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Editorial

Eating Less and Exercise – Lose the Weight

Mohsin Masud Jan

Editor

Losing weight is based on two ideas, eating less and exercise. First about exercise. From a medical point of view, exercise has so many diverse benefits that all those fit enough to exercise regularly must do it. you do not have to run a few miles every day or do some strenuous gym stuff for exercise to be 'useful'. Even a ten or fifteen minute brisk walk five days a week will provide most health benefits associated with exercise. And that is fine for most people. One important bit of advice particularly for older people that have been relatively inactive. Before starting any programme of significant exercise, getting a heart check might be a good idea. As far as losing weight is concerned, exercise though a useful 'adjunct' is of little use as a primary method for weight loss. It takes a lot of pretty strenuous physical activity to burn off the calories consumed in just one hamburger eaten without any fries, regular soda or a milk shake. When I say that exercise is a useful adjunct, of course moderate exercise does burn off some calories and also helps other systems by improving circulation of blood to all parts of the body and perhaps increasing how many calories the body burns during inactivity. Some investigations suggest that exercising or even a brisk walk is more beneficial if done on a relatively empty stomach. Dieting is the best to lose weight. Dieting requires self discipline. There are some diets in which you can eat as much as you want except for this or that food group. But few of these diets can be adhered to for any period of time and it is well known that once a diet is stopped, most dieters will regain the weight they lost while on the diet. So, most physicians and other health care professionals will always recommend dietary changes that can be sustained. The simple equation that comes to play in weight gain or loss is the number of calories consumed and the number of calories burned up. Average males or females require about fifteen hundred calories a day (does go up or down based on the body size) to sustain normal 'metabolic' processes in the body. What that means is that even at a state of perfect rest, our body is still functioning and burning calories. So, the only effective way to lose weight is to cut down on a number of calories consumed in a day. Starvation type diets are useless except for certain short term goals like being able to fit into a slim-cut wedding dress.

A good diet is not only helpful in losing weight or in maintaining weight loss but is also important for general health and prevention of some medical

problems. There is much confusion about what to eat or not to eat. First let me present two basic principles that I have mentioned before about a healthy diet. Firstly, eat whatever you want but mostly plants. Secondly, avoid food that your grandmother would not recognize as food. What the latter suggests is to avoid most 'pre-cooked food'. Of course a generation ago there were foods that were cooked are stored but unlike those today they did not contain preservatives besides salt, vinegar or sugar, and there were no flavor enhancers for taste improvement. In essence, all processed foods or pre-cooked foods that come from a store freezer that only need to be heated before being eaten should be mostly avoided.

Also some fats are better than others. In general, fats derived from plants are healthier than those derived from animals. However, some butter on toast, or 'ghee'(clarified butter) are all perfectly healthy if used sparingly. The same is true of 'red meat' as long as it is lean and the fat has been trimmed by the butcher.

Past dietary recommendations to avoid fatty foods led to an unintentional side effect. People starting consuming more starch to feel full. This is probably part responsible for the present epidemic of obesity and adult onset Diabetes (Type II) that we see in many countries including the United States. Fat and fatty foods including meat are better at making people feel full than starchy foods. So peostarch if they eat less fat.

Dietary recommendations suggest that whole grains like whole wheat are better than white flour. That processed meats (sausages, bacon) should be avoided, that red meat is fine as long as the fat has been trimmed, though white meat is probably better. That home cooked meals or freshly cooked meals are superior to those brought from a store and are pre-cooked. And animal origin fats are not dangerous if used in moderation though vegetable origin oils are better when used for cooking. The most important recommendation is that almost all traditional forms of foods that are a part of most cultural traditions are just fine as long as they are used in a varied diet and eaten in moderation. And that home cooked food is the best, but an occasional visit to a local restaurant or fast food outlet is quite alright. And chose whatever diet you want to that will help you lose weight but then stick with a basic simple diet plan that helps you keep the weight off.

Mean Platelet Volume and Thrombocytopenia as Hematological Predictive Indicator of Patients' Outcome in Medical Intensive Care Unit

Inayatullah Memon¹ and Hamid Raza²

ABSTRACT

Objective: The present study determined the predictive significance of mean platelet volume (MPV) and low platelet count (thrombocytopenia) as hematological indicator of patient outcome in medical intensive care units (ICU).

Study Design: Observational study.

Place and Duration of Study: This study was conducted at the Department of Pathology and Medical ICU, Indus Medical College Hospital, Tando Muhammad Khan, Sindh from April 2017 to March 2019.

Materials and Methods: Critical subjects admitted to medical intensive care units of the hospital were selected according to inclusion and exclusion criteria. A sample of 300 (n=300) patients was selected and analyzed to meet criteria of study. 5-10 ml of venous blood sample was collected for study parameters. Data was analyzed on SPSS 21.0 IBM, Incorporation USA at 95% confidence interval.

Results: Thrombocytopenia was noted in 70 (23%) and severe thrombocytopenia in 19 (6.3%) patients (P=0.0001). Thrombocytopenia and severe thrombocytopenia were noted in 14 (4.6%) of non- survivors vs. (1.6%) in survivors (P=0.0001). Normal and elevated MPV in survivors and non- survivors were noted in 195 (65%) vs. 40 (13.3%) and 14 (4.6%) vs. 51 (17%) respectively (P=0.0001). Platelet counts and MPV in survivors and non- survivors were noted as 378457±459 vs. 123153±366 (x10⁹/L) (P=0.0001) and 9.83±1.23 vs. 14.73±3.53 fl respectively (P=0.0001). ROC curve shows area under curve (AUC) of 0.913 (91.3%) (P=0.0001).

Conclusion: Thrombocytopenia and elevated MPV are useful hematological indicators to predict the poor patient outcome and mortality.

Key Words: Thrombocytopenia, Mean Platelet Volume, Intensive care unit.

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INTRODUCTION

Thrombocytopenia is a common hematological finding in intensive care units (ICU) admitted patients. Infectious such as the malaria and sepsis and non-infectious agents such as the drugs are known causative agents.¹ In addition to the platelet counts, the mean platelet volume (MPV) has currently researched parameter of prognostic significance in ICU patients.¹⁻³ MPV is a measure of platelet size, function and activation.³

In pathological conditions of accelerated platelet consumption, the MPV is found elevated. When platelets are consumed rapidly, it results in low platelet counts called the thrombocytopenia. Fresh platelets released from bone marrow in circulation have high MPV. Bone marrow released fresh platelets have large size, more dense granules and are physiologically active. The enzyme systems and metabolic reactions do occur rapidly in young platelets. For example, the content of platelet activator thromboxane A₂ (TxA₂) is very high in young platelets compared to older one. Recently, interest has been seen in research in platelet counts and MPV indices as simple indicators of patient outcome in ICU⁴⁻⁶ and brain stroke and myocardial infarction.⁷ In intensive care units admitted patients, the frequency of thrombocytopenia has been reported in range of 13 - 44%.⁸ Why the frequency of thrombocytopenia is high in intensive care unit admitted patients is not known. It is considered as multi- factorial in ICU setting. In majority of cases, it is not easy to reach to the proper exact cause. Malignancy, invasive catheters, sepsis, and medications such as the cephalosporin have been reported as causative agents of thrombocytopenia. Heparin, an anticoagulant, is a

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common cause of thrombocytopenia. This is called the heparin-induced thrombocytopenia (HIT). Many confounding factors are working together; hence pointing out the exact cause of thrombocytopenia is a challenging job. Thrombocytopenia and elevated MPV have been linked to high mortality in critically ill ICU patients.^{1,8,9} Platelet count $<150 \times 10^9/L$ is termed as thrombocytopenia; however; for ICU settings the cut point $<100 \times 10^9/L$ is considered as thrombocytopenia. Platelet counts $<50 \times 10^9/L$ is termed as severe thrombocytopenia.^{9,10} Because of bleeding tendency and thrombosis, the platelet counts considered a marker of survival and mortality among ICU patients.^{11,12} In critically ill ICU patients, the thrombocytopenia may cause bleeding, organ failure and mortality.^{10,13,14} A Korean study recently reported on the thrombocytopenia in the ICU as marker of poor patient outcome.¹⁵ A few studies are available from developing countries such as Pakistan. This prompted the researchers to analyze the frequency of thrombocytopenia and mean platelet volume (MPV) in critically ill ICU patients and their effects on the patient outcome in medical intensive care units at our tertiary care hospital.

