tertiary care hospital from January 2017 to September 2017 were included in this study. Repeated samples from the same patient as well as culture negative were excluded. Bacterial concentration of 10<sup>5</sup> CFU/ml was considered as significant attained after inoculating 1 ul of urine on Cysteine Lactose Electrolyte deficient agar.<sup>12</sup> The culture media was then incubated at 37°C for 24 to 48 hours.<sup>12</sup> Identification of the microorganisms was done through Gram staining, biochemical tests and serology. Analytical profile index API-20E (Biomerieux, France) was used to identify Enterobacteriaceae family and associated organisms according to manufacturer's directions. Antibacterial susceptibility of the isolates was done using Modified Kirby-Bauer disk diffusion method following CLSI 2017 protocol. Commercially available standard antibiotic discs (Oxoid UK) were used. The zones of inhibition were measured and recorded according to the CLSI guidelines 2017.<sup>13</sup> Amikacin (30 µg), imipenem (10 µg), nitrofurantoin (300 µg), gentamicin (30 µg), ceftriaxone (30 µg), ceftazidime (30 µg), amoxicillin/clavulanic acid (20/10 µg), ciprofloxacin (5 µg), trimethoprim/ sulfamethoxazole (1.25/23.75 µg), ampicillin (25 µg), vancomycin (30 µg), linezolid (30 µg), teicoplanin (30 µg), piperacillin/tazobactam (100/10 µg) were used. *S. aureus* (ATCC 25923), *E. coli* (ATCC 25922) and *P. aeruginosa* (ATCC 27853) were used as control strains.

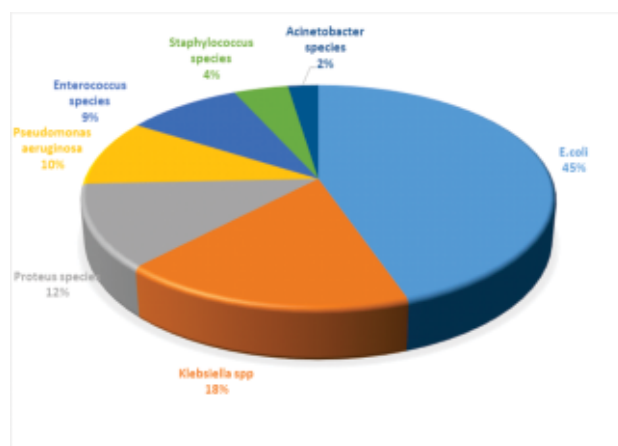
### RESULTS

Out of a total 1440 urine specimens, 206 (14%) yielded bacterial growth. The isolate yielding bacterial growth 126 (61.1%) urine cultures were from female patients and rest 80 (38.8%) male patients. The age of the patients presenting with UTIs ranged from 1 to 67 years with large numbers around 45 years of age. Gram negative bacteria constituted the major bulk with a total of 178 (86%) isolates. *E. coli* 92 (44.6%), *P. aeruginosa* 20 (9.7%) and *Klebsiella pneumoniae* 36 (17.47%) accounted

**Table 1:** Antimicrobial Resistance pattern of Gram Negative Rods

Antibiotics	<i>E. coli</i> n=92	<i>Klebsiella</i> spp n= 36	<i>Proteus</i> spp n=25	<i>Pseudomonas</i> <i>aeruginosa</i> n=20	<i>Acinetobacter</i> spp n=5
Ampicillin	97%	100%	100%	-	100%
Co trimoxazole	92%	92%	97%	-	80%
Gentamicin	38%	42%	44%	50%	40%
Amikacin	30%	28%	32%	25%	40%
Ciprofloxacin	68%	72%	52%	60%	60%
Co-amoxyclav	78%	69%	64%	-	-
Nitrofurantoin	32%	28%	25%	20%	20%
Ceftriaxone	71%	75%	60%	-	60%
Ceftazidime	71%	75%	60%	60%	60%
Piperacillin/ Tazobactam	41%	46%	40%	45%	60%
Imipenem	36%	40%	32%	35%	40%

for the major bulk i.e. 86% of the total culture positive Gram negative isolates while Gram positive bacteria accounted for only 28 (14%) of total isolates as shown in Figure 1.

**Figure 1.** Spectrum of Pathogens isolated (n=206)**Table 2:** Antimicrobial Resistance pattern of Gram Positive Cocci

Antibiotics	<i>Enterococcus</i> spp n=19	<i>Staphylococcus</i> spp n= 9
Penicillin	90%	100%
Co trimoxazole	-	77%
Gentamicin	-	33%
Amikacin	-	33%
Ciprofloxacin	42%	44%
Co-amoxyclav	32%	33%
Nitrofurantoin	26%	44%
Cefoxitin	11%	33%
Vancomycin	11%	0%
Linezolid	0%	0%

## DISCUSSION

Bacterial infections of the urinary tract are one of the most frequent cause for seeking medical attention in community.<sup>14</sup> Effective management of patients suffering from bacterial UTIs commonly relies on the identification of the bacterial isolate and the selection of an effective antibacterial agent used for the treatment of bacterial organisms is in question.<sup>15</sup> Antimicrobial resistance is a serious public health threat now a days. Treatment failure is result of resistance developed by different bacterial pathogens against commonly used antimicrobials. In this study, the bulk of the urinary isolates were from female patients (61%) as UTIs are frequent in females due to anatomy of urethra. Mean age of the patients was around 44 years. The most common urinary tract bacteria was found to be *E. coli*, a frequent causative agent of UTIs. A similar study conducted at Department of Microbiology, Armed Forces Institute of Pathology, Rawalpindi in 2010 and at Mayo Hospital, Lahore in 2013 revealed *E. coli* as the most common bacteria accounting for 63% and 80% of the total culture positive isolates.<sup>16,17</sup> A similar study conducted in Peshawar, Khyber Pakhtunkhwa Pakistan has revealed similar results showing *E. coli* (77%) as the predominant uropathogen.<sup>18</sup> However, the frequency of *E. coli* as the causative agent of UTIs was found to be 80 - 90 % in two similar studies carried out in Canada and Ethiopia in the recent years. It was almost the double as compared to 45% of *E. coli* in our study.<sup>19,20</sup> In this study, 64% of *E. coli* isolates were susceptible to imipenem, the result being comparable with similar study carried out at AFIP and a similar study conducted in Peshawar in 2013.<sup>16,18</sup> These results are also comparable to earlier studies carried out in India where 96% of *E. coli* isolates were susceptible to

imipenem.<sup>11</sup> The results of this study are contrary to a similar study conducted in Lahore, Pakistan, where *E. coli* showed 44% resistance to carbapenems.<sup>17</sup> This proves the injudicious use of antimicrobials limiting the use of oral antibiotics for UTIs. As far as the antimicrobial sensitivity of quinolones to *E. coli* is concerned, the susceptibility to ciprofloxacin was 32% comparable to a study conducted in Pakistan and India.<sup>11,17,18</sup> However, the situation is quite different with *E. coli* isolated in a study carried out in London where 94% of bacterial isolates were susceptible to ciprofloxacin.<sup>10</sup> These contrasting results clearly suggest the injudicious use of quinolones in this part of the world has led to deteriorating susceptibility to this important antimicrobial group. Similarly, another important oral antimicrobial used for empirical treatment of uncomplicated UTIs in our setup is trimethoprim/sulfamethoxazole. The susceptibility of *E. coli* to cotrimoxazole was found to be only 8% in this study and 46% in another local study, which is quite low as compared to similar studies conducted in Tunisia and other parts of the world.<sup>8,18</sup> In this study, the susceptibility of *E. coli* to nitrofurantoin was 68% compared to 94% in a study done in London.<sup>10</sup> Nitrofurantoin is effective against many Gram positive and Gram negative urinary isolates and activity of this antimicrobial is greatly enhanced at pH 5.5 and below. It is a cheap antimicrobial and can be given orally for months for the suppression of chronic UTIs. In our study 74% of Enterococcal isolates were sensitive to nitrofurantoin. It shows that nitrofurantoin is still effective against majority of the urinary isolates and can be used prophylactically for recurrent urinary tract infections. The second most common urinary isolate in this study was *Klebsiella* spp which is consistent to other contemporary studies where the second commonest reported isolates was also *K. pneumoniae*.<sup>17,18,21</sup> In this study, *Klebsiella* spp. isolates showed better susceptibility against Imipenem after nitrofurantoin and amikacin. The antimicrobial susceptibility of Enterobacteriaceae other than *E. coli* has revealed that imipenem was among the most effective antibiotics with amikacin and nitrofurantoin, similar to other local studies.<sup>18</sup> In vitro activity of oral antimicrobials such as trimethoprim/ sulphamethoxazole and ciprofloxacin was quite low comparable to other studies performed in Pakistan, which is a worrying trend as far as the oral antibiotics are concerned.<sup>18</sup> The results of this study were almost similar to a study carried out at AFIP, rawalpindi in 2010.<sup>16</sup> *Pseudomonas aeruginosa* was responsible for 10% of the cases of this study. Carbapenems,

amikacin, ceftazidime and antipseudomonal penicillin such as piperacillin are the recommended antibiotics to treat UTIs caused by *P. aeruginosa*. The antimicrobial susceptibility profile of *Pseudomonas aeruginosa* in this study revealed that a good percentage of the isolates were sensitive to antipseudomonal penicillins followed by imipenem and amikacin. These results are slightly different from an earlier study carried out at AFIP, rawalpindi in 2010, when 86% of the isolates were sensitive to ceftazidime and imipenem followed by antipseudomonal penicillins (76%).<sup>16</sup> This is a worrying trend with an indication that *P. aeruginosa* is gradually developing resistance against carbapenems and antipseudomonal third generation cephalosporins. The antimicrobial susceptibility of *Acinetobacter* spp. causing UTIs in the studied population revealed high degree of resistance to most of the routinely used antibiotics necessitating its susceptibility testing for newer drugs. All the uropathogens showed high degree of resistance to trimethoprim/sulphamethoxazole. This is possibly due to the opportunistic nature of the organism and its versatility in causing nosocomial infections in hospitalized patients especially those fitted with catheters. The antibiogram of enterococcal isolates showed that 89% isolates were susceptible to vancomycin, teicoplanin and all isolates were susceptible to linezolid. The antimicrobial susceptibility of the enterococcal isolates against amoxicillin/clavulanic acid and ciprofloxacin was quite low. Resistance to antimicrobials has been noted ever since the first use of these agents and is increasing with each passing day.<sup>22</sup> The fact that 78% of *E. coli* and 69% of *K. pneumoniae* isolates were resistant to amoxicillin/clavulanic acid and ampicillin is of immense importance which implies that these antibiotics can no longer be considered for empirical therapy in urinary tract infection. Empirical treatment for nosocomial UTIs with multi-drug resistant isolates remains challenging with many authorities recommending parenteral Carbapenem especially where ESBL producing isolates are involved.<sup>23</sup> The increasing rates of resistance to uropathogenic isolates warrants evaluation of other antimicrobials such as fosfomicin which can safely be given orally and is highly effective against many uropathogens.<sup>24</sup> The results of this study will benefit clinicians to know the local pattern of antimicrobial susceptibilities and formulate the empirical antibiotic strategies in patients presenting with UTIs.



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## NEED AND JUSTIFICATION OF HISTOPATHOLOGICAL ANALYSIS OF ELECTIVE CHOLECYSTECTOMY IESSED SPECIMEN FOR CHOLELITHIASIS

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### ABSTRACT

Gallbladder is a small pear shape organ on right side of abdomen below the right lower ribs, just below the liver and chronic cholelithiasis is found in patients with gallbladder cancer, prevalence of which is higher in adults. Cholecystectomy is first line of surgical remedy to manage and treat the patients. Gallbladder cancer is most common malignant tumor of biliary tract worldwide with shortest median survival. The aim of study was to enhance the awareness of disease of worst prognosis; otherwise potentially curable by high lighting the fact that histopathology of gall bladder is not restricted to only those which have morphological abnormalities.

**Objective:** The incidence of gallbladder cancer in routine histopathology analysis of electively cholecystectomised specimens, not show any preoperatively morphological abnormalities.

### Material and methodology

**Study Design:** A cross sectional study on 285 patients including both male and female between age of 20-65 years. Place and Duration of Study: the study was carried out at Ch. Mohammad Akram Teaching And Research Center, Rainwind Road and Social Security Hospital, MangaMondi, Lahore. For the period of sept-2016 – Dec.-2018 Methodology: 285 patients were presented in surgical department both gender and their names, age, sex and socioeconomic status were noted and their cholecystectomyiesed specimen without any obvious gross abnormal findings were submitted for Histopathological diagnosis.

**Result:** out Off 285 patients 31.57% (90) were male and 68.42 (195) were female and 21 patient having the gallbladder carcinoma and no malignancy in 264 patients. All the detected 21 patients were females.

**Keywords:** Carcinoma, Gallbladder, Gallstones, Cholecystectomy. Macroscopic.

Chronic cholethiasis is found in patients with cancer of gallbladder which is pear shaped organ below the liver on right side of abdomen, prevalence of which is higher in adults up to 70% in white race of developed countries.<sup>(1)</sup> Cholecystectomy is first line of surgical remedy to manage and treat the patients.