MATERIALS AND METHODS

The present observational study was conducted at the Department of Pathology and medical ICU, Indus Medical College Hospital, Tando Muhammad Khan, Sindh. The study covered duration of 2 years from April 2017 to March 2019. Critical subjects admitted to medical intensive care units of the hospital were selected according to inclusion and exclusion criteria. Both male and female, adult age and suffering from sepsis were included. Those having history of aspirin intake, smoking and in moribund condition were excluded. A sample of 300 patients was selected and analyzed to meet criteria of study. Patients were divided into 2 groups according to the platelet counts. Group 1- was defined as normal platelet counts (normo-thrombocytosis) and Group 2- was defined as low platelet counts (thrombocytopenia). Subjects who meet the inclusion and exclusion criteria were studied. Written consent was taken from the legal heirs of the patients. They were informed that the study will never inflict damage, even a tiny damage, to the patient. Self-willing volunteers were included in the study protocol. A signed consent was taken on a proforma in writing. Biodata of patients were taken including drug history. Medical history was asked by a medical officer and recorded in a pre-structured proforma. Medical officers strictly followed the inclusion and exclusion criteria. Participants were finally examined by a Consultant Physician. 5-10 ml of venous blood sample was collected from each participant. Age, gender distribution, body weight, BMI and systemic blood pressure were noted. Blood glucose, hemoglobin blood

urea nitrogen (BUN) and serum creatinine were detected by standard methods by a Consultant Pathologist. Blood glucose was estimated by "hexokinase" method. Blood was analyzed on hematology analyzer. Platelet counts $>150 \times 10^9/L$ was defined as normo-thrombocytosis and $<150 \times 10^9/L$ was termed the thrombocytopenia. For ICU settings the cut point of thrombocytopenia was taken at $<100 \times 10^9/L$. Platelet counts $<50 \times 10^9/L$ was defined as severe thrombocytopenia. Normal mean platelet volume (MPV) was taken as 8.5 – 11.5 fl.^{9,10} Institute's ethical permission was taken in writing. Confidentiality of patients Biodata and laboratory findings was maintained by keeping the record in lockers. Data was analyzed on SPSS 21.0 IBM, Incorporation USA. Statistical comparison between groups was carried by Student's t-test (numerical data) and Chi square test (categorical data). 95% confidence interval ($P \leq 0.05$) was taken statistically significant.

RESULTS

Demography characteristics of study subjects are shown in table 1. Age, gender distribution, body weight, BMI, hemoglobin and systemic blood pressure shows non-significant differences between Normo-thrombocytosis and thrombocytopenic subjects ($P > 0.05$). Blood glucose, blood urea nitrogen (BUN) and serum creatinine differed significantly between Normo-thrombocytosis and thrombocytopenic subjects ($P < 0.05$). Platelet counts and MPV differed significantly between survivors and non-survivors ($P < 0.05$) as shown in table 2, 3 and 4.

Table No.1: Characteristics and laboratory findings of study subjects (n=300)

	Group 1. Normo- thrombocytosis (n=230)	Group 2. Thrombocytopenia (n=70)	P-value
Age (years)	51.7±9.6	51.7±9.6	0.091
Male	123 (%)	37 (%)	0.078
Female	107 (%)	33 (%)	
Body wt. (kg)	83.5±12.5	84.3±13.7	0.90
BMI (kg/m ²)	30.67±3.45	29.7±4.5	0.93
Systolic BP (mmHg)	130.4±19.3	126.3±17.5	0.97
Diastolic BP (mmHg)	76.6±11.5	79.0±13.3	0.89
Blood Glucose (R) (mg/dl)	120.3±13.2	139.01±29.3	0.049
BUN (mg/dl)	11.9±0.73	15.03±0.70	0.023
Serum creatinine (mg/dl)	3.03±1.23	1.2±0.09	0.003
Hemoglobin (g/dl)	13.03±1.03	12.98±1.09	0.059
Platelet Counts ($\times 10^9/L$)	423457±256	70457±457	0.0001
MPV (fl)	10.3 ±1.45	15.73±3.23	0.0001

Normo-thrombocytosis and thrombocytopenia were noted in 230 (77%) and 70 (23%) of total 300 subjects respectively (P=0.0001). Of 70 patients, the severe thrombocytopenia was noted in 27% (n=19) patients.

Table No.2: Platelet counts among survivors and non- survivors (n=300)

	Survivors	Non-Survivors	Total	p-value
Normo-thrombocytosis	197 (65.6%)	33 (11%)	230 (77%)	0.0001
Thrombocytopenia	33 (11%)	18 (6%)	51 (17%)	
Severe thrombocytopenia	5 (1.6%)	14 (4.6%)	19 (6.0%)	
Total	235 (%)	65(%)	300 (100%)	

Table No.3: MPV among survivors and non-survivors (n=300)

	Survivors	Non-Survivors	Total	p-value
Normal MPV	195 (65%)	40 (13.3%)	235 (78.3%)	0.0001
Elevated MPV	14 (4.6%)	51 (17%)	65 (21.6%)	
Total	209 (69.9%)	91 (30.3%)	300 (100%)	

Table No.4: Platelet counts and MPV among survivors and non- survivors (n=300)

	Survivors	Non-Survivors	p-value
Platelet counts	378457±459	123153±366	0.0001
MPV	9.83±1.23	14.73±3.53	0.0001

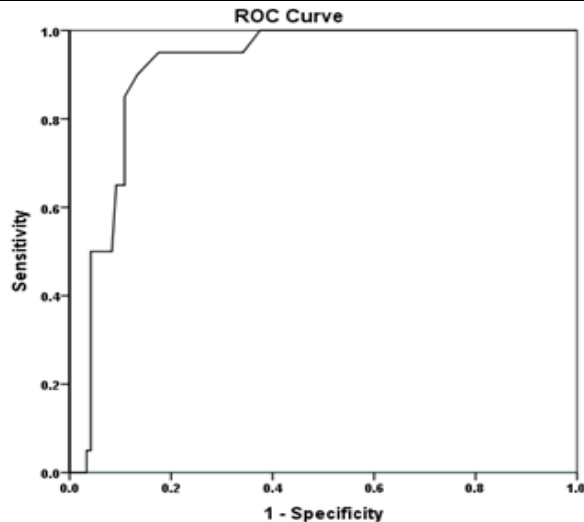


Figure No.1 Receiver Operating Characteristic curve as model of predictive.

Table No.5: Area Under the Curve

Test Result Variable(s): Predicted probability				
Area	Std. Error ^a	P-value ^b	95% Confidence Interval	
			Lower Bound	Upper Bound
0.913	0.026	0.0001	0.762	0.964

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Platelet counts in normo-thrombocytosis and thrombocytopenic were noted as 423457±256 and 70457±457 (x10⁹/L) respectively (P=0.0001). Mean platelet volume (MPV) in normo-thrombocytosis and thrombocytopenic was noted 10.3 ±1.45 and 15.73±3.23 fl respectively (P=0.0001) (table 4). Logistic regression model of MPV prediction of patient survival is shown in table 5. ROC curve shows area under curve (AUC) of 0.913 (91.3%) and highly significant P value (P=0.0001).

DISCUSSION

The present study determined the predictive significance of mean platelet volume (MPV) and low platelet count (thrombocytopenia) as a marker of patient outcome in medical intensive care units. The present study reports the thrombocytopenia and MPV as possible hematological indicator of patient outcome prognosis in ICU patients. The findings are in agreement with previous studies.^{1,2, 8,9} Above studies^{1,2, 8,9} reported the prognostic significance of thrombocytopenia. They reported that the thrombocytopenia is associated with increased mortality in ICU patients irrespective of the cause. In present study, thrombocytopenia was noted in 70 (23%) out of 300 subjects (P=0.0001) and severe thrombocytopenia in 19 (6.3%) patients (P=0.0001). Thrombocytopenia and severe thrombocytopenia were noted in 14 (4.6%) of non- survivors vs. (1.6%) in survivors (P=0.0001). The findings are in agreement with previous reported frequency of 13 - 44%.⁸ However, Fadaei et al² detected thrombocytopenia in 35% of patients that is inconsistent to present and previous studies.⁸ Thiery-Antier et al reported thrombocytopenia in 48.4% patients and severe thrombocytopenia (platelet count <50 × 10⁹/l) in 14.8% patients.¹⁶ Findings of Thiery-Antier et al¹⁶ are discordant to the present study; as thrombocytopenia was noted in 23% and severe thrombocytopenia in 19 (27%) patients. In present study, the Platelet counts in normo-thrombocytosis and thrombocytopenic were noted as 423457±256 and 70457±457 (x10⁹/L) respectively. The findings are in agreement with previous studies.¹⁷⁻¹⁹ that have reported platelet counts of similar range. In present study, the MPV was elevated to 15.73±3.23 fl in thrombocytopenic patients. Normal and elevated MPV in survivors and non-

survivors were noted in 195 (65%) vs. 40 (13.3%) and 14 (4.6%) vs. 51 (17%) respectively (P=0.0001). Platelet counts and MPV in survivors and non-survivors were noted as 378457 ± 459 vs. 123153 ± 366 ($\times 10^9/L$) (P=0.0001) and 9.83 ± 1.23 vs. 14.73 ± 3.53 fl respectively (P=0.0001). ROC curve shows area under curve (AUC) of 0.913 (91.3%) (P=0.0001). Logistic regression model shows high predictive value of MPV as marker of non-survivor (AUC=0.913) (P=0.0001). Elevated MPV of present study is in agreement with previous studies.³⁻⁷ The study by Kucukardali et al⁷ reported high MPV in ICU patients; however, they concluded that the MPV was not predictable of mortality that is in disagreement to present and previous studies.^{2,7,8} Huczek et al¹⁷ reported that the MPV was elevated in patients and correlated with age and hypertension in ICU patients. The finding of elevated MPV is in full agreement with the present study. Nalbant et al¹⁸ reported the MPV was elevated in variceal upper gut bleeding but the correlation was not found. Again, the finding of elevated MPV is in agreement to the present study. The present study included heterogeneous group of patients. To the best of knowledge, the present study is first time reporting on the thrombocytopenia and MPV from Pakistan in the ICU patients. We detected significant difference in thrombocytopenia and MPV values between the ICU survivors and non-survivors. MPV has emerged as a predictive risk factor for myocardial infarction and brain stroke¹⁹ and sepsis.²⁰ Kisacik et al²¹ reported the MPV values were high in active ankylosing spondylitis and rheumatoid arthritis patients compared to controls. Coban et al²² reported elevated MPV in familial Mediterranean fever (FMF) and concluded the MPV may indicate the increasing risk atherosclerotic in FMF patients. Yilmaz et al²³ reported that the platelet indices including MPV are of diagnostic and prognostic value in animals and humans beings with endotoxemia. Becchi et al²⁴ reported that the platelet count and MPV showed a correlation with during the course of sepsis when expressed as means and frequency distributions. We conclude that the low platelet count (thrombocytopenia) and elevated MPV may help to predict the patient outcome in ICU settings. The present study is a unique contribution to the medical literature that demands more future studies with large sample size. The limitations of present study are a small sample size, heterogeneous patients belonging to peculiar ethnicity, hence results cannot be generalized. We suggest both thrombocytopenia and high MPV may be used as a easy and inexpensive hematological predictive indicator of patient outcome in ICU patients.

CONCLUSION

Mean platelet volume and thrombocytopenia are the common hematologic abnormalities that might be considered as a prognosis monitor of patients' outcome

in ICU settings. Severe thrombocytopenia with elevated mean platelet volume may be useful indicator of poor prognosis and mortality. The simple, effortless and cost-effective hematological findings of platelet count and mean platelet volume should be extensively investigated to predict severity of the critical illness and patients' outcome in medical intensive care units.

Author's Contribution:

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Diagnostic Accuracy of Multidetector Computed Tomography (MDCT) in Evaluation of Varices in Cirrhotic Patients

CT in Detection Of
Esophageal Varices in
Cirrhosis

Abdul Sattar¹, Sadia Anjum¹, Saeeda Rana² and Nasreen Hamid³

ABSTRACT

Objective: To evaluate the diagnostic accuracy of Multidetector Computed Tomography in detection of esophageal varices in cirrhotic patients comparing with Upper GI endoscopy results.

Study Design: Observational study.

Place and Duration of Study: This study was conducted at the Department of Nishtar Medical Teaching Hospital from Oct, 2016 to Oct, 2017.

Materials and Methods: Total 172 patients with liver cirrhosis and portal hypertension (Portal vein diameter > 13mm) on ultrasound were included in the study. After unenhanced scanning, helical images were obtained during the hepatic arterial and portovenous phase. Negative oral contrast was given to all patients 30 to 45 minutes before examination. Endoscopic diagnosis of esophageal varices was obtained from medical record of the patients. Using SPSS-18, data was analyzed and diagnostic accuracy, positive predictive value, negative predictive value, sensitivity and specificity were calculated.

Results: 172 patients were included in study according to inclusion criteria. Patients mean age was 45.01±6.48 years with range of 25(35-60) years. Male patients were 55.81 % (n=96), and 44.18% (n=76) were female. The overall mean duration of disease was 43.82±12.55 months, with range of 45(19-64) months. MDCT scan was true positive for 126 and true negative for 23 patients. False negative were 23 and false positive only 3 patients. Diagnostic accuracy, positive predictive value (PPV), negative predictive value (NPV), sensitivity and specificity of MDCT were 84.88%, 97.61%, 50.00 %, 84.24%, and 84.46% respectively.

Conclusion: MDCT is a new non-invasive diagnostic modality with significantly high accuracy in diagnosis of varices in cirrhotic patients with portal hypertension that are comparable with upper GI endoscopy.