The important predisposing risk factors for the gallbladder cancer (GBC) are chronic cholelithiasis, with higher risk than the general population<sup>(2)</sup>. The socioeconomic issue can delay the access to cholecystectomy for the cholelithiasis, which is increasing the rate of gallbladder cancer.<sup>(3,4)</sup> GBC is most malignant tumor of biliary tract worldwide with shortest median survival<sup>(1,5)</sup> with higher incidence in women than in men<sup>(6)</sup>, among female higher parity and gravidity increases the risks<sup>(7)</sup>. Other risks factors as annotated are gallbladder abnormalities,

infection<sup>(8)</sup> exposure to heavy metals, medications like methyl dopa, isoniazid and smoking<sup>(3,4)</sup> but important risk factor is gallstones for development of gallbladder cancer among general population.<sup>(9)</sup> 70- 90% of which have positive history of gallstones<sup>(3,4)</sup>. The surgical resection is the first line management and for chronic cholecystitis with lithiasis. The objective this study was to put the emphasis on the need of histopathology of cholecystectomies specimen of gallbladder looking benign, because histopathology analysis is restricted to those which are associated with abnormality. A study conducted on 220 patients with symptomatic cholelithiasis, 203 reveals chronic inflammatory process in gallbladder and 06 (2.8%) adenocarcinoma with lithiasis<sup>(10)</sup>. Another cross sectional study on 250 patients showed that gallbladder carcinoma on routine Histopathological analysis after elective cholecystectomy was observed in 18 (7.2%) Anal vol. 22-1. Similarly a study of 500 patients with

routine cholecystectomy denotes 460 patients of chronic cholecystitis, 06 showed gangrenous cholecystitis and 01 reported gallbladder cancer i.e. adenocarcinoma<sup>(7)</sup>. From above statistics it is observed the carcinoma is presented up to 12%<sup>(5)</sup> in patients with cholelithiasis. So histopathology examination of all cholecystectomy is therefore mandatory, keeping in view the high prevalence of malignancy up to 12%. It is commonly practiced that the Histopathological analysis of cholecystectomy specimens is restricted to those one which have macroscopic abnormality and discarding those specimens which lacks any gross findings with justification of lowering the patients financial expenses and reducing pathologist's workload which is contradictory to global practice of entire submission of gallbladder specimen for Histopathological reporting for the sole purpose of identification of discrete cancer in early stage. Hence this study will play an ride to understand the emphasis for histopathology analysis in cases with cholelithiasis.

## METHODOLOGY

For this study 285 patients were enrolled from surgical wards of Ch. Mohammad Akram Teaching Hospital and Research Centre Raiwind Road and Businessman Social Security Hospital, Manga Mondhi, Lahore in duration of September 2016 to December-2017. With either gender with age of 20-65 years going for cholecystectomy for gallbladder stones. The patient was evaluated clinically and advised abdominal ultrasound (for existent of stones and features of chronic cholecystitis). Relevant laboratory investigations i.e. complete blood count (CBC) random glucose level, urea and creatinine and PT & APPT. was done as protocol. All cholecystectomy specimens without any obvious gross abnormality were sent for histopathology reporting on routine H & E stained slides from pathology department. The collected data was analyzed by using computer software program of SPSS 20 version. Mean and stander deviation (SD) were used. Chi-square test was applied and p- value of <0.05 as significant.

## RESULT

A total number of 285 patients were enrolled with mean age 40.13 ± 11.35 years, with minimum and maximum ages of 20-65 years. The mean gallbladder stone size 6.91 ± 1.9 mm with minimum and maximum of 06 – 12 mm. Frequency of gender distribution revealed that three were 90 male and 195 female patients. Histopathology of the cholecysec-

tomyiesed specimen showed malignancy in 21 (7.31%) patients and no malignancy in 264 patients. (92.63%). All the detected 21 specimens were in of female gender which reflects highly significant difference between genders. It was observed in the study that stone size was < 08 mm in 175 cases in

**Table 1:** Descriptive statistics

	Minimum	Maximum	Mean	Std Deviation
Age(years)	20	65	40.13	11.35
Stone size(mm)	6.00	12.00	7.65	± 1.66
Duration of disease() months	03	11.00	4.81	±2.55

which 13 harbor the malignancy and no in 162 cases. Similarly 110 cases having stone size > 8mm in which 08 having malignancy while 102 were free of it. Statistically insignificant difference was there for the size of stone and malignancy Numbers of stones were also stratified and frequency distribution of stones showed that single stone was found in 51 patients and two and three were present in 66 and 74 patients respectively and multiple stones were in 94 cases.

## DISCUSSION

Chronic cholecystitis with lithiasis is consider a major contributing factor for carcinogenesis, tissue proliferation, and release of growth factors with cytokines and damage to DNA to develop into porcelain gallbladder<sup>(8,9)</sup> which is associated with gallbladder cancer<sup>(7)</sup>.

Cholelithiasis, biliary stones and chronic inflammatory diseases i.e. primary sclerosing cholangitis (PSC) are reported to be associated with higher incidence of GBC.<sup>(7)</sup> Cholecystitis with microlethiasis is likely to be asymptomatic as compared with macrolethiasis.<sup>(11)</sup> Therefore the practice of cholecystectomy for all symptomatic cholecystitis may not be treating the patients who are at high risk of having malignancy<sup>(12)</sup>. Unsuspected gallbladder cancer is mostly diagnosed incidentally after routine cholecystectomy. Lack of preoperative suspicion and absence of serological markers on history of patients and clinically examination of are likely contributing for advance stage of cancer. It is evident in some others studies that percentage of gallbladder cancer is in accordance with this study<sup>(12-14)</sup>. Samad A et-all reported 1.1% ± 0.5 occurrence of tumor in those who underwent cholecystectomy because of

**Table 2:** Gender distribution

		Carcinoma		Total
		Yes	No	
Gender	Female*	21	174	195
	Male	0	90	90
Total		21	264	285

Chi-square value = 7.313

\*p-value = 0.005(significant) as compared to males

**Table 3:** Distribution of Carcinoma according to stone size

		Carcinoma		Total
		Yes	No	
Stone size(mm)	<8	13	162	175
	>8	08	102	110
Total		21	264	285

Chi-square value = 0.00004

p-value = 0.96 (insignificant)

**Table 4:** Distribution of Carcinoma according to number of stones

		Carcinoma		Total
		Yes	No	
No. of stones	<2	09	108	117
	≥	12	156	168
Total		21	264	285

Chi-square value = 0.02

\*p-value = 0.78 (insignificant)

cholecystitis with lithiasis.<sup>(13)</sup> various international studies<sup>(17-18)</sup> have quoted different incidence of GBC ranging 0.17% to 12.4 %<sup>(10,17,18)</sup>.

In this study, mean age 40.12± 11.92 years, the male were in lower number than female. In a study by Sidique et-all showed male to female ratio 1:7<sup>(6)</sup> and other studies showed female preponderance.<sup>(20-21)</sup> in another study the age of patients was 19-80 years with mean of 32.25±5.3 years. Higher rate of gallbladder cancer has been reported in female<sup>(22)</sup> in the region of Chili, India and Pakistan<sup>(23)</sup>.

## CONCLUSION

The estimate of gallbladder cancer in patients of cholelithiasis without gross / macroscopic abnormalities is significant. So Histopathological examination of cholecystectomyiesed specimens for identification of discrete cancer is highly recommendable for guideline and help to prevent the mortality and morbidity.

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## FREQUENCY OF NEUROPATHY AMONG TREATMENT NAÏVE PATIENTS INFECTED WITH HUMAN IMMUNODEFICIENCY VIRUS

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Human Immunodeficiency virus<sup>1</sup> causes acquired immunodeficiency syndrome,<sup>2,3</sup> in which the immune system of body totally fails to develop any defense against the foreign invaders.<sup>2,3</sup> HIV/AIDS is a global problem and it results nearly 25 million deaths worldwide. Developing countries like Pakistan have issues regarding Public Health. Currently, epidemic of HIV/AIDS is established in Pakistan and there is a threat of an expanded

HIV/AIDS outbreak in the country.<sup>2,4,5</sup> Pakistan had an estimated 98,000 people living with HIV (PLHIV) by the end of 2009, with 5,256 PLHIV registered in 17 Anti retro viral treatment (ART) centers by end of 2011.<sup>6</sup> With the advent of highly active antiretroviral therapy (HAART), HIV-related morbidity and mortality has declined. Survival and life quality has improved significantly in HIV-infected patients with access to HAART but on the

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other hand risk of chronic non infectious diseases is on rise like neuropathy.<sup>4,7-11</sup>

Neuropathies affect quality of life of patients living with HIV. Peripheral neuropathies like distal symmetrical sensory neuropathy is the most common form encountered today and is one of the few that are specific to HIV infection or its treatment.<sup>7,9,11</sup> In the pre-ART era, neuropathies were categorized according to the CD4 count and HIV viral load. In the early stages of HIV infection when CD4 count is high, the inflammatory demyelinating neuropathies predominate. Prevalence of neuropathy continues to rise as patients with HIV infection are living longer. In an observational cohort of 50 patients, sixteen patients (32%) were symptomatic and 34(68%) were neuropathy free. Of them 13 (81%) were on ART and three (19%) were not on ART.<sup>8</sup> In an Indian study, mean CD4 count was  $687 \pm 170/\text{mm}^3$  in patients without neuropathy while  $497 \pm 201/\text{mm}^3$  in patients with neuropathy.<sup>12</sup>

HIV and neuropathy are both chronic diseases that significantly affect quality of life of patients. When they intersect, the treatment regimens required for both diseases can be overwhelming for patients. The present study was planned to determine the local prevalence of neuropathy in HIV patients which will ascertain a benchmark for health professionals and help devise certain guidelines to cater it.

## MATERIAL AND METHODS:

### STUDY DESIGN:

It was across sectional survey done at the HIV Clinic, Jinnah Hospital, Lahor. The study was conducted over a period of 6 months. Consecutive non-probability sampling was done and a total sample size of 237 was taken.

### INCLUSION CRITERIA:

- Patients with age ranging from 20 to 60 years
- Male, female
- Cases of HIV determined by HIV RNA

detected by PCR within last 6 months

- Never taken highly active antiretroviral therapy (HAART) determined by history

### EXCLUSION CRITERIA:

- Patients with diabetes ,chronic liver disease, chronic kidney disease, on medication for psychiatric illnesses e.g. antidepressants, anxiolytics, patients with history of suicidal attempt and those having severe anemia were excluded.

### SAMPLE SELECTION.

Patients between 20 to 37 years of age, 154 males and 83 females having +ive PCR for HIV RNA(in last 6 months), Never taken highly active antiretroviral therapy (HAART), were included in the study where as Patients with diabetes, chronic disease liver(determined by ultrasound showing coarse echo texture of liver involving >50% of total size), chronic kidney disease( determined by creatinine > 2mg/dl), on medication for psychiatric illnesses e.g. antidepressants, anxiolytics, history of suicidal attempt and Patients with severe anemia determined by hemoglobin < 8mg/dl were excluded from the study.

Informed consent was taken from all participants after explaining the purpose of study. Clinical examination for diminished vibration sense in great toes, decreased or inability to discriminate between sharp and dull sensation in the feet and absent or weakened bilateral ankle reflexes. Neuropathy was labelled if one of three signs found bilaterally and symmetrically. All other variables of interest like CD4 count and HIV viral load were recorded in patients with and without neuropathy. Unique identifier instead of name of patient was recorded as per policy of Punjab AIDS control program.

## RESULTS

In our study population of 237 treatment naïve patients, having mean  $26.41 \pm 5.674$  ranged from 18 to 37 years, 122 patients (51.5%) were less than 25 years of age while remaining 115 patients (48.5%) were either 25 years or above. 154 patients (65%) were male and 83 (35%) were female.

Out of 237 patients 157 patients (66.2%) had

viral load < 1000 copies whereas 80 patients (33.8%) had > 1000 copies. Among all patients CD4 count ranged from 725 to 1425, mean  $1085.6 \pm 221.3$ .

116 patients (48.9%) turned out to be neuropathic. (Table I) Out of these 116 patients 61 were < 25 years of age and 55 were > 25 years old, there was no significant relation between age and neuropathy ( $p=0.738$ ), whereas out of 116 neuropathic patients 83 were male and 33 were female, the difference turned out to be statistically significant ( $p=0.038$ ). Our study also showed that among the 116 neuropathic patients 81 were diagnosed as HIV +ve for > one year, again a statistically significant relation was found between the duration since diagnosis of HIV and development of neuropathy ( $p=0.001$ ).

While comparing viral load with neuropathy only 80 out of 157 patients having viral load < 1000 copies and 36 out of 80 having viral load > 1000 copies had neuropathy ( $p=0.386$ ). The 116 patients with neuropathy had mean CD4 count =  $1094.61 \pm 20.524$ , while those without neuropathy had mean CD4 count =  $1077.02 \pm 20.643$  ( $p=0.542$ ).