Key Words: MDCT, Upper GI Endoscopy, Varices, Portal Hypertension

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INTRODUCTION

Cirrhosis is the end stage of every chronic liver disease, resulting in fibrosis, disorganization of architecture and nodule formation that results in portal hypertension that is associated with ascites, hepatic encephalopathy and esophago-gastric varices.¹ Reported incidence of esophageal varices in cirrhotic patients has been 90 %.² In patients who survive after the initial variceal hemorrhage, a cascade of complications may be initiated that can include hepatic encephalopathy, spontaneous bacterial peritonitis and hepatorenal

syndrome. Therefore, identification of at risk individuals and subsequent prophylactic therapy is most important. Hemorrhage occurs in 25 to 40% of patient with cirrhosis and is associated with a 30% mortality rate. The larger the size of varices, higher the risk of hemorrhage.³

Patients with liver cirrhosis, undergo for esophageal screening by endoscopy due to significant mortality associated with varices bleeding.⁴ Moderate to large varices (≥5mm diameter), that are found in 30 % of cirrhotic patients on endoscopy had high risk of hemorrhage.

Endoscopic variceal ligation is indicated in large varices.⁵

Risk of variceal hemorrhage can be reduced by 50% with early diagnosis by screening that is why screening is recommended after first diagnosis by follow up. MDCT is less expensive, well tolerated and less invasive method of screening with high sensitivity and specificity in comparison with endoscopy that has limited compliance. Because of high prevalence of liver cirrhosis in our country with life threatening varices, we planned to conduct this study to evaluate the diagnostic accuracy of CT scan in detection of esophageal varices in cirrhotic patients.⁷

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MATERIALS AND METHODS

We conducted this study at Radiology Department of Nishtar Medical Teaching Hospital, Punjab including 172 patients from Oct, 2016 to Oct, 2017. Patients mean age, percentage of male and female were collected. Patients having liver cirrhosis with portal hypertension for one year were included in the study to determine the diagnostic accuracy of MDCT in detection of esophageal varices. After unenhanced scanning, helical CT images were obtained during the hepatic arterial phase. MDCT images were taken with a 7.5 mm slice thickness on 16 slice Toshiba scanner. All patients received negative oral contrast media over 45-60 minutes before examination. Endoscopic diagnosis of esophageal varices was obtained from the medical record of the patient.

Data was analyzed using computer program SPSS-18. Descriptive statistics were applied to calculate mean and standard deviation for quantitative variables. Frequencies and percentages were calculated for the qualitative variables. Sensitivity, specificity, PPV, NPV and diagnostic accuracy of CT scan was calculated. Effect modifier were controlled by stratification. Chi-square test was applied post stratification and p-value ≤ 0.05 was considered as significant.

RESULTS

Total 172 patients fulfilling inclusion criteria were included. Patients mean age was 45.01 ± 6.48 years with range of 25(35-60) years. Females were (n=76) 44.18% and 55.81% (n=96), were male. Mean duration of disease was 43.82 ± 12.55 months, with range of 45(19-64) months. MDCT scan was true positive for 126 and true negative for 23 patients. False negative were 23 and false positive only 3 patients. Among positive varices found on endoscopy, 57.7% were male and 42.3% were female. Diagnostic accuracy, positive predictive value (PPV), negative predictive value (NPV), sensitivity and specificity of MDCT were 84.88%, 97.61%, 50.00%, 84.24%, and 84.46% respectively.

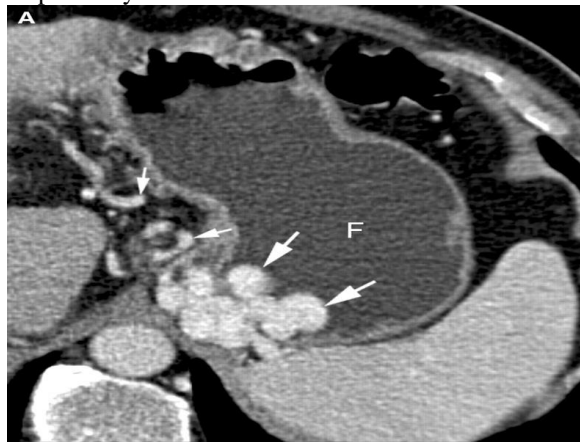


Figure No.1: Varices on Multi-Detector CT scan.

The stratification according to gender, age, and duration of disease was done and sensitivity, specificity and diagnostic accuracy were also calculated post stratification. Sensitivity among male was 83.4%, 85.5% among female patients, and 86.4% in patients of age ≤ 45 years. Post stratification association of outcome with age, gender, and duration of disease were calculated using chi square test considered $p \leq 0.05$ as significant. The results showed significant association with gender, age and duration of disease.

Table No. I: Diagnostic accuracy of ct scan in evaluation of esophageal varices in cirrhotic patients (n=172)

CT Findings	Endoscopic Findings		Total
	Positive	Negative	
Positive	True positive(a) 123 (71.51%)	False positive (b) 3 (1.74%)	a + b 126 (73.25%)
Negative	False negative(c) 23 (13.37%)	True negative (d) 23 (13.37%)	c + d 46 (26.75%)
Total	a + c 146 (73.25%)	b + d 26(15.11%)	172 (100%)

Accuracy = True +ve + True -ve / (True +ve+ True -ve/ False +ve+False -ve) x 100 = 84.88%

PPV = True +ve / (True +ve + False +ve) x 100 = 97.61%

NPV = True -ve / (True -ve + False -ve) x 100 = 50.00%

Sensitivity = True +ve / (True +ve + False -ve) x 100 = 84.24%

Specificity = True -ve / (True -ve + False +ve) x 100 = 88.46%

DISCUSSION

Significant morbidity and mortality associated with variceal bleeding justifies screening and surveillance of cirrhotic patients with portal hypertension. Upper GI endoscopy is invasive, expensive and have relatively poor compliance in routine clinical practice. MDCT angiography and capsule endoscopy are emerging noninvasive modalities for evaluation of esophageal varices.⁸ Cancer screening of patients with chronic liver parenchymal disease by MDCT has better diagnostic accuracy, compared with ultrasound as reported by several investigators, however it remains controversial.⁹ MDCT with 16 or more detectors providing isotropic or near isotropic data sets that enables multiplanar details. With the use of high resolution techniques, comparable results were obtained in detection of esophageal varices against upper GI endoscopy. MDCT imaging show high potential to detect or exclude the presence of esophageal varices in cirrhotic patients. MDCT imaging in cirrhotic patients has significantly high positive predictive value (PPV) in detecting esophageal varices (97.6%), along with an impressive negative predictive value (NPV) in excluding clinically significant esophageal varices (50%).¹¹ Detection of

esophageal varices was high i.e. 84.3% and 88.5% as sensitivity & specificity respectively in our study in comparison with Kim et al. who reported that the overall sensitivity of MDCT for detecting esophageal varices of any size were less than 70% due to poor detection of small varices; however sensitivity for large varices was very high (92%). High detection rate of varices by MDCT is clinically much important, as the ultimate goal of screening for esophageal varices is to decrease morbidity and mortality due to variceal bleeding.¹² CT size criteria (4mm) for differentiation of high-risk varices was used as an effective threshold in our study, comparing with 5mm used by Perri et al. as Cut-Off¹³. In our study male patients were more than female patients. Most of the patients were of age <45 years. Endoscopy found 84.90% varices among them most were male patients. Sensitivity of CT scan among male was 83.4% and 85.5% among female patients. Furthermore, significant association was observed in diagnostic accuracy of CT after the stratification with respect to age, gender and duration of disease at 5% level of significance.¹⁴ Results of our study support the need to develop a sensitive and non-invasive method of accurately detecting the presence of esophageal varices. Additional benefit of evaluating images obtained for another purpose is to reduce risks of radiation exposure and no additional costs would be incurred. Additional clinical information would be given to the clinicians in a given patient with cirrhosis.^{15,16}

CONCLUSION

Our results have demonstrated that routine liver MDCT allows the evaluation of the presence and grading of esophageal varices. As the accuracy of esophageal varices with clinically relevance on liver MDCT is good, even as detected by endoscopists. MDCT imaging which is highly acceptable to patients prove to be cost-effective and suitable promising tool for screening of esophageal varices in cirrhotic patients.