When we cross tabulated CD4 count with gender, 154 male patients had mean CD4 count  $1099.2 \pm 217.4$  and 83 female patients had mean CD4 count  $1060.3 \pm 227.4$ , results were non-significant ( $p=0.196$ ). Among the 116 patients having neuropathy 35 patients, diagnosed as HIV+ for < 1 year, had mean CD4 count =  $1089 \pm 196.54$  while 81 patients, diagnosed as HIV+ for > 1 year, had mean CD4 count =  $1097 \pm 231.95$  ( $p=0.688$ ). On comparing the mean CD4 count of patients having neuropathy with the viral load we found that out of 116 patients 80 patients having viral load < 1000 copies had mean CD4 count =  $1105.06 \pm 223.96$  while 36 patients having viral load > 1000 copies had mean CD4 count =  $1071.39 \pm 215.70$  ( $p=0.633$ ) again the result was non significant.

## DISCUSSION

Human immunodeficiency virus has appeared as epidemic in Pakistan, infected patients are prone to develop the non-communicable diseases like neuropathy, thyroid dysfunction and diabetes mellitus etc. In our population HIV epidemic is expanding among injection drug users (IDUs), female sex workers and transgender sex workers<sup>2,3</sup> There is a significant difference among developed and developing countries regarding momentum of communicable and non-communicable diseases..

Neuropathy was present in 116 patients (48.9%) among sampled population. Presence of neuropathy in about half of the population is an alarming situation which needs urgent attention because it may aggravate the prior morbidity and may lead to

poor quality of life. Our results agree with study results of Reminder Pal et al that showed the prevalence of neuropathy in treatment naïve HIV positive patients to be 43%<sup>13</sup>. Similarly in other studies done by Duby Tribuvan et al<sup>12</sup> and Daenna staylor et al<sup>14</sup> the prevalence of peripheral neuropathy in treatment naïve HIV positive patients was 40% and 19% respectively. In our study Neuropathy was more common among males (83%) as compared to females (33%) ( $p=0.038$ ) whereas statistics are exactly opposite, the difference may be due to the

**Table 1:** Frequency Distribution of sampled population by Neuropathy in HIV+ patients

Neuropathy		Frequency	Percent
Valid	No	121	51.1
	Yes	116	48.9
	Total	237	100

**Table 2:** Cross tabulation between Time since Diagnosis > 1 Year & Neuropathy

		Neuropathy		Total
		No	Yes	
Time since Diagnosis > 1 Year	No	96	35	131
	Yes	25	81	106
Total		121	116	237

Using Pearson chi square test = 0.001 (significant)

**Table 3:** Cross tabulation between Viral Load & Neuropathy

		Neuropathy		Total
		No	Yes	
Viral Load	Less than 1000 copies	77	80	157
	More than 1000 copies	44	36	80
Total		121	116	237

Using Pearson chi square test = 0.386 (non -significant)

**Table 4:** Cross tabulation between CD4 Count & Neuropathy

	Neuropathy	N	Mean	Std.	Std. Error
				Deviation	Mean
CD4 Count	Yes	116	1094.61	221.050	20.524
	No	121	1077.02	222.201	20.200

Using Pearson chi square test = 0.542 (non -significant)

fact that majority of female patients remain undiagnosed in our population due to difference in treatment seeking behavior. At times cultural peculiarities skew the data recorded in manners quite unrelated to the disease or pathology thereof. This has been noted by Deanna Saylor et al in the case of

differences between HIV behavior in developed countries and sub Saharan Africa<sup>14</sup>. They have noted the incidence of peripheral neuropathy in general is quite high among the Ugandan population. They have cited figures of large variation among South African (4%) and Rawanda59%). They find the way anti-retroviral therapy is initiated among the African is different from those in the west. This may be easily noted in population groups with strong cultural or religious back grounds. A woman in a Muslim society like ours does not commonly move independently across gender divide of the society. This maybe an explanation for relatively lower incidence of HIV infection in the Muslim societies and still lower among the women folk. The same can be offered as an argument that since Muslim teachings strictly discourage intra gender sexual relationships the likelihood of one getting STDs is less likely unlike the western societies who have removed all barriers to such contacts among people.

While determining the effect of viral load and CD4 count on neuropathy in HIV treatment naïve patients, the results were statistically non-significant (p value =0.38 & p=.542 respectively, same as the results of an Indian study done by duby et al. Duration of infection was found to be significantly related to the development of neuropathy. In the light of this small scale study drawing conclusive inferences is not wise until large scale more scientifically planned studies are carried out to test the true incidence of neuropathy among those who are HIV positive. The group is growing steadily even in our country hence the need for such studies cannot be but reiterated.

### CONCLUSION:

It is concluded that the frequency of neuropathy is high in treatment naïve patients infected with human immunodeficiency virus i.e. 48%.Time elapsed since diagnosis has parallel relationship with neuropathy, so these patients should be routinely evaluated for neuropathy for early diagnosis to improve morbidity.

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## ROLE OF ALKALINE PHOSPHATE IN DIAGNOSIS OF TUBERCULOUS PLEURAL EFFUSION

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### ABSTRACT

**Background:** Pleural cavity is a space between parietal and visceral pleura that surrounds the lungs. Excessive accumulation of fluid in pleural cavity is called as pleural effusion. Alkaline phosphatase is an enzyme found in pleural effusion, used to differentiate tuberculous from non tuberculous effusions.

**Objective:** To evaluate the diagnostic accuracy of alkaline phosphatase (ALP) in distinguishing tuberculous pleural effusion and taking pleural biopsy as gold standard .

**Material and methods:** This cross sectional study was conducted at Department of Chest Medicine, Mayo Hospital, Lahore. The Non probability, consecutive sampling technique was used. Informed consent was obtained. Demographic details were obtained. Then USG guided 20cc pleural fluid aspirated under aseptic condition and 5cc blood sample was collected by using 5cc syringes. Pleural fluid samples were sent to Pathology Deptt of the Mayo Hospital for ALP. Then reports were analysed for ALP level and patients positive for TB and negative for TB were grouped. Then pleural tissue was obtained by Abrahams' pleural biopsy needle on all patients for culture. Culture was labeled as positive or negative for tuberculosis. Data was entered and analyzed on SPSS version 20. Sensitivity, Specificity, PPV, NPV were calculated and diagnostic accuracy of ALP was determined by taking pleural biopsy as gold standard.

**Results:** The mean age of patients was  $34.82 \pm 11.82$  years; male to female ratio was 2.1:1. By using ALP, TBE was diagnosed positive in 139 (66.2%) patients and negative in 71(33.8%) patients. The sensitivity of ALP was 97.67% with specificity of 83.95% and the diagnostic accuracy of ALP of TBE was 92.38%.

**Conclusion:** ALP is useful and reliable diagnostic tool with high accuracy in distinguishing tuberculosis pleural effusion taking pleural biopsy as gold standard in patients having pleural effusion.

**Keywords:** Tuberculosis ,Pleural Effusion, Diagnostic Accuracy, Alkaline Phosphate, Pleural Biopsy

Tuberculosis prevalence is continuously increasing all over the world. Pakistan ranks 8th for high incidence of tuberculosis worldwide.<sup>1</sup> Yearly near about 0.3 million new cases arise, the prevalence of tuberculosis is 297 per 100,000 populations in Pakistan.<sup>1</sup> The tuberculosis program of Pakistan is failed to meet the WHO's 2005 target of 70% cases detection and 80% cure. Deficiency of knowledge about the disease sign and symptoms causes under use of services, delay in establishing diagnosis and poor treatment compliance.<sup>2</sup>

Tuberculosis occurs disproportionately which involve malnourished homeless people and those people who are living in congested and substandard houses, through inhalation of airborne droplets that contain viable organisms and mycobacterium

tuberculosis infection starts.<sup>3</sup> Occurrence of exudative tuberculous effusion was 53.6%.<sup>4</sup>

Pleural effusion is a common complication of tuberculosis patch. Pleural effusion can be used for diagnosis of different related diseases through analysis of fluid which is obtained from pleural space. Sometime fluid analysis alone is sufficient to meet the demand for making diagnosis.<sup>5</sup> Tuberculous and non tuberculous pleural effusion can be differentiated through various parameters. Alkaline phosphate is being used in previous studies to differentiate exudative from transudative pleural effusion.<sup>6</sup> A very useful parameter for differentiating TB from non TB pleural effusion can be alkaline phosphatase activity which is very simple and non-invasive. In one study to diagnose tuberculous

pleural effusion, the sensitivity and specificity of alkaline phosphatase were 90 and 80% for pleural fluid.<sup>6</sup> Sensitivity of alkaline phosphatase estimation for the diagnosis of exudative pleural effusion is 100% and specificity is 85.7% in one other study.<sup>7</sup> One of the study by Isabel Gazquez et al. Reported that the sensitivity and specificity of pleural alkaline phosphatase for exudative were calculated as 97% and 75% respectively.<sup>8</sup>

Rationale of this study is to find the diagnostic accuracy of alkaline phosphatase (ALP) in distinguishing TB and non TB exudative pleural effusion by taking pleural biopsy and culture as gold standard. So we want to conduct this study to confirm whether ALP is useful to differentiate between TB and non TB pleural effusion in local population as there was no local study available which can help us in implementing its use.

### **Tuberculous pleural effusion**

If Pleural fluid ALP >71IU/L, then tuberculous exudative was labeled. If Pleural fluid ALP ≤71IU/L, then pleural effusion was not labeled as tuberculous. On pleural culture, presence of Mycobacterium tuberculosis (more than 1/high power field) was confirmed as tuberculous pleural effusion.

### **MATERIALS AND METHODS:**

This Cross sectional study was conducted at Department of Chest medicine, Mayo hospital Lahore. The sample size estimated is 210 is calculated by using 95% confidence level, 5% margin of error for sensitivity and 7% margin of error for specificity and taking expected percentage of tuberculosis 53.6%<sup>4</sup> and sensitivity of 90%<sup>6</sup> specificity of 80%<sup>6</sup> of ALP to differentiate tuberculosis. Non probability and consecutive sampling was done. An inclusion criterion was Male and female patients aged 15-55 year and diagnosed as cases of exudative pleural effusion during last 7 days. Exclusion criteria was inaccurate sample or sample not enough to run tests, history of smoking >10 packs per year, COPD, asthma and history of previous thoracocentesis (within previous 4 weeks

on medical record).

210 patient fulfilling inclusion criteria were selected from OPD of Department of Chest, Mayo Hospital, Lahore. Informed consent was obtained. Demographic details (name, age, gender, duration of pleural effusion) were obtained. Then 20cc pleural fluid sample and 5cc blood sample was collected by using 5cc syringes. Pleural fluid samples were sent to Pathology Deptt of the Mayo Hospital for ALP. Reports were then analysed for ALP level and patients were labeled as having tuberculous or not (as per operational definition). Then pleural tissue was obtained by Abrahams' pleural biopsy needle on all patients and sample was sent to the laboratory of the hospital for culture. Culture was labeled as positive or negative for tuberculosis (as per operational definition). All this information was noted on a pre-designed proforma.

Data compilation and analysis was done on SPSS version 20. Mean and standard deviation was calculated for age and ALP. Frequency and percentages were calculated for gender and tuberculosis pleural effusion (on ALP and pleural culture). Sensitivity, Specificity, PPV, NPV were calculated using 2 by 2 table and diagnostic accuracy of ALP was determined by taking pleural biopsy as gold standard. Data was stratified for age, gender and duration of effusion to deal with effect modifiers. Post-stratification chi-square test was done. P-value of equal to or less than 0.05 was considered significant.

### **RESULTS:**

In our study total 210 cases were enrolled in department of Chest Medicine, Mayo Hospital, Lahore. The mean age of the patients was 34.82 ± 11.82 years with minimum and maximum ages of 16 & 57 years respectively.

In our study 68.10% patients were males and 31.90% patients were females. The male to female ratio was 2.1:1.

Results also showed that the mean duration of PE was 5±1.19 months with minimum and maxi-

mum duration of 3 & 7 months.

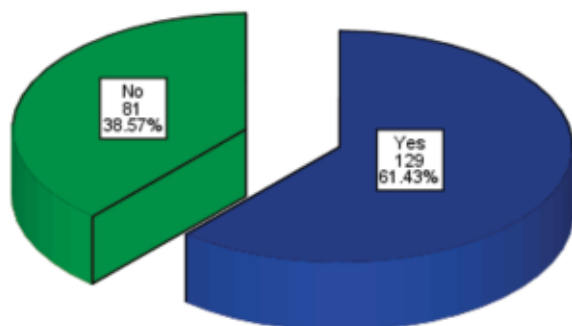
Our results showed that by alkaline phosphate, TBE was diagnosed positive in 139(66.2%) patients and it was diagnosed negative in 71(33.8%) patients. Table#1

In this study by plural biopsy the TBE was diagnosed positive in 61.43% patients and it was diagnosed as negative in 38.57% patients. Fig#1

The study results showed that the sensitivity of alkaline phosphate was 97.67% with specificity of 83.95%, the PPV value was 90.65%, NPV value was 95.77% and the diagnostic accuracy of alkaline phosphate of TBE was 92.38%. Table#2

**Table 1:** Frequency distribution of AP TBE

		Frequency	Percent
Alkaline Phosphatase TBE	Yes	139	66.2
	No	71	33.8
	Total	210	100.0



**Fig 1:** Frequency distribution of biopsy TBE

**Table 2:** Comparison of ALP with biopsy for TBE

		Biopsy TBE		Total
		Yes	No	
Alkaline Phosphate TBE	Yes	126	13	139
	No	3	68	71
Total		129	81	210

Sensitivity	97.67%
Specificity	83.95%
Positive Predictive Value	90.65%
Negative Predictive Value	95.77%
Diagnostic Accuracy	92.38%

## DISCUSSION:

There are multiple causes of exudative pleural effusion, tuberculosis is one of them.<sup>9</sup> To differentiate tuberculous from non-tuberculous pleural effusion multiple biochemical tests were used in the past. Especially protein levels and specific gravity were used to differentiate between exudative and transudative pleural effusion. Now alkaline phosphatase is an advance marker present in pleural effusion.<sup>10,11</sup>

In our study the sensitivity of alkaline phosphate was 97.67% with specificity of 83.95%, the PPV value was 90.65%, NPV value was 95.77% and the diagnostic accuracy of alkaline phosphate of TBE was 92.38%.

According to Jhadhv AA study sensitivity and specificity of alkaline phosphatase is 90% and 80% respectively to diagnose tuberculous pleural effusion. And this study also explains that pleural fluid and serum fluid alkaline phosphatase ratio has 90% sensitivity and 80% specificity.<sup>5</sup>

In one study which was conducted in India by Mushtaq A. Lone et al.<sup>12</sup> in 2002 the estimated of alkaline phosphatase was 100% and specificity was 85.71% for exudative pleural effusion.

EL-Habashy MM showed sensitivity and specificity values were 90% and 80% for pleural alkaline phosphatase activity for the diagnosis of tuberculous pleural effusion<sup>6</sup>.

The study of Salimuddin Aziz et al.<sup>13</sup> which was conducted in Karachi regarding alkaline phosphatase was helpful to differentiate tuberculous from malignant pleural effusion.

Estimation of alkaline phosphatase activity in pleural fluid was demonstrated a useful test in diagnosis of tuberculosis.<sup>14</sup>

The study conducted by Irene Tsiloni et al. showed that both alkaline phosphatase and adenosine deaminase have comparable specificity in distinguishing exudative and transudative pleural effusion but sensitivity of adenosine deaminase was higher than the alkaline phosphatase.<sup>15</sup>

Miguel Perpina and Francisco Carrion has also mentioned the superiority of alkaline phosphatase in pleural effusion as a diagnostic biochemical marker.<sup>16</sup>

So our study showed that alkaline phosphatase is a useful and easy test to differentiate between TB and non-TB pleural effusion. Further mega studies are needed for confirmation of the results.

### CONCLUSION:

ALP is useful and reliable diagnostic tool with high accuracy in distinguishing tuberculosis pleural effusion taking pleural biopsy as gold standard in patients having pleural effusion

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## FREQUENCY AND ANTIMICROBIAL SENSITIVITY PATTERN OF BACTERIA ISOLATED FROM BLOOD STREAM INFECTION (BSI): A SINGLE CENTRE STUDY.

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### ABSTRACT

**Background and Objectives:** The aim of our study was to isolate and identify pathogenic bacteria from blood cultures submitted to Fatima Memorial Hospital Microbiology Laboratory and to evaluate the sensitivity pattern of these bacteria to various antimicrobials.

**Methods:** The study analyzed data of blood cultures processed in FMH microbiology laboratory from 1st January to 31st July 2017. Total of 2092 blood specimens were received from FMH hospital; 152 were positive for bacterial isolates. Antimicrobial sensitivity testing to different appropriate drugs were tested by Kirby-Bauer disc diffusion method and the antimicrobial sensitivity pattern of the bacteria were noted.

**Results:** Total of 2092 blood specimens was received for culture, out of which 152 (7.2%) were positive for bacterial isolates. The paediatric department sent 88% of positive blood cultures and 12% positive blood cultures were from other wards. In positive samples 96 (63.2%) were drawn from males and 56 (36.8%) were drawn from females. The age distribution of the positive specimens were as follows: infants were 105 (69.1%), children were 29 (19.1%), neonates were 13 (8.6%) and adults were 5 (3.3%). Among these positive blood cultures, 47 (31%) were positive for *S. aureus*, out of which 12 (25.5%) were MRSA based on oxacillin disc (1). *S. epidermidis* was positive in 23 (15%) blood cultures, among these 3 (13%) were MRSE and 1 (4.3%) was MSSE. All gram-positive organisms were sensitive to vancomycin. Among Enterobacteriaceae, positive Enterobacter were 28 (18.4%), positive cultures for *Escherichia coli* and *Klebsiella sp.* 13 (8.5%) each, *Salmonella typhi* were positive in 21 (13.8%) Among non-fermenter gram-negative bacteria, *Acinetobacter* 6 (4%) and *Pseudomonas species* 1 (0.6%) were identified. Gram-negative bacteria were sensitive to ciprofloxacin, amikacin, meropenem, tazocin and sulzone. *E. coli* showed resistance to 3rd generation cephalosporins and were sensitive to ciproxin, tazocin and sulzone. *Acinetobacter* were resistant to carbapenems and sensitive to doxycycline while *Pseudomonas* was also sensitive to all the tested antibiotics.

**Conclusions:** Most of the positive blood cultures were from the paediatric department (88%) and 69% positive blood cultures were from infants. *Staphylococcus aureus* is (31%) most common gram-positive organism & showed sensitivity to 3rd generation cephalosporins, augmentin & gentamicin. All gram-positive bacteria were sensitive to vancomycin. Enterobacter (18.4%) most common gram-negative organism, which showed sensitivity to ciprofloxacin, meropenem, tazocin & sulzone.

Blood is usually sterile. Bacteremia is the presence of bacteria in the blood, which could be transient in the course of many diseases and is asymptomatic. Septicemia, on the other hand is invasion of blood with bacteria releasing their toxins and could be a major cause of morbidity and mortality in all age groups especially in infants and children. Nowadays wide variety of antibiotics are

available to treat blood stream infections (BSI), but at the same time a constant change is seen in the type & frequency of microbial isolates and their sensitivity pattern in different settings, thus requiring need for constant review to reduce the mortality & morbidity especially in infants and children by initiating the appropriate antibiotics at an early stage. Isolation of bacteria from blood culture is a

gold standard for diagnosis of blood stream infections (BSI),<sup>(1,3,4)</sup>

The aim of this study was to analyze the data of blood cultures submitted to our FMH microbiology laboratory, to identify, assess frequency of various bacteria and evaluate their sensitivity / resistance patterns in our centre.

### MATERIALS & METHODS:

The present study analyzed data of blood cultures processed in FMH microbiology laboratory from 1st January to 31st July 2017. Total of 2092 blood specimens were received from FMH hospital; 152 were positive for bacterial isolates. Antimicrobial sensitivity testing to appropriate different drugs according to the growth isolated was carried out by Kirby-Bauer disc diffusion method and the antimicrobial sensitivity pattern of the bacteria were noted.

These samples were collected from patients admitted to various wards of the FMH, with full aseptic measures in specified blood culture broth (paediatric/ adult) and transferred to the microbiology laboratory of FMH. The culture tubes were incubated overnight at 35°C. After 24 hours of incubation these samples were sub-cultured on Blood & Mac Conkey's agar plates and again incubated at 35°C overnight. If these plates showed growth of organism, identifications of growth was based on colony morphology, Gram's staining and appropriate biochemical tests (API kits/bench tests) to reach the species level. Antibiotic sensitivity testing to different antibiotics based on the type of growth was performed on Muller Hinton's agar by standard Kirby Bauer method (Monica cheesbrough vol:2). Gram- positive isolates were tested against-cefixime, ceftriaxone, cefaclor, augmentine, gentamicin, ciprofloxacin, penicillin, oxacillin, vancomycin, meropenem. Gram- negative isolates were tested against cefixime, ceftriaxone, cefaclor, ciprofloxacin, amikacin, meropenem, ceftazidime, sulzone, tazocin, imipenem, colistin & doxycycline. If plates didn't showed any growth they were kept at

37°C for a week and subculture was repeated daily. The blood culture broth were discarded after a week. Statistical analysis was done by using SPSS version 17.

### RESULTS

Total of 2092 blood specimens for culture were received, out of which 152 (7.2%) were positive for bacterial isolates. The paediatric department sent 88% of positive blood culture samples in our laboratory and only 12% positive blood cultures were from all other wards. Positive samples drawn from males were 96 (63.2%) and from females were 56 (36.8%) (Table I).

The age distribution of patients with positive specimens was as follows: Infants were 105 (69.1%), children were 29 (19.1%), neonates were 13(8.6%) and adults were 5 (3.3%). Most of the specimens were from paediatric age group and only few from adult age group (Table II). Frequency distribution of Ward of patients with positive blood culture samples at FMH is detailed in Table III.

Most common Gram-positive organism isolated were Staphylococcus aureus (31%), staphylococcus epidermidis (15%), MRSA (25.5%) and methicillin resistant staphylococcus epidermidis (MRSE) was (13%) and MSSE was (4.3%). Gram-negative organisms included: Enterobacter (18.4%), SalmonellaTyphi (13.8%), Escherichia coli (8.5%), Klebsiella species(8.5%), Acinetobacter (4.0%), and Pseudomonas species (0.6%) (Table IV).

Antimicrobial sensitivity to appropriate drugs were tested by Kirby-bauer disc diffusion method. Staphylococcus aureus & epidermidis were sensitive to third generation cephalosporins, augmentine & gentamicin but showed resistance to penicillin & ciprofloxacin. All gram-positive were sensitive to vancomycin . Gram-negative bacilli were mostly sensitive to 3rd generation. Acinetobacter were sensitive to doxycycline, colistin & polymyxin-B . Klebsiella species were resistant to 3rd generation cephalosporins & ciprofloxacin, but were sensitive to meropenem, imipenem, tazocin & sulzone.

Escherichia coli isolates were resistant to 3rd generation cephalosporins & were sensitive to ciprofloxacin, tazocin and sulzone. Pseudomonas were sensitive to ciprofloxacin, amikacin, meropenem, sulzone, imipenem & tazocin and resistant to ceftazidime & co-trimoxazole. (Table V & VI)

## DISCUSSION:

Blood stream infection (BSI) continues to be a major cause of morbidity and mortality in hospitalized patients. To prevent complications and reduce mortality from BSI, it is important to recognize the cause of infection and to start the effective antibiotic therapy immediately. Multidrug-resistant (MDR) organisms are now becoming a great threat in health care setting making the choice of empirical antimicrobial therapy challenging.

The present study includes children of all age groups (88%) and (69.1%) positive blood cultures are from infants, children (19.1%), neonates (8.6%) and adults (3.3%), this was different from the study of Karki et al from Nepal<sup>(5)</sup> which showed highest blood culture positivity among neonates followed by infants and it decreased with increasing age. The overall blood culture positivity showed male preponderance (63.2%) & females (36.8%) which is similar to other studies conducted in other cities in Pakistan<sup>(4)</sup>, Nepal<sup>(5)</sup> & Nigeria<sup>(11)</sup>.

In our study the blood culture positivity is 7.2% which is much lower than reported from other centers in Pakistan i.e. 16.6%<sup>(1)</sup>, 27.6%<sup>(10)</sup>, 27.9%<sup>(3)</sup>, 12.2%<sup>(2&18)</sup>, 62.8%<sup>(13)</sup>, 18.4%<sup>(16)</sup>. Internationally similar low positivity 6.6% reported from Iran<sup>(9)</sup>, Nepal 4.2%<sup>(5)</sup>, Kabul 12.2%<sup>(2)</sup> and from India high positivity about 42%<sup>(6)</sup> has been reported.

Most common Gram-positive organism isolated in our study is staphylococcus aureus (31%), followed by staphylococcus epidermidis (15%) & MRSA (25.5%). These results are similar to other studies carried at other centres in Lahore as noted by shahla et al<sup>(3)</sup> at SIMS also reported staphylococcus aureus (24.1%), staphylococcus epidermidis (20.8%) and high oxacillin-resistant (31.25%). In children hospital Butt et al<sup>(10)</sup> from children hospital Lahore, reported staphylococcus aureus (9.5%), high incidence of staphylococcus epidermidis (24.8%) & Escherichia coli (31.6%) in their neonatal nursery unit. Kumhar et al<sup>(6)</sup> from India also reported staphylococcus aureus (24.4%), staphylococcus epidermidis (7.9%). Studies from Nepal<sup>(5)</sup> showed very high incidence of staphylococcus aureus (65%). A multi-centred study in 6 countries including Agha Khan Hospital Karachi reported MRSA

(11%). Nearly all above mentioned studies showed 100% sensitivity to vancomycin, in case of staphylococcus aureus.