Author's Contribution:

Concept & Design of Study: Abdul Sattar
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 Data Analysis: Saeeda Rana, Nasreen Hamid
 Revisiting Critically: Abdul Sattar
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Frequency of Metabolic Syndrome in Patients with Hypertension

Bilal Habib¹, Shoaib Ahmed², Imran Aftab³, Raza Farrukh⁴, Ali Zulqernain⁵ and Moizza Sahar⁶

ABSTRACT

Objective: To determine the frequency of metabolic syndrome among the hypertensive patients reporting in the outpatient department of a tertiary care hospital.

Study Design: Cross-sectional study.

Place and Duration of Study: This study was conducted at the Medical OPD of General hospital, Lahore. The present study was conducted from June 2017 to December 2017 over a period of six months.

Materials and Methods: Adult known hypertensive patients of age between the ages 19-50 years were included in the study. The patients satisfying the selection criteria of study were incorporated in the study after informed written consent. Physical examination and laboratory investigations were carried out where required. The data was analyzed using SPSS version 16. Mean \pm standard deviations (SD) were recorded for quantitative variables while frequencies were obtained for qualitative variables. The level of significance marked by p-value was determined using independent sample t-test and Chi square test respectively. The p-value of ≤ 0.05 was considered significant.

Results: A total of 156 known cases of hypertension were enrolled in the study which included 57(36.54%) males and 99(63.46%) females. The patients were screened for MS using the Adult Treatment Panel III-A (ATP-III-A) criteria. Their blood pressure and waist circumference were recorded and fasting blood samples were drawn to measure serum glucose, HDL-cholesterol and triglyceride levels. MS was found in 65.38% (n=102) patients while 34.36% (n=54) patients did not fulfill the ATP-III-A criteria for MS.

Conclusion: MS is highly prevalent among the hypertensive patients and almost two thirds of the study population was found to have MS along with hypertension.

Key Words: Dyslipidemia, Obesity, Metabolic syndrome, Hypertension, ATP-III-A.

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INTRODUCTION

Metabolic Syndrome (MS) is a disorder characterized by concurrence of several known cardiovascular risk factors like obesity, dyslipidemia, insulin resistance and hypertension¹. In 1998 World Health Organization (WHO) suggested the first modern definition of MS according to which insulin resistance manifested by

raised blood glucose or type II diabetes mellitus was the central pathology. Apart from insulin resistance, hypertension, dyslipidemia, elevated BMI (Body Mass Index) and increased urinary albumin excretion were among the other benchmarks of condition². Apart from insulin resistance, an individual with any two of the following features could be considered as a patient of MS:

- Blood pressure greater than or equal to 140/90 mm Hg or a patient taking anti-hypertensive drug/s.
- Plasma triglyceride level ≥ 150 mg/dl.
- High density lipoprotein (HDL) cholesterol less than 35mg/dl and 39mg/dl in males and females respectively.
- Body mass index (BMI) higher than 30kg/m² and/or waist/hip ratio (WHR) greater than 0.9 and 0.85 in males and females respectively.
- Urinary albumin excretion ≥ 20 μ g/min.

The Third Adult Treatment Panel of The National Cholesterol Education Program (NCEP ATP-III) suggested another criterion for the diagnosis of MS. According to this definition a patient is said to have MS if any three of the following five criteria are found in an individual:

1. Hypertension denoted by a blood pressure greater than 130/85 mmHg.

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2. Fasting blood sugar more than 110 mg/dl.
3. Central obesity marked by waist circumference of greater than 40 inches in males and 35 inches in females.
4. Fasting HDL-Cholesterol level of below 40 mg/dl in males and less than 50 mg/dl in females.
5. Fasting triglycerides level beyond 150 mg/dl.

This definition was modified by American Heart Association (AHA) later on and is well-known as the Adult Treatment Panel III-A (ATP III-A) criteria for defining MS. The only change in the criteria is that cutoff value of fasting blood sugar levels has been reduced to 100 mg/dl from 110 mg/dl³.

The dysfunctional adipose tissue and insulin resistance play an important role in the development and pathogenesis of MS. As a matter of fact the dysfunctional adipose tissue has a vital part in the progression of obesity that eventually leads to insulin resistance⁴.

Prevalence of MS is subject to variation depending upon the definition and criterion used for the diagnosis. It also varies with age, gender, race and ethnicity of the study population⁵. Regardless of the criteria used prevalence is high and increasing among the western people, which may be due to outbreak of obesity epidemic⁶.

Hypertension which is one of the components of MS may lead to various complications including renal parenchymal damage, peripheral vascular disease and left ventricular enlargement⁷. According to JNC VII (seventh report of Joint National Committee on prevention, detection, evaluation and treatment of high blood pressure) guidelines patient may be diagnosed as a hypertensive, if the systolic and diastolic blood pressures are beyond 140 mmHg and 90 mm Hg respectively. As per JNC VII data more than 50 million people in USA and above one billion worldwide are hypertensives⁸. This study was aimed at finding out the frequency of MS amongst the hypertensive patients in Pakistan. To the best of our knowledge no such data is available for Pakistani population.

MATERIALS AND METHODS

This was a cross sectional study conducted in medical outpatients department of General Hospital Lahore during from June 2017 to December 2017. The study population comprised of 156 subjects. The study included hypertensive patients were 19 to 50 year old belonging to both genders having hypertension. The purposive non-probability sampling technique was applied. The ATP- III-A criterion was used to diagnose the MS in these patients. They were divided in two groups depending upon the presence (Group A) and absence of MS (Group B) according to this criterion. The mercury sphygmomanometer was used to measure the blood pressure according to the standard procedure. The patients were ensured resting comfortably for more

than five minutes in supine or sitting position. It was recorded thrice and the mean value was recorded. The measuring tape was used to measure the waist circumference after the patients were asked to hold breath at the end of expiration. As per ATP- III-A, males with waist circumference more than 40 and females more than 35 were labeled to have met the criteria for metabolic syndrome.

RESULTS

This study comprised 156 patients with the age group of 19 to 50 years including males and females. They were cases of hypertension taking antihypertensive medicines. The informed consent was obtained from them. Personal information of the patient and history was taken. Clinical examination was done and observations were recorded. Metabolic Syndrome was found in almost two third of the study population (65.38%) as shown in Figure 1. The mean values of different parameters of MS and age were compared among the two groups as shown in Table 1. The mean age of patients in group A was 42.35 ± 6.28 years as compared to 42.00 ± 8.15 years in group B which was statistically non-significant ($p=0.766$). The mean \pm SD systolic blood pressure of group A patients was significantly higher than the group B patients and the value was 166.36 ± 29.50 mm Hg in comparison to 152.33 ± 15.39 mm Hg respectively with a p value of 0.031. However no significant difference in diastolic pressure of two groups was found and mean diastolic pressure of group A was 103.18 ± 16.77 mm Hg while that of group B was 100.00 ± 10.39 mm Hg with statistically non-significant p value of 0.42. As shown in table 3, the mean waist circumference of patients in Group A was 42.84 ± 4.01 inches in contrast to 40.14 ± 2.82 inches in group B patients with a highly significant p-value (<0.001). We observed that insulin resistance marked by fasting blood sugar level >100 mg/dl was also found to be significantly higher in group A (132.71 ± 50.31 mg/dl) than in group B (89.56 ± 7.36 mg/dl) having a highly significant p-value of <0.001 . It was observed in present study that the mean HDL-cholesterol levels of group A was 41.29 ± 5.09 mg/dl compared to 48.72 ± 4.78 mg/dl in group B (p-value <0.001). The mean triglyceride level was 205.03 ± 91.38 mg/dl in group A while it was significantly lower ($p<0.001$) in group B at 141.33 ± 33.95 mg/dl.

The frequency of MS was compared between two genders and the results are shown in Figure 2. It was observed that MS was more prevalent among female hypertensive patients. The frequency of MS among the male hypertensive patients was 47.36% as compared to 75.75% in the female hypertensives.

The mean values of study parameters were compared for quantitative differences between the two genders (Table 2). The mean age of the male participants of

present study was less (mean age = 40.63±7.63 years) as compared to females (mean age= 43.15±6.37 years) with a statistically significant difference (p=0.029). We could not find a significant difference in the systolic or diastolic blood pressure among two genders. The mean systolic pressure of male patients was 154.89±19.03 mm Hg compared to 155.83±21.82 mm Hg (p=0.374) while the mean diastolic pressure was 99.89±12.08 mm Hg in males and 103.33±10.73 mm Hg among females (p=0.893). The central obesity measured by mean waist circumference had non-significant association with gender i.e. 41.92±4.07 inches in males and 41.89±3.74 inches in females (p=0.960). The difference in mean fasting blood sugar of two genders was statistically non-significant with a p value of 0.49 and the level was 114.42±56.59 mg/dl and 119.70±38.34 mg/dl in males and females respectively. As show table 3, the statistical difference in the mean F Cholesterol level was highly significant between the two genders i.e. mean HDL-cholesterol of 42.05±4.71 mg/dl in males and 44.90±6.58 mg/dl in females (p=0.005).The mean triglyceride levels of the two genders were not significantly different i.e. 195.37±67.21 mg/dl vs. 175.85±89.27 mg/dl in males and females respectively (p=0.154).

Figure 3 shows the frequency of MS criteria in each group. As all the study participants were hypertensives, therefore no difference in the frequency of hypertension could be established between the two groups. The obesity criterion of MS denoted by the waist circumference was met by 88.24% patients in group A as compared to 72.22% participants from group B fulfilling the criteria with a non-significant p-value of 0.12. The most striking difference was in HDL-Cholesterol criteria. The ATP-III-A criterion for HDL was met by 76.47% subjects in group A while none of the patients in group B fulfilled the HDL criteria which was statistically a very significant difference (p<0.001). The frequency of triglyceride and fasting blood sugar criteria were remarkably different amongst the two groups. Almost two-thirds (67.75%) of group A patients met the criteria for both triglycerides and fasting blood sugar while only 11.11% patients of group B met the triglyceride criteria and none of the group B participants had the fasting blood sugar criteria fulfilled (p<0.001).

The observations of the study were recorded in MS word and Excel data sheet. The data was entered and analyzed by using SPSS (Statistical package for social sciences) version 19. The interpretation of the p - value was done as follows.

- p >0.05 Difference insignificant
- *p < 0.05 Difference significant
- **p < 0.05 Difference considerably significant
- ***p < 0.05 Difference very significant

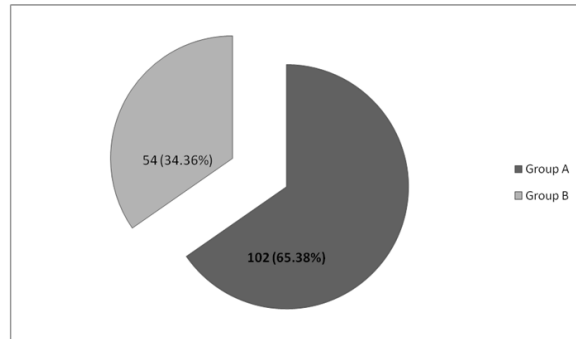


Figure No.1: Frequency of Metabolic Syndrome in the total study population (n=156)

Group A: Hypertensive patients with metabolic syndrome

Group B: Hypertensive patients without metabolic syndrome

Table No.1: Physical & Biochemical parameters of hypertensive subjects with and without metabolic syndrome

Parameter	Group A (n=102)	Group B (n=54)	p-value
Age (Years)	42.35±6.28	42.00±8.15	0.766 [†]
Systolic BP (mm Hg)	166.36±29.03	152.33±15.35	0.031*
Diastolic BP (mm Hg)	103.18±16.77	100.00±10.39	0.42 [†]
Waist Circumference (inches)	42.84±4.01	40.14±2.82	<0.001***
Fasting Blood Sugar (mg/dl)	132.71±50.31	89.56±7.36	<0.001***
HDL-Cholesterol (mg/dl)	41.29±5.09	48.72±4.78	<0.001***
Triglycerides (mg/dl)	205.03±91.38	141.33±33.95	<0.001***

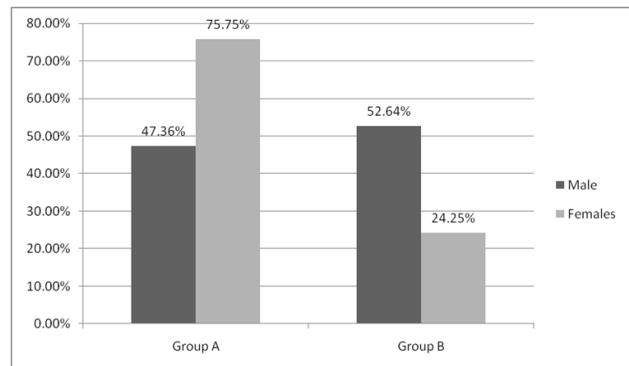


Figure No.2: Gender Distribution of Metabolic Syndrome

Values are expressed as percentages

Group A: Hypertensive patients with metabolic syndrome (n=102)

Group B: Hypertensive patients without metabolic syndrome (n=54)

Table No.2: Physical & Biochemical parameters of study subjects according to gender

Parameter	Males (n=57)	Females (n=99)	p-value
Age (Years)	40.63±7.63	43.15±6.37	0.029*
Systolic BP (mm Hg)	154.89±19.03	155.83±21.82	0.374†
Diastolic BP (mm Hg)	99.89±12.08	103.33±10.73	0.893†
Waist Circumference (inches)	41.92±4.07	41.89±3.74	0.960†
Fasting Blood Sugar (mg/dL)	114.42±56.59	119.70±38.34	0.490†
HDL-Cholesterol (mg/dL)	42.05±4.71	44.90±6.58	0.005**
Triglycerides (mg/dL)	195.37±67.21	175.85±89.27	0.154†
Leptin (ng/ml)	9.33 ±5.61	34.64±24.69	<0.001**
Cortisol (ng/ml)	458.95±214.0 9	454.44±191.4 8	0.824†

Values are given in terms of mean ± SD.