In our study, most common Gram-negative bacilli were enterobacter (18.4%), salmonellatyphi (13.8%), Escherichia coli (8.5%), klebsiella (8.5%), acinetobacter (4.0%) and pseudomonas (0.6%). These findings were similar to some studies<sup>(1,3, and 11)</sup> and differ from others. Most common gram-negative organism usually reported were Escherichia coli, klebsiella, pseudomonas & acinetobacter<sup>(1,2,5&9)</sup>.

The microbial sensitivity pattern for staphylococcus aureus & epidermidis showed sensitivity to 3rd generation cephalosporins, augmentine & gentamicin, but showed resistance to penicillin & ciprofloxacin as in other studies<sup>(1,3,5, and 11)</sup>. All gram-positive including MRSA were sensitive to vancomycin<sup>(1,2,3,4, and 6)</sup>. Gram-negative bacilli were mainly resistant to 3rd generation cephalosporins (ceftriaxone), and showed good sensitivity to aminoglycoside (amikacin), imipenem, sulzone, tazocin & ciprofloxacin. Acinetobacter species were sensitive to doxycycline only and resistant to carbapenems. Pseudomonas only single isolate showed sensitivity to amikacin, meropenem, sulzone, tazocin and ciprofloxacin. These results were comparable with studies conducted at national and international level<sup>(1-6,11-14)</sup>.

The rational and appropriate use of antibiotics requires understanding of common pathogens and their antibiotic susceptibility pattern in a community. Specially in a tertiary-care hospital, as it is seen to be periodically changing over the time. Moreover, gram-negatives that were ESBL producers, were found to be multi-drug resistant; but nevertheless majority of such isolates were sensitive to imipenem/meropenem and to amikacin.

The main factors causing the increase in antimicrobial resistant bacteria are poor infection control measures & in appropriate use of antibiotics. Specific strategies for rational use of superfluous antibiotics and combination antibiotic therapy may help to check the emergence of resistance.

## CONCLUSION:

BSI caused by multidrug-resistant bacteria is a serious problem in health care settings. It is need of the hour to continuously evaluate the sensitivity pattern of local isolates in order to formulate a rationale antibiotic policy

*Table 5: Sensitivity Pattern of Gram-Negative Microorganism*

*(Table content is obscured by a large light blue rectangle)*

*Table 4: Frequency distribution for organism identified in positive blood culture samples at FMH.*

Microorganism	Frequency	Percent	Cumulative Percent
staphylococcus aureus	47	31.0	23.0
MRSA	12	25.5	30.3
E coli	13	8.5	38.8
Klebsiella	13	8.5	47.4
Acinetobacter	6	4.0	51.3
Enterobacter	28	18.5	69.7
Stapylococcus Epidermidis	23	15.0	82.2
MRSE	3	2.0	84.2
MSSE	1	2.0	86.2
Salmonella Typhi	21	13.8	100.0
Total	152	100.0	



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**AUTHOR'S CONTRIBUTION**

**DSL:** Designed, worked on methodology & literature review of the study .**AE :** helped in analysis of results by SSPS 17 & formation of tables. **AB:** Proof reading & final layout . **SR:** Overall supervision of the project.

**FUNDING:** None

**Conflict of Interest:** None

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## OUTCOME OF EMERGENCY OBSTETRICS REFERRAL TO TEACHING HOSPITALS AFTER TRIAL OF LABOR

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### ABSTRACT

**Background:** Most obstetric complications develop during pregnancy, labor and in postnatal period. Though pregnancy and labor is a physiological process but even in women without an apparent risk factor complications may arise or these may have potential to become life threatening. In our country most of births take place at home or local clinics by traditional birth attendants, LHV's, nurses, untrained personnel and may be associated with fetomaternal complications. Skilled birth attendants can provide timed care.

**Objective :** To determine fetomaternal outcome in referred cases

**Study Design:** Descriptive case series

**Settings:** Obstetrics and Gynecology Unit 1, JHL, From 15th Jan 2016- 15th Jan 2017

**Results:** Total admissions were 230. Most patients belong to age group 26-30(N=56)(42%), PG(N=86)(37%), G2-5(N=100)(43%), G6 or more(N=44) (19%). Labor monitored by TBA (N=130) (56.5%), LHV's(N=88)(33%), doctors(N=12)(5%). Patients presenting within 12- 24 hours of trial of labor(n=124) (53%) and after 24 hours(n=42)(18%). Most common presentation was obstructed labor (n=80)(34%) followed by APH(n=50)(30%), ruptured uterus(n=64) (19%), maternal shock(n=16) (7%), Malpresentation(n=8) (3.4%). More than half (n=136)(59%) had abdominal delivery, 36 patients (15%) had vaginal delivery and only 8(3.4%) had instrumental deliveries. PPH observed in(n=40)(17%), vaginal/cervical tear(n=30) (13%), wound infection (n=24)10%, obstetrical hysterectomy(n=8) (3.4%) and sepsis (n=6)2.6%. Out of 230 patients, 10 were admitted in intensive care unit and 2 patients expired. Regarding perinatal outcome, 60 were stillbirths, 80 neonates had meconium staining, 104 were neonatal admissions in NICU and nursery. 84 babies delivered with low APGAR at 1 and 5 minutes.

**Conclusion:** Women empowerment, raising awareness and education among community, regular training courses and supervision of health personnel and eliminating quacks are advocated at all level to improve outcome of obstetrical emergencies.

**Key Words:** Emergency obstetric referral to high volume centre, Mortality of delayed obstetric referral, Impact factor regarding Fetomaternal mortality in emergency obstetric referral.

Obstetric and fetal complications along with their management have effects on a pregnant mother or her fetus. Though labor is a physiological process, time around delivery and the postnatal period is most vulnerable for both mother and newborn. Annually almost 300,000 maternal deaths and over 2.5 million stillbirths and similar number of neonatal deaths occur world wide.<sup>1,2,3</sup>

Census done in 2017 showed that Pakistan is 5th populous country of world with 207,774,520 million populations. 34% pregnant women living in urban while 74% in rural areas. Birth rate is 21.9/1000 and total fertility ratio is 2.68 children

born/woman.<sup>4</sup>

The Pakistan Demographic and Health survey (PDHS) 2012-2013 reported that 75% of women received antenatal care at least once during pregnancy.<sup>5</sup> According to WHO report 2015 percentage of women delivered by Skilled Birth Attendant (SBA) is 55%. These SBA may be trained midwives, LHV's, Nurses and doctors. While 45% are delivered by untrained personnel or quacks resulting in higher morbidity.<sup>6</sup> Delivery conducted by untrained birth attendant has 4.67 times higher mortality as compared to SBA.<sup>7</sup> Current figures show that worldwide 830 women die every single day due to compli-

cations during pregnancy and childbirth and more than one million children remain motherless.<sup>8</sup> More than 99% of the women who die from pregnancy-related complications live in low- and middle-income countries.<sup>9</sup> During pregnancy and labor characteristics associated with increased maternal and perinatal morbidity and mortality are suboptimal antenatal care, antepartum hemorrhage, hypertensive disorders, operative or instrumental vaginal deliveries, obstructed labor, fetal malposition. Postpartum characteristics that are associated with maternal morbidity are seizures or convulsions, hemorrhage, anemia, hospitalization and the receipt of medical treatment.<sup>10</sup> In Pakistan Postpartum hemorrhage is main cause of maternal morbidity and mortality. Anticipating PPH and vigilance in postpartum period, active management of 3rd stage of labor and using misoprostol can reduce blood loss in low resource remote settings.<sup>11</sup>

Uterine rupture in pregnancy is catastrophic complication with a high incidence of fetal and maternal morbidity. Uterine rupture puts mother's life in danger and result in 100% fetal mortality. Incidence of uterine rupture in unscarred uterus in developed countries is 1 in 8434(0.0125) pregnancies while in developing countries 1 in 920 pregnancies(1.1%). Causes of uterine rupture are vigorous use of oxytocin, prostaglandins and uterine pressure in aim to deliver baby. Many authors have considered multiparity a risk factor for uterine rupture. Golan et al noted that, in 19 of 61 cases (31%), uterine rupture occurred in women with a parity of more than 5.<sup>12</sup> Women with prior CS are more vulnerable to uterine rupture. According to WHO In developing countries like Pakistan, uterine rupture with previous cesarean section has been associated with, lack of antenatal care, grand multiparity, obstructed labor, injudicious use of oxytocic drugs, low socioeconomic status and hence difficult access to better health facility rather than prior CS.<sup>13</sup>

It is estimated that 2.9 million neonatal deaths and 2.6 million stillbirths occur worldwide annually.<sup>14</sup> 36% of all these deaths ensue in the first 24 h

after birth. These deaths are preventable by implementing appropriately trained staff, suitably equipped facilities, and the obligatory life-saving commodities for mother and neonate.<sup>15</sup>

#### SUBJECTS AND METHODS:

This study was carried out at Jinnah hospital Lahore in Gynae unit 1 for a period of 6 month from 15-01-16 till 15-01-17. It is 1500 bedded hospital, having Obstetric patients attendance above 300 in OPD/day, 100-150 patients are managed in each emergency in labor room and more than 1200 births/month(in 3 units)

All patients who were received in emergency after a trial of labor outside the hospital by TBAs, LHV's, nurse or doctor at home or at some clinic were carried out. Thorough history was taken regarding age, obstetric history, antenatal visits, trial of labor, duration of trial, condition at presentation. Patients were managed according to their condition on presentation on individual basis and were assessed by senior person on floor. Further plans were based on fetomaternal evaluation. Salient components of management were adequate hydration, analgesia, antibiotics and arrangement of blood. Partogram maintained. Mode of delivery planned according to obstetric condition keeping maternal and fetal safety at top priority. Postpartum complications noted. Perinatal complication in term of meconium staining, fetal distress, intrapartum death or IUD, APGAR score at 1 and 5 minutes and need for nursery admissions were noted. Outcome measures were patient's demographic features, obstetric details, delivery attendant (LHV, TBA, Midwife, doctor, nurse), mode of delivery, maternal and perinatal mortality and morbidity. All cases were managed and all information recorded on pre-designed proforma.

**RESULTS:****Table 1:** According to age distribution

Age(Years)	Number of patients (n=230)	%
20-25	64	27.8%
26-30	96	41.7%
31-35	50	21.7%
36-40	20	8.6%

**Table 2:** Gravidity of patients

Gravidity/Parity	No: of patients(n=230)	%
Primigravida	86	37.3
Gravida 2-5	100	43.4
Gravida 6 or more	44	19.1

**Table 3:** Labor details

Parameters	Number(n=230)	%
Birth attendant		
TBA	130	56.5
LHV	88	38.2
Doctor	12	05.2
Duration of trial of labor before referral		
Less than 12 h	64	27.8
12-24 h	124	53.9
More than 24 h	42	18.2

**Table 4:** Maternal condition at presentation

Presentation	Number(n=230)	%
Obstructed labor	80	34.7
Vaginal bleeding	70	30.4
Neglected transverse lie	8	3.4
Ruptured uterus	44	19.1
Impending rupture	12	5.2
Hypovolemic shock	16 (2CPR done)	6.9

**Table 5:** Mode of delivery

Mode	Number(n=230)	%
Abdominal delivery	136	59.1
Instrumental delivery	8	3.4
Spontaneous Vaginal delivery	36	15.6

**Table 6:** Maternal Morbidity and Mortality

Morbidity	Number(n=230)	%
Ruptured uterus	44	19.1
Scar dehiscence	10	4.3
PPH	40	17.3
Obstetrical hysterectomy	8	3.47
Genital tract trauma	30	13
Puerperal sepsis	6	2.6
Bladder injury	4	1.7
Wound infection	24	10.4
No morbidity	64	27.8
ICU admission	10/230= (4.3%)	
Mortality	2 out of 230	

**Table 7:** Perinatal outcome(Total births =230)

Outcome	N=230
APGAR less than 5 at 5 min	24
Meconium staining/distress	80
Still birth	60
NNU admission	104

**DISCUSSION:**

Most obstetric complications occur during delivery or may rapidly progress to become life threatening. Estimated 15% of pregnant women in developing countries experience pregnancy related complications and nearly 530,000 women worldwide die annually with 95% of their deaths occurring in Asia and Africa.<sup>16</sup> In developed countries obstetric care is at peak while developing countries are still striving to achieve it. In comparison to its neighbors as well as developing countries with a similar level of economic development and international investment in MNH worldwide, Pakistan has had remarkably limited success in reducing maternal and newborn deaths<sup>17</sup>.

In our study conducted over a period of 12 months we had 230 patients who were referred to Jinnah hospital Lahore in gynea unit 1 after having a trial of labor outside the hospital by traditional birth attendants, LHVs and doctors. Most of patients belonged to age group 26-30 years(n=96)(41%) which is comparable to local study conducted at sheikh Zaid hospital Rahim Yar Khan in 2012 and a similar study carried out at Fatima Memorial Hospital in 2011.<sup>18,19</sup>

More than two third patient (n=100) (43.4%) had kids up to 2-5. Primigravida (n=86) 37.3% and patients having 6 or more kids were(n=44) 19%. These results are in contrast to a study carried out at Abbasi Shaheed Hospital Karachi where PG were upto 65%.<sup>20</sup>

According to WHO report 2015, about 55% of births are conducted by SBA (Skilled birth attendants) in Pakistan and other developing countries<sup>6</sup>. But our study showed that almost half of laboring



patients (n=130) 56.5% were managed by TBA, (n=88)38% labors were managed by LHVs and only (n=12) 5% patients had a trial of labor by doctor. This difference may be due to social pressure by family and patient's preference for delivery by traditional birth attendant rather than hospital.

Study carried out at Nigeria by Okafor show delay of more than 12 h by the TBAs before referrals in (75.6%) of the patients, our study showed (n=124) 53% of referrals had delay for more than 12 hours. Most common reason for referral was obstructed labor (n=80) (34%) and vaginal bleeding (n=70) (30%), ruptured uterus (n=44) 19.1% in our study. These results are contrary to the same study carried at Nigeria where obstructed labor was noted in 19% patients and vaginal bleeding observed in just 10% and no referral with ruptured uterus.<sup>21</sup>

Modes of deliveries were abdominal in about 60%, SVDs 15%, Instrumental deliveries 3.4%. Vaginal deliveries ratio were comparable to study at Nigeria, indications for cesarean delivery were same obstructed labor, fetal distress, meconium staining and malpresentation which were similar to study carried out by Rakhshan N.<sup>21-22</sup>

Maternal morbidities in our study were ruptured uterus 19%, PPH(17%), vaginal/cervical tears 13%, Peuperal sepsis 2.6%, wound infection 10% and rate of obstetrical hysterectomy was 3%. One mother passed away inspite of all efforts. She presented in shock with ruptured uterus. Our study had resemblance in many ways with study carried out by B.Zahid. In this study Peuperal sepsis 2%, genital tract trauma 16%, obstetrical hysterectomy 2% which were quiet comparable to our study. While wound infection rate was half (5%) as compared to 10 % in our study. Other morbidities contrary to our study were ruptured uterus 5%(1/3rd of our study) and PPH 10% (about half of our study).<sup>23</sup>

Regarding perinatal outcome, out of 115 births, 30 had still births, 40 had meconium staining, 12 had APGAR Score less than 5 at 5 minutes. Baby with meconium and low APGAR admitted in nursery. Out of 52 admissions in nursery 12 babies expired in first 24 hours. A report on early neonatal mortality and stillbirth determines that in Pakistan a child being delivered has the highest risk in the world of both intrapartum stillbirth and death within first 24 hours of birth<sup>[24]</sup>. And it is evident with statistics that in contrast to neighboring countries and in comparison to other developing countries with interchangeable economic development and international investment in MNH worldwide. Pakistan is lagging behind

astoundingly and acquired insubstantial success in reducing maternal and newborn deaths<sup>[17,25]</sup>. The Pakistan Demographic and Health Survey (PDHS) 2012-13 reports a perinatal mortality rate of 75 per 1000 pregnancies and neonatal mortality rate of 55 per 1,000 live births<sup>[26]</sup>.

It is evident by the analysis of article that fetomaternal morbidity and mortality is caused by substandard care given by TBA and quacks as most of patients are managed by them outside proper health facility. Most of our women are delivered by untrained birth attendants. A lack of life-saving delivery care may be attributed to an inability to recognize an impending complication, failure to reach an appropriate level of care in a timely manner, a lack of appropriate care provision at the facility or to iatrogenic causes, for example from unsafe labor augmentation or unhygienic practices.<sup>[27,28,29]</sup>

### CONCLUSION:

Barriers to reach a health facility are lack of education, poverty and not involving woman in decision making. Women empowerment, raising awareness and education among community, regular training courses and supervision of health personnel and eliminating quacks are advocated to reduce maternal/fetal complications during pregnancy and child birth.

Not only the above mentioned implementations must be carried out but there is room for improvement in tertiary care hospitals. Inadequate staff, logistics problems and maltreatment of health personnel with patients are deterrent to seek antenatal and intrapartum care.

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## UTILIZATION OF PUNJAB PUBLIC SECTOR HEALTH CARE SERVICES BY MOTHERS-COMMUNITY PERCEPTION

Naheed pirzada

### ABSTRACT

**Introduction:** Inadequate utilization of maternal health care services by mothers is constantly being a major challenge among middle and low socio economic countries. Pakistan remained accountable for not meeting the targets of Mellinium development goals number 4 and 5,largly due to poor access and usage of skilled health care providers services.

This study was intended to explore the hurdles that inhibit the mothers to approach the government sector health care services and to unveil the gaps other than money that play as the leading obstacles in utilizing such facility by mothers.

**Methodology:** To gather an in depth understanding of the human behavior, a Qualitative study was carried out comprising of six in depth interviews and one focus group discussion, using non probability purposive sampling. . Codes were extracted followed by reduction and sub themes, and finally themes.

**Results/ Discussion:** Five themes were derived from in depth interviews and focus group discussions. Financial as well as social and cultural barriers, attitude and behavior of health care providers, previous exposure of health facility and quality of care. Infrastructure, supplies, non availability of medicines, transport constrains and time costs remained dominant factors in refraining from use of health care services.

**Recommendations:** There is Strong need of strengthening the bond between consumers and health care providers. Better responsiveness in terms of reduced waiting time along with efficient addressing coupled with refurbishing and ensuring the availability of maximum services under one roof, high quality liaison, skilled medical staff and sympathetic behavior can build confidence in government sector hospitals.

**Key words:** Perception, utilization, skilled, Health care providers', barriers

Women have a basic human right to be protected when they undertake the risky enterprise of pregnancy and child birth. Every death in pregnancy and child birth is a multiple personal tragedy. It is not only a health system malfunction but the under-utilization of health services by mothers. Interventions are needed to curb maternal and infant mortality. We cannot close our eyes to the overwhelming figure of 170/100,000 maternal deaths every year due to pregnancy related complications in Punjab, Pakistan.<sup>1</sup>

In Punjab, health services are provided through a tiered referral system of health care facilities with increasing level of coverage from primary to secondary and tertiary health facilities. Outreach and community based activities focus on immunization, sanitation, communicable disease control, maternal child health and family planning services. Private

sector in service provision caters to almost 70% of the population. It is obvious that certain obstacles prevent Pakistani mothers from seeking health care services. This study is projected to identify the constraints mothers face during pregnancy and delivery in accessing the health care delivery center

According to United Nations, one out of three women receives adequate care during their pregnancies in developing regions. In Sub-Saharan Africa, majority of the pregnant mothers do not seek health care and deliver without skilled birth attendants. Many of the maternal deaths are avoidable and are the result of direct causes which are hemorrhage, sepsis, hyper-tension, unsafe abortion and obstructed and prolonged labor. By reducing the high risk pregnancies through adequate utilization of health care services, many of the maternal and infant deaths can be avoided.<sup>2,3</sup>

The high number of maternal deaths reflects inequities in access to health services. The maternal mortality ratio in developing countries in 2013 was 230 per 100,000 live births versus 16 per 100,000 live births in developed countries. More than half of these deaths occur in sub-Saharan Africa and almost one third occur in South Asia.<sup>4,5</sup> Neonatal outcomes are inextricably connected to maternal health and therefore to the quality of care a mother receives during labor, delivery and the immediate postpartum period, the highest risk period for both mothers and babies. Maternal complications and maternal deaths, add significantly to impact newborns ability to survive and thrive. Neonatal deaths are concentrated in the low and middle income countries where maternal mortality is highest, utilization of health services is lowest and the quality of available care is not up to the mark e.g. sub-Saharan Africa.<sup>6,7</sup>

Reaching to a maternal health facility does not imply that morbidity or mortality could be avoided, if the services are inefficient and the qualities of services which are being provided are not effective. Moreover, the availability of services does not ensure that it would be utilized with best possible outcomes. There exists a strong relationship between the quality of the services being provided and the patterns of services being utilized.<sup>8</sup> The lives of most of the mothers could be saved if they had access to some basic health care services. These include skilled care during and after child birth which can only be put into practice by the quality of the medical and technical expertise, health education, knowledge and information, the equipment and quality assurance system in practice.<sup>9</sup>

A study conducted in Pakistan addressing the challenges in access to and utilization of reproductive health care has thrown light on the obstacles a mother usually faces in reaching out to health centers e.g. her inability to travel alone as and when they wished because they are unable to go to health facility unaccompanied. Male family member or an elderly person from the family such as her mother in

law must accompany them.<sup>10</sup> Access to and availability of quality medical care are both necessary but not sufficient factors to improve the utilization of health services. In addition other factors conducive to improve maternal and neonatal outcomes are joint family structure, mass media exposure, literacy status, gender discrimination and socio-economic status of mothers were significantly associated with the health seeking behavior of the mothers.

In a study conducted in Africa to understand the community factors and perceptions that influence women's health care seeking behavior showed that programs aimed at reducing the three delays in seeking care include primary prevention by education and services, developing secondary prevention through early detection and treatment and to address the economic, social and physical factors operating at the community, at household and individual level as well as at the larger social and political environments.<sup>11</sup>

### Research Question

The underlying factors compelling women to abstain from seeking health care facilities or preferring private over the public health care sector, if they ever choose to avail them and how to strengthen the track between consumers i.e. the mothers and the health care providers.

### DATA AND METHOD

It is qualitative study which aims to gather an in depth understanding of human behavior and reasons that govern such behavior. The non-probability purposive sampling design has been used for the study. Qualitative data has been obtained by using analytical induction approach. We included the females who gave birth to a child more than 6 months back to reduce the recalled bias. Irresponsible mothers who did not provide much information were not a part of this study sample. The selection criteria for this study was three categories of women (i) who have not utilized any health care facility for maternal services ii) who have utilized private sector over public sector iii) who utilized and seek help from



public sector health care. The sample was taken from two different areas of Lahore, Jinnah hospital and Basti saidan shah Lahore, where three in-depth interviews at each place were done.

In depth interviews were conducted for the study sample. Interviews were guided by question guide that was made to cover the range of issues that deters the mothers from seeking health care services. The interview guide which included some of specific questions regarding maternal health care and utilization of health care services, was used to extract the contents. As well as some of the broader questions related to experiences. All the women who have been selected and volunteered to participate in study were given an explanation of the purpose of study and provided verbal informed consent.

The interviews were conducted in Urdu and local language to make interviewee more comfortable to answer and explain the issues they have been facing. The interviewer used probing and question rephrasing to clarify the questions and obtained details from mothers. Data analysis was conducted using qualitative technique i.e. familiarizing, reading and rereading Through case analysis the codes were extracted followed by reduction and sub themes, and finally themes were generated.

After analysis there were many barriers found that abstain the use of health care facilities either public or private sector. The following five themes were derived from in depth interviews and focus group discussions (financial as well as social and cultural barriers, attitude and behavior of health care providers, previous exposure of health facility and quality of care).

### **Financial Barriers**

Under the financial barrier as the major theme, certain sub-themes emerged. The public sector health care facilities are sometimes expensive due to non-availability of some diagnostic services and undue expenses associated with those available. "We belong to very low socioeconomic status so can't afford the expenditure of the public sector hospital

and prefer to deliver at home". Few of the participants, were of the opinion that public sector hospital is best regarding financial issues, free medication and lab test facilities and values their hard earned money. "We don't have extra money to waste in private clinics as they are indulged in the art of money making by being expensive and prescribing costly medicines."

Some mothers concern was that since they can't go alone to the distant hospitals so prefer to go to nearby private clinics to avoid the loss of time (long waiting) and hard earned money of their husbands.

Physical location of the facility is a major contributing factor to the utilization of the health services." I have to travel by multiple buses to reach the government facility. This not only adds to my expenses but also my children at home get neglected" said one of the respondents. "Once I was turned away as I went on the wrong day and it was too costly to contemplate returning to the same facility."

### **Attitude and behavior of health care providers**

Mostly the medical staff of the government sector misbehave with the mothers in the labor room which was expressed as dissatisfying regarding the quality of care they had both during the antenatal care and delivery procedure. "When I was in labor, they used to shout at me when I walked slowly, neither were they sympathetic to my condition. Even nurses hurled abuses at me."

Another issue conveyed by the relatives was of the successive visits to the medical store rather than providing a complete list of the needed medicines at a single time. "My husband was made to visit the pharmacy multiple times. They came up with a new medicine slip every half an hour. This practice surely adds to the vows of both the patient and the accompanying partner.

### **Previous exposure**

There were mixed past experiences related to the public set up which compelled many women to change their choice. The availability of nearby local

private clinics is usually the source of first contact point for antenatal health care visits and later using public sector hospital for delivery. "I had my last delivery in the public hospital. My baby was serious and was immediately shifted to 'baccha ward' (nursery) where he revived". Another mother complained of the shortage of beds in the labour room. "My daughter was delivered in government hospital where two patients were made to lie on a single bed and the lady doctor had no time to cater to her".

"I got scared of hospitals after my last pregnancy, doctors kept on assuring throughout my antenatal period that I would have a normal delivery but at the delivery time they suddenly decided for section without giving any authentic reason. Since then I decided not to go to any hospital."