*significant at p< 0.05

**highly significant at p<0. 01

***very highly significant at p<0.001

†not significant

n is the number of patients

t test was applied to analyze the data

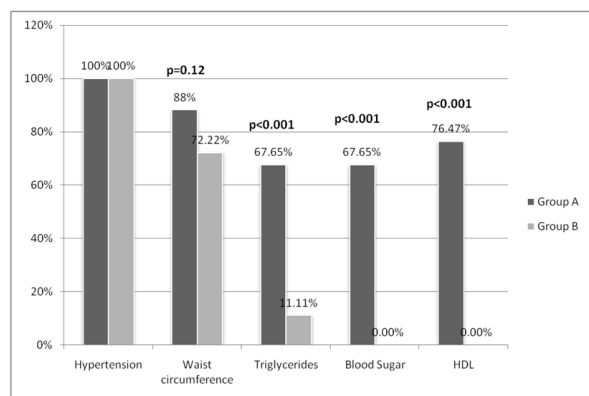


Figure No.3: Frequency of components of metabolic syndrome among study groups

Values are expressed as percentages

DISCUSSION

There is an alarming increase in the prevalence of cardiovascular diseases in recent years all over the world. Hypertension is considered as important risk factor for cardiovascular complications like cardiac failure and stroke⁸. Hypertension is one of the basic components of the metabolic syndrome along with obesity, insulin resistance and dyslipidemia¹. It also plays a key role in the pathogenesis of various features of metabolic syndrome⁹. The high frequency of MS is observed among the hypertensive patients in this study. It is supported by a recent survey showing high frequency in South Asian immigrants indicating their unique body structure and fat distribution¹⁰.

There is a report of prevalence of MS almost three times more in age group of 40 to 59 years than in other age groups and same is the finding of this study¹¹. The present study showed high frequency of MS among study groups that implies that hypertensives have more tendency of developing metabolic abnormalities than the general population¹².

The higher frequency of MS in females than males observed in this study is in accordance with the other studies already reported in the literature^{13,14}. Obesity is becoming more common in females than males all around the world especially in South Asian countries which is alarming. This may explain the higher frequency of MS in females than males¹⁵.

Central obesity indicated by the waist circumference is a component of MS showing close association with it. There is intimate relation of waist circumference and abdominal obesity leading to cardiovascular diseases. Ulas et al have also identified the central obesity as the most frequent component of MS. Waist circumference, a measure of adiposity has been found as one of the most important parameter useful in identifying the MS^{16,17}.

Comparing the individual parameters of MS between the two groups revealed that all the parameters including systolic blood pressure, waist circumference, dyslipidemia (low HDL-cholesterol and high triglyceride) and fasting blood sugar were significantly higher in the hypertensive patients with MS (group A) than the hypertensives alone (group B). The results of Hsu et al and Su et al also revealed a strong association of these parameters with MS among hypertensive patients^{18,19}.

However no significant difference was found in the diastolic blood pressure of two groups (p=0.42). Mule et al also had similar results with non-significant difference in the diastolic blood pressure of their study groups and the stronger association of systolic blood pressure with MS²⁰. Contrary to present result Khan et al reported a stronger association of diastolic blood pressure rather than the systolic blood pressure⁹. Thus the type of hypertension more strongly associated with MS in present study was systolic one although diastolic blood pressure was also higher in the MS group but statistically significant level was not reached. Both the systolic and diastolic blood pressures signify different disease processes leading to a common outcome that is hypertension.

The gender based comparison of the patients with MS (group A) showed that dyslipidemia manifested by

hypertriglyceridemia and low HDL-cholesterol was more profound among males, and statistically significant differences were present which was not in agreement with the observation of Beigh and Jain²¹. However this was in congruence with the observation of Hsu et al¹⁸.

The results of present study suggest that hypertensive patients should undergo regular clinical screening to prevent the development of MS and its hazardous outcomes. The general population should be educated for life style modifications to improve physical activity.

CONCLUSION

MS is highly prevalent among the hypertensive patients and almost two thirds of the study population was found to have MS along with hypertension.

Author's Contribution:

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 Revisiting Critically: Bilal Habib
 Final Approval of version: Bilal Habib

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

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Viral Hepatitis B and C in Hemodialysis Patients: A Study from Khyber Pakhtunkhwa, Pakistan

Mufti Baleegh-ur-Raheem Mahmood¹, Ahmad Zeb Khan¹, Najmuddin², Irfan Mirza³, Fazli Subhan² and Rahmat Ali Khan⁴

ABSTRACT

Objective: Viral hepatitis has high prevalence in hemodialysis dependent patients. We aimed to find the prevalence of viral hepatitis B and hepatitis C in hemodialysis dependent patients of Khyber Pakhtunkhwa (KPK), Pakistan. This study was also directed to assess the basic infection control measures practiced in different dialysis units of the region.

Study Design: Descriptive / cross-sectional study.

Place and Duration of Study: This study was conducted at the multiple hemodialysis centers of KPK, Pakistan, conducted from April 2017 to March 2018.

Materials and Methods: It was a survey of the hemodialysis patients in multiple hemodialysis centers of KPK. The study involved obtaining information from each dialysis center regarding the number of patients positive for viral hepatitis. Centers were also asked to report the measures adapted by them regarding infection control and monitoring of their patients.

Results: A total of 10 centers reported their data. Of the total population of 953 dialysis dependent patients, 169 (17.7%) patients were HCV positive, 31 (3.3%) patients were hepatitis B positive, and 08 (0.8%) patients were positive for both hepatitis B and C. Therefore a total of 208 (21.8%) patients were positive for markers of viral hepatitis B and C. Nine centers reported 03 monthly screening for viral markers but None of the centers reported using PCR based testing. Only 01 dialysis center reported adequate surface disinfection after each and every cycle. Majority of centers reported adequate internal machine disinfection practices (07 centers performing machine rinsing after every cycle of hemodialysis and 09 centers performing machine disinfection every day or every week). None of the centers reported re-use of dialyzers. Only 36 (55.4%) of the total 65 dialysis technicians working in these 10 centers were reported to be vaccinated against hepatitis B infection.

Conclusion: We conclude that our dialysis centers have a higher prevalence of viral hepatitis. Inadequate general infection control measures especially inadequate Surface disinfection can prove to be important risk factors for transmission of viral hepatitis among hemodialysis patients.

Key Words: Hemodialysis, End Stage Renal Disease (ESRD), Viral Hepatitis, Hepatitis B, Hepatitis C.

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INTRODUCTION

Infection caused by hepatitis B and C viruses is common in chronic kidney disease patients.¹

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These infection play an important role in the causation of kidney diseases. Hepatitis C is associated with Membrano proliferative Glomerulonephritis usually with Cryoglobulinemia, Mesangial-proliferative glomerulonephritis, Membranous nephropathy and Thrombotic microangiopathy.² Hepatitis B infection is also associated with renal diseases such as membranous nephropathy, Membranoproliferative glomerulonephritis, and polyarteritis nodosa which may involve renal vasculature.³ The adverse effect of viral hepatitis on mortality of hemodialysis patients is established for both viral hepatitis B and C virus.^{4,5,6}

Chronic kidney disease patients on maintenance hemodialysis are at a higher risk for developing hepatitis B and hepatitis C infection due to multiple risk factors including, frequent use of Intravenous injections, blood transfusions, surgical interventions, poor sterilization and sanitation practices of hemodialysis centers, and hemodialysis procedure

itself. Prevalence higher than that for general population is expected to be found in Hemodialysis dependent patients. Fissell et al sampled the population of the ‘Dialysis Outcomes and Practice Patterns Study’, which primarily included hemodialysis patients from developed world. They reported a mean prevalence for HCV of 13.5% in their multicenter data.⁷ In a second study from the same population, the mean prevalence of hepatitis B was 3.0% per center.⁸ Centers from South East Asia, Africa, and Middle East where viral hepatitis is more prevalent in the general population^{9, 10} were not included.

Studies in Pakistani hemodialysis population report prevalence figures of 12.4%¹¹ for HBV, and 23.7 to 68%^{12, 13} for HCV. The prevalence of viral hepatitis increases with the duration of hemodialysis as these patients are persistently exposed to the risk factors for acquisition of these viral infections.¹⁴

Considering implications of viral Hepatitis in patients with chronic kidney disease, it is desirable to develop epidemiological figures, ascertain causation, and to develop prevention and treatment strategies. This study was aimed to clarify the Prevalence of hepatitis B and hepatitis C infection in hemodialysis dependent population of Khyber Pukhtunkhwa (KPK), Pakistan.

MATERIALS AND METHODS

As there is no central record of hemodialysis centers and their patient population, the regional centers were contacted for the provision of their data. These centers were asked to include the data pertaining to their hemodialysis dependent patients, of all ages and both genders. A total of 10 centers agreed to provide their patient data for the purpose of this study. These centers included the following:

1. Institute of Kidney Diseases, Hayatabad Medical complex, Peshawar.
2. Department of Nephrology, Khyber Teaching Hospital Peshawar.
3. Department of Nephrology, Lady Reading Hospital Peshawar.
4. Dialysis Unit, Ayub Teaching Hospital. Abbottabad.
5. Dialysis Unit, Mardan Medical Complex. Mardan.
6. Dialysis Unit, Saidu Group of Hospitals. Swat.
7. Dialysis Unit, Kuwait Teaching Hospital. Peshawar.
8. Dialysis Unit, Alkhidmat Hospital. Peshawar.
9. Ittefaq Dialysis center, Peshawar.
10. Saidu Dialysis Center, Swat.

These centers constitute the majority of hemodialysis centers in our province. Six of these centers are government hospitals where hemodialysis is provided free of cost to the patients. These centers provide healthcare services to most of the population in their areas. Two of the participating centers are charity hospitals, again providing hemodialysis free of cost or

at subsidized rates. Two centers were private centers and operated on commercial basis. Therefore it is safe to assume that these centers catered to the majority of hemodialysis dependent patients in the province.

Data was collected over a period of one year, from April 2017 to March 2018, after the approval by the research and ethical committee.

Approval was obtained from the hospital research and ethical committee. All of these centers were asked to provide the data regarding the total number patients registered for Hemodialysis and the number of Anti-HCV-Ab and HBs-Ag positive patients being dialyzed at that center. This information was collected on a Performa. This proforma also contained questions pertaining to basic infection control measures.

RESULTS

A total of 10 centers responded to our request for submission of data. A total of 953 patients were being dialyzed at these centers.

Viral Prevalence: Off the total population of 953 dialysis dependent patients, 169 (17.7%) patients were HCV positive, 31 (3.3%) patients were hepatitis B positive, and 08 (0.8%) patients were positive for both hepatitis B and C. Therefore a total of 208 (21.8%) patients were positive for markers of viral hepatitis B and C. Table 1& Figure 1.

Table No.1: Prevalence of viral hepatitis b & c in hemodialysis dependent patients. Cumulative data from all ten centers

Patients negative for HBC & HCV	HCV positive patients	HBV positive patients	Patients positive for both HCV & HBV	Total patients positive for either or both HCV & HBV	Grand total of the number of patients. (total study population)
745 (78.1%)	169 (17.7%)	31 (3.3%)	08 (0.8%)	208 (21.8%)	953

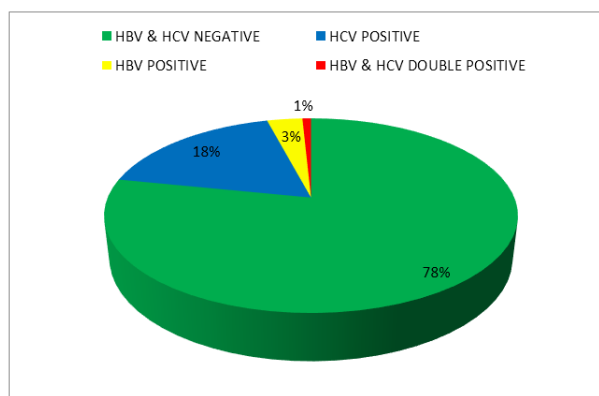


Figure No.1: Prevalence of viral hepatitis in hemodialysis dependent patients

Viral Testing: All the centers but one reported regular 03 monthly screening of their patients for viral

hepatitis. Six out of the total 10 centers were testing the viral serology using ICT based method, while 04 centers were utilizing ELISA based testing for viral screening. None of the centers reported using PCR based testing.

Disinfection Practices: Participating dialysis centers were asked about their practices of SURFACE DISINFECTION of machine and other patient contact surfaces. Only 01 dialysis center reported surface disinfection after each cycle. Five centers reported the surface disinfection after every duty shift, while the remaining 04 centers were performing surface disinfection once daily or once weekly.

Regarding dialysis machine rinsing, 07 centers reported machine internal rinsing after every cycle while in the remaining 03 centers the dialysis machines were rinsed after every 08 hourly shifts.

Regarding machine internal disinfection, 01 center reported machine disinfection after every shift, while the remaining 09 centers were performing machine disinfection every day or every week. Figure 2.

None of the centers reported re-use of dialyzers.

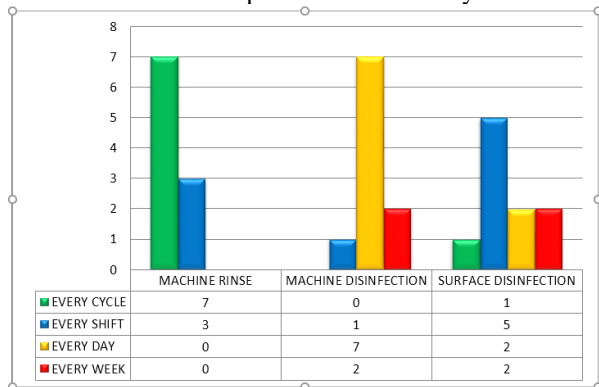


Figure No.2: Hemodialysis machine and surface disinfection practice

Staff Protection And Infection Control: These dialysis centers were asked about basic infection control measures including hand hygiene, eye protection, gowns and gloves. Seven out of 10 centers reported observing infection control measures. A total of 65 dialysis technicians were working in these 10 centers and only 36 (55.4%) were reported to be vaccinated against hepatitis B infection.

DISCUSSION

This survey aimed to determine the prevalence of viral hepatitis B and C in our local hemodialysis population. The total prevalence for viral hepatitis B and C was 21.8%. HBV was found in 3.3% patients, HCV was positive in 17.7% patients, and 0.8% patients were found to be positive