In contrast some mother think that private sector health care provider do not bother to provide holistic approach to care of patients rather they prefer to save time, increase the expenses by enhancing the number of C- sections as compared to normal deliveries in maternal services. "Private sector is a machine to make money they do not wait for normal delivery as it takes more time then C-section"

### **Social and Cultural Barriers**

We thrive in a patriarchal society where husbands and mothers in laws are the dominant decision makers and possess the power to decide when and which services are to be availed. This lack of autonomy and empowerment are the basic factors contributing to the less utilization of health care services. "I was forced by my in-laws to seek the services of their ancestral 'dai' which resulted in the death of my baby. It was then only that my husband decided to take me to a public hospital the next time I conceived".

### **Quality of Care**

Care that is safe, effective and ensures dignity and satisfaction of the patient is lacking in the government sector health facilities. "Sometimes the staff shows abusive behavior, with no maintenance

of privacy and the lady doctors are too busy to listen to our pleas". "I doubt sterilization and cleanliness is a part of their agenda. A patient is always at a greater risk of getting other infections when visiting the government facilities".

Few mothers admitted that although the doctors worked under deficient conditions and are overburdened due the massive patient turn-over, this does not give them the liberty to be disrespectful towards them. "It is true that they have to manage a number of patients, with excessive pressure but they should be sympathetic and must interact in a proper manner so that the patient and her relatives are aware of the situation".

### **DISCUSSION**

Our results confirmed most of the trends found in the previous researches. Affordability barriers including the infrastructure, supplies, medicines and transport and time costs remained dominant factors in refraining from use of health care services. One thing that needs to be recognized is that sometimes a trade-off exists between availability and affordability where the private clinics are more easily geographically accessible as compared to the government hospitals and these factors are also evident from previous literature.

Although the provision of health care was recognized by the family members but the well-being of the mothers was not taken as a priority. Lack of spousal communication and the restrictions imposed by the in-laws were recognized as a major social and cultural barrier to the practice of using health care services which were also endorsed by the existing studies.

There were mixed views regarding the attitudes and behaviors of the health personnel but the dissatisfaction pertaining the quality of the care they received, incomplete guidance leading to marked up stress and frustration of the patients and their attendants was enough for them to contemplate the wisdom behind their decision to visit such a facility again. Thus, one bad experience places a question

mark on the credibility of future decisions. Embarrassing physical examinations, previous outcomes and mistreatment deterred mothers from seeking health assistance and this was reflecting in the literature review as well. ,

Certain respondents were not accustomed to using hospital services as they were habitual to deliver at home like other women in their families. Their distrust in the healthcare workers and strong religious conviction and beliefs were reflected in their health care seeking practices.

### CONCLUSION AND RECOMMENDATIONS

This study revealed that the behavior of the medical staff is not encouraging and facilitating enough to lessen the dilemmas of the poor mothers. Adding to their hurdles is the unsupportive attitude of their in-laws. The entire system of health care comprising of multiple sittings, never-ending pharmacy visits and the long hours of waiting in queues contribute to the less utilization of health sector facilities. The bond between the health care providers and seekers is not as strong as it should be owing to a number of factors discussed above

A few interventions or measures that can improve the quality of care will help to bridge the gap. Better responsiveness in terms of reduced waiting time along with efficient addressing coupled with refurbishing and ensuring the availability of maximum services under one roof, high quality liaison, skilled medical staff and sympathetic behavior can build confidence in government sector hospitals. Patriarchal thinking and conventional cultural issues should be addressed simultaneously to enhance utilization.

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## A KNOWLEDGE, ATTITUDE AND PRACTICE(KAP) STUDY ON DENGUE PREVENTION IN URBAN LAHORE

Maaz Ahmad

### ABSTRACT

**Background:** Dengue Fever (DF) is an emergent disease in Pakistan. It is endemic in some parts of country and contributes annual outbreaks of dengue.

**Objective:** The objective of this study was to evaluate the knowledge, attitude, and practices (KAP) of the community residing in Walled city, Lahore about Dengue fever.

**Materials and Methods:** A descriptive cross-sectional study of 100 families in Walled city, Lahore was conducted through interviews using pretested questionnaire. The questionnaire was designed to assess the knowledge, attitude, and practices (KAP) regarding Dengue fever. Only those who gave their consent to participate were included in the study. The data was analyzed by using the Statistical Package for Social Sciences (SPSS) statistical software, version 20.

**Results:** The community had an inadequate knowledge about DF and its vector. Also, people had inadequate knowledge of DF prevention methods and the biological control of dengue vectors. Similarly, they were practicing preventive measures application which was inadequate. 54.1 % respondents belonged to the age group of 30 – 45 years, 88 % respondents were married and 42.12 % respondents were high school certificate (31.21 %). All the respondents (70%)knew the word”Dengue” through the media. Majority of them(60%) were aware of fever as a main symptom of dengue fever. Other features were not known to most of the respondents. No one was capable to identify larva and pupa of dengue mosquito. Also no one was aware of breeding places, biting habits of dengue mosquito and transmission of dengue fever and preventive measures. Though the dengue teams visited many houses(60%) but they neither trained the community about identification and breeding places of various developmental stages of dengue mosquitoes nor they educated them to prevent dengue. Majority of the teams(98%) did not inspect the houses thoroughly .Social resistance was also shown by the community. Majority(90%) was not knowing any satisfactory treatment of dengue fever. Most of the respondents (60%) were considering dengue fever quite serious. Majority of respondents had this opinion that this was the responsibility of government to control dengue. A casual attitude was found in the respondents about dengue and their living practice was being reflected by this attitude. Dengue was not a priority problem in their minds. Mosquito repellants were applied by some respondents(20%),however coils/mats were used by 40% respondents off and on.

**Conclusion:** This study demonstrated that knowledge and attitude towards Dengue is inadequate.

**Keywords:** Dengue, attitude, knowledge, practice.

Dengue fever is caused by a mosquito-borne human viral pathogen that belongs to the genus *Flavivirus* of the family *Flaviviridae* (single-strand, non-segmented RNA viruses). There are four dengue serotypes (DEN-1, DEN-2, DEN-3, and DEN-4).<sup>1</sup> Dengue fever predominantly occurs in Southeast Asia, the Americas, Africa and the Caribbean Islands. There has been a gradual global upsurge in the number of dengue cases in the last decade.<sup>2</sup> Dengue is transmitted in humans by two

species of *Aedes* mosquitoes namely, *Aedes aegypti* (principal vector) and *Aedes albopictus*. Although infection with one dengue serotype confers lifetime immunity against reinfection by the same serotype, there is no evidence of cross immunity. Therefore, it is possible for one to be infected with dengue fever several times during one’s lifetime. There are two main forms of dengue disease, dengue fever and the more severe dengue hemorrhagic fever (DHF). Infection with any of the four serotypes can produce



a broad range of clinical manifestations including asymptomatic infection, mild flu-like symptoms, and the more severe hemorrhagic fever.<sup>3</sup> The hemorrhagic fever usually results when someone who had prior infection with a particular dengue serotype becomes infected with a different serotype. The cross reaction of antibodies to the dengue antigens is thought to result in this disease.<sup>4</sup> In severe cases, patients may suddenly deteriorate, develop hypothermia and go into circulatory shock, a condition known as dengue shock syndrome.<sup>5</sup> This syndrome is associated with 40–50% fatality if untreated or mistreated. When properly treated, the case fatality can be reduced to 5% or less.<sup>6</sup> Every year, there are more than 100 million cases of dengue worldwide and of these, 2000–3000 cases (mostly children) result in death.<sup>7</sup> In tropical areas where dengue fever is endemic, dengue hemorrhagic fever is confined to children younger than 15 years of age.<sup>8</sup> However, in Pakistan, all ages are affected with highest incidence among those over 15 years old. Treatment for dengue fever entails mainly supportive therapy. Because there is no vaccine to protect against this disease, great emphasis is placed on control and preventive measures.

The WHO and Centers for Disease Control and Prevention recommends limited reliance on insecticidal control and emphasis on community educational campaigns that emphasize residents' responsibility in reducing vector breeding sites.<sup>9,10</sup> This view is supported by prior research showing that community education can be more effective in reducing dengue vector breeding sites than chemicals alone.<sup>11</sup>

Recent outbreaks of dengue in Pakistan and the paucity of relevant studies on knowledge, attitudes and practices regarding dengue transmission and infection necessitated development of the study. Further, although investments have been made in media campaigns to increase awareness about dengue by government, non-governmental and private institutions in Jamaica, no assessment has been conducted to determine the impact of such interventions or to identify gaps in knowledge and

practice regarding dengue infection.

## METHODS

### Study setting

Lahore was hit by Dengue Fever(DF)in 2011.It was a huge epidemic affecting the whole community residing in Lahore in one way or other having more than 20 thousands dengue patients and more than 300 casualties. There are 10 towns in Lahore .One town was randomly selected..Walled city is one of such community located in this town. Inside Lohari was the community randomly selected for this study. It is a thickly populated community and to capture a representative sample of the population with 95% confidence and a 5% margin of error, we estimated that a total of 100 persons were required .So a sample unit of 100 families was randomly selected to evaluate the knowledge, attitude, and practices (KAP) of residents of this sample unit for dengue.

### Study design and participants

There are 10 towns in Lahore district. One locality was selected after multistage sampling. A cluster of 100 families was randomly selected .In this study ,a community inside Lohari gate was the study population in this study. A descriptive cross-sectional study was conducted during May 2015 concerning Knowledge, Attitudes, and Practices of DF prevention. Head of each residential unit was enlisted for study. Participation in the study was voluntary and no incentives were provided.

### Study instruments and data collection

After enrolment in the study, every respondent was interviewed with a pre-designed questionnaire. Informed consent (verbal or written) was taken from all the respondents and confidentiality was ensured throughout the study. Prior to use of the KAP questionnaire. The study instrument, Questionnaire, was developed following an extensive review of the literature and then was translated into local language The questionnaire was pretested among two separate groups of 14 residents in Inside Lohari who were excluded from the main study. The questionnaire covered the following areas: (1) demographic

information (district, sex, age, occupation, and education); (2) health information relating to dengue disease and dengue vector (3) knowledge about dengue symptoms, signs, and transmission modes; (4) attitude towards dengue; (5) preventive practices against dengue e.g. methods used to reduce breeding sites, and reduce potential human-mosquito contact (repellents, bed nets, and window screens, etc). Data were collected from a total of 100 respondents.

### Data Analysis

The data were analyzed using SPSS software package version 20. Simple frequency tables were prepared for the socio-demographic variables and for knowledge, attitudes and preventive practices. Responses to questions were coded such that correct answers were scored 1 and incorrect answers were scored 0.

## RESULTS

### 1. Knowledge

#### i) Knowledge about Disease

All the respondents(100%) had heard about Dengue. Majority of them(70%) came to know through electronic and print media. 20% were informed by dengue team whereas local dispensary informed 3% and general practioners 's role was 5%.Contribution of Imam masjid was only 2%.Out

**Table 1:** Knowledge about Dengue fever

Indicators of Knowledge about the Disease	Yes(%)
i.Knowledge about the name of disease?	100
ii.Source of awareness about dengue?	
a.Dengue team ?	20
b.Nearby health facility?	3
c.Imam masjid ?	2
d.your family physician?	5
iii.Personal observation of dengue case?	12
iv.Awareness of Signs/symptoms of dengue?	
a.Fever	60
b. Headache?	15
c. Joint pain?	10
d. Muscle pain?	10
e. Pain behind the eyes(Retro orbital)?	0
f. Rash?	0
g. Abdominal pain?	0

of all respondents, only 12% had observed dengue patients in hospitals and not at home. Majority (60%) knew about fever as a feature of dengue fever,15% were aware of headache,10% were knowing joint pain and muscle pain as signs/symptoms of dengue fever. But no one was aware of retro-orbital pain, rash and abdominal pain.(Table.1)

#### ii) Knowledge about the Dengue Vector

Majority was not much aware of Dengue mosquito. Only few respondents (5%) observed dengue mosquito in flying mode only. No one else was aware of actual shape of eggs, larva and pupal stage of dengue mosquito. About habitat and breeding places only 8% gave the idea of standing water whereas 5% respondents were knowing about uncovered water containers and desert coolers as breeding places.3% were aware of discarded tyres for breeding of mosquitoes. No one else was aware of other breeding places e.g. bottom tray of refrigerator, air conditioners, electric water cooler, water pots for birds and pets, flower pots, leaking water taps, fountains, junk, lids of gutters and manholes. Very little knowledge was found about the biting

**Table 2:** Knowledge about Dengue fever

Indicators of Knowledge about Dengue Vector(Aedese aegypti mosquito)	Yes(%)
i. Personal observation of developmental stages of Dengue mosquito	
a. live larva of Dengue mosquito	0
b. live pupa of dengue mosquito	0
c. eggs of dengue mosquito	0
ii. Knowledge about breeding places of dengue mosquito?	
a. uncovered water containers at home?	5
b. desert coolers at home?	5
c. tray at the bottom of refrigerator at home?	0
d. old discarded tyres on the roof or inside home ?	3
e. water pots for birds at home?	0
f. leaking taps?	0
g. flower pots withstanding water at home?	0
h. junk at home?	0
i. fountains at home?	0
j. covers of gutters/manholes at home?	0
k. water pots for pets at home?	0
l. lower tray of airconditioner/electric water cooler at home?	0
iii. Knowledge about the biting habits of dengue mosquito?	
a. Likely to bite at night?	23
b. Likely to bite in day time?	0
c. Likely to bite at any time?	12

habits of mosquitoes. In the opinion of 12% respondents, dengue mosquito could bite any time. 23% were of opinion of biting at night time.(Table 2)

**iii. Knowledge about transmission of Dengue disease**

Some respondents(16) were aware about disease transmission but 15% were of the opinion of person to person transmission through contact.22% were holding sharing of food items and utensils responsible and 2% were conveying about blood transfusion. No one was aware of name of Dengue mosquito i.e. Aedese aegypti and its exclusive role in spreading the disease. Dengue fever could be spread through all mosquitoes in the opinion of 4% reospondants. Very few (2%) were quoting houseflies as transmitters (Table 3).

**Table 3:** Knowledge about transmission of Dengue disease

Indicators of Knowledge about transmission of Dengue disease	Yes(%)
i. Knowledge about dengue disease mode of transmission	
a. Person to person contact?	15
b. Sharing eatables, utensils ?	22
c. Blood transfusion?	2
ii. Knowledge about the transmitter of dengue disease virus?	16
iii. Knowledge about the actual name of dengue mosquito?	0
iv. Knowledge about the exclusive role of Aedese mosquito in spreading dengue?	0
v. Knowledge about other mosquitoes spreading dengue?	0
vi. Knowledge about dengue spread through all types of mosquitoes? Dengue fever?	4
vii. Knowledge about the role of housefly in spreading dengue?	2

**iv. Knowledge about Dengue Prevention**

Dengue surveillance teams have been deployed to do the dengue surveillance and impart health education but surveys that this particular task is not adequately addressed. In this particular community, majority of respondents(60%) were claiming of dengue teams visits and 20% were reporting regular visits by dengue teams but 15% respondents had reported about the entry of teams into homes

whereas 2% respondents reported that thorough inspection was carried out by these teams. 5% respondents were receiving health education and some material but no one else was given health education or material. Dengue teams. Some respondents (5%) were not found receiving any preventive advice by the dengue teams. Respondent or his any family member were not found to be familiar with actual shape of larva or pupa of dengue mosquito nor they were found trained to detect these stages in their home at various different breeding places. Respondents were not found remembering the dengue toll free number nor they were linked with local health authorities in any way. 20% respondents were aware to reduce mosquito bite through window screens and

**Table 4:** Knowledge about prevention

Indicators of Knowledge about prevention	Yes(%)
i. Knowledge about importance of sharing the disease with your family/friends/colleagues?	2
ii. Knowledge about importance of sharing the disease at any forum?	10
iii. Knowledge about dengue teams?	
a. Home visiting of dengue teams ?	60
b. Regular home visits of dengue team ?	20
c. Entry into home by dengue team?	15
d. Inspection of home by the dengue team?	2
e. Distribution of dengue information literature by the dengue team?	5
f. Discussion with family members?	0
g. Imparting health education material?	5
h. Showing dengue vector developmental stages live?	0
i. Conveying preventive methods to avoid dengue?	5
j. Provision of training to detect/identify dengue vector developmental stages?	0
iv. Knowledge of Coordination with local health authority?	0
v. Knowledge of Dengue Toll free number?	0
vi. Knowledge of preventive measures?	
a. Window screens and bed nets?	20
b. Insecticide sprays	18
c. Covering water containers	10
d. Removal of standing water	10
e. Mosquito repellants	5
f. Cutting down bushes	0
g. Pouring chemicals in standing water	0
h. Larvae eating fish	0
i. Mosquito repellent plants if grown in homes?	0

bed nets reduce mosquito bite, whereas 18 % were knowing the role of Insecticide sprays to reduce mosquitoes and prevent Dengue. Covering water containers reduce mosquitoes and removal of standing water could prevent mosquito breeding was in the knowledge of 10% respondents.5% respondents were knowing the role of mosquito repellants to prevent mosquito bite. However no one was having the importance of cutting the bushes around houses, larvae eating fish or mosquito repellent plants.(Table.4)

#### v. Knowledge about Disease Management

Majority(90%) was not knowing any satisfactory treatment of dengue fever, however 30% respondents were of this opinion to prefer their family physician. Few respondents were knowing some local remedies for the treatment of dengue fever(Table.5)

**Table 5:** Knowledge about Disease Management

Indicators of Knowledge about Disease Management	Yes(%)
i. Knowledge about effective treatment of dengue fever	10
ii. Preference of family physician in case of illness?	30
iii. Belief in locally prepared remedies?	13

#### 2. Attitude

Majority of respondents (60%)were considering dengue fever quite serious.25% were feeling at risk of dengue but 13% were of this opinion that dengue could be prevented. Only 5% respondents felt the need of hospitalization for every dengue patient. Majority of respondents had this opinion that this was the responsibility of government to control dengue(Table.6)

**Table 6:** Attitude of the respondents

Indicators of Attitude	Yes(%)
i. Serious consideration of dengue?	60
ii. Feeling at risk of dengue disease?	25
iii. Considering dengue as a preventable disease?	13
iv. Consideration of hospitalization of every dengue patient ?	5
v. Considering control of dengue as state responsibility?	80

#### 3. Practice

It was observed that the majority of community (76%) did not allow dengue teams to enter their house due to multiple psycho-social reasons but the people did not try to be equipped with knowledge for dengue prevention. Respondents were found in habit of reacting in a non social manner. They did not bother to discuss with their family, friends, colleagues, neighbours at all. They were not taking any

**Table 7:** Practice pattern of the Respondents regarding Dengue prevention

Indicators of Practice pattern of the Respondents	Yes(%)
i. Desirous to know the dengue disease?	0
ii. Response to dengue team?	
a. Showing reservation to dengue team	76
iii. Sharing dengue disease and its prevention?	
a. Neighbours?	0
b. friends?	0
c. family?	0
iii. Regular plan of inspection of your home regarding dengue prevention?	0
iv. Appointing any of your family member as a focal person for indoor dengue surveillance?	0
v. Laison with some government responsible person for conveying information about dengue vector for its management?	0
vi. Preventive practices?	
a. Updating through media?	0
b. Regular home cleanliness?	20
c. Elimination standing water around the house?	6
d. Checking roof top regularly for any junk/tyres?	2
e. Cutting down bushes in the yard ?	0
f. Covering water containers in the home	0
g. Insecticide sprays	4
h. Screening windows	0
i. Screeing doors?	0
j. Mosquito eating fish in your fountains	0
k. Mosquito repellent oil/lotion?	40
l. Mosquito mat/coils to repel mosquitoes	23
m. Bed nets to reduce mosquitoes	0
n. Checking desert coolers regularly?	0
o. Checking Air conditioner bottom tray regularly?	0
p. Check Refrigerator tray regularly fordengue vector?	0
q. Changing water of electric water cooler tray regularly?	0
r.. Changing water of the flower pots regularly?	0
s. Changing water of the pots for birds regularly?	0
t. Changing water of the pots for your pets daily?	0
u. Leaking tap in house?	0



responsibility at home for maintenance of cleanliness or fixing responsibility to any member of the family residing in that house for regular inspection and keeping the house neat and clean. Respondents were found least interested in developing coordination relationship with local health authorities and media people. Only 20% respondents were found maintaining the cleanliness of their houses. 6% were taking the responsibility to eliminate standing water around the house to reduce mosquitoes. Only 2% respondents were found having the habit of checking their roofs regularly. 40% respondents reported using mosquito repellent oil/lotion whereas 23% respondents used mat/coil to repel mosquitoes. No respondent was found keeping the environment clean by cutting down bushes around his residence, covering water containers, screening doors and windows, breeding larvae eating fish, cultivating mosquito repellent plants, using bed nets, checking desert coolers, checking air conditioners, electric water coolers, checking flower pots, water pots for birds, water pots for pets and leaking water taps. (Table.7)

## DISCUSSION

Near about all the residents were aware of the name "Dengue" mostly due to this reason that there was an epidemic in 2011 then every year dengue is spreading to other parts of the country. Media played a major role.<sup>1</sup> The knowledge level on dengue fever reported in this study is comparable to findings in similar KAP studies conducted in Grenada and Thailand. Most respondents were not able to correctly relate the symptoms of dengue apart from a few who identified fever, an obvious symptom. Fever was also the most frequently recalled symptom in a similar study conducted in India. The poor knowledge of the spectrum of symptoms associated with dengue means it may be confused with most other causes of fever such as the flu. The implication of this is that presentation to the clinic may be delayed until complications arise.

Majority of respondents got information from electronic and print media.<sup>2</sup> Role of dengue team was not up to the mark only some of the respondents got benefitted. No general practitioner or family physician played much positive role. Similarly imam masjid or local government dispensary did not participate in conveying information to the public.

All the dengue patients seen were in various hospitals. Most people were not aware of all the symptoms/signs of dengue fever, however majority knew that fever was a mandatory part of dengue. Only few were aware of generalized pain and aches all over the body in dengue fever. The remaining signs/symptoms were not known to any one. As far as dengue vector was concerned, only few persons observed flying dengue mosquitoes, otherwise no one was aware of any developmental stage of dengue mosquito.<sup>3</sup>

Knowledge about breeding places of dengue mosquitoes was very poor. Only few persons guessed of standing water on ground otherwise no one was aware of other breeding places like uncovered water containers, desert coolers, tray at the bottom of refrigerator, old discarded tyres, water pots for birds, flower pots with standing water, junk, fountains, leaking water taps and tray of air conditioner/ electric water cooler. Very few knew the biting habits of mosquitoes.

Few respondents were aware about disease transmission. Some were of this opinion that dengue might be spreading through contact or ingestion and blood transfusion. No one was aware of name of Dengue mosquito i.e. *Aedes aegypti* and its exclusive role in spreading the disease. Transmission through mosquitoes was not in the knowledge of respondents.

Regarding preventive measures, dengue surveillance teams had been visiting as reported by majority of respondents but detailed inspection of inside of houses was not reported. Few respondents were given health education and some material. Very few respondents received any preventive advice by the dengue teams. Respondent or his any family member were not found to be familiar with actual shape of larva or pupa of dengue mosquito. No respondent was trained to detect these stages in their home at various different breeding places. Dengue toll free number was not conveyed to the respondents. No link was developed with local health authorities. Some but not majority of respondents were aware of importance of door/window screening, bed nets, insecticide sprays, covering water containers, removal of standing water, mosquito repellents, cutting the bushes around houses, larvae eating fish or mosquito repellent plants and pouring chemicals in standing water.

Majority was not knowing any satisfactory treatment of dengue fever, however some respondents preferred their family physician instead of hospitals.

Majority of respondents thought dengue fever a serious problem. Some felt at risk of dengue but few were of this opinion that dengue could be prevented. Very few respondents felt the need of hospitalization for every dengue patient. Majority of respondents had this opinion that this was the responsibility of government to control dengue.<sup>5</sup>

While conducting survey it was felt that the majority of community did not allow dengue teams to enter their house for thorough inspection due to cultural aspects and some recent mishaps of robbery but the people did not show much enthusiasm to learn. They did not bother to discuss with their family, friends, colleagues and neighbours at all.<sup>6</sup> They could not manage at home for maintenance of cleanliness or fixing responsibility to any member of the family residing in that house for regular inspection and keeping the house neat and clean. Respondents were found not having coordination with local health authorities and media people. Few respondents were found maintaining the cleanliness of their houses. Very few were taking the responsibility to eliminate standing water around the house to reduce mosquitoes and checking their roofs regularly. Some respondents were using mosquito repellent oil/lotion and mat/coil to repel mosquitoes.<sup>8</sup> No respondent was found keeping the environment clean by cutting down bushes around his residence, covering water containers, screening doors and windows, using bed nets, checking desert coolers, air conditioners, electric water coolers, flower pots, water pots for birds, water pots for pets and leaking water taps. Community was not aware of breeding larvae eating fish and cultivating mosquito repellent plants.<sup>9</sup>

No significant association was found between preventive practices and socio-demographic characteristics of the participants. There was no correlation between knowledge about dengue and preventive practices ( $p=0.34$ ).

## CONCLUSION

In conclusion, community under discussion had an inadequate knowledge about DF and its vector. Also, people had inadequate knowledge of DF prevention methods and the biological control of dengue vectors. Similarly, they were practicing preventive measures application which was inadequate. There is a need to make community people aware of different preventive practices and reduce

this knowledge application gap. Television may play an important role in conveying health information to the public. We submit that in spite of our study limitations our findings highlight the need for further information, education and communication programs to identify barriers to action and to seek ways to translate population knowledge about dengue into positive preventive practices that would ultimately reduce the transmission of dengue in this part of the world

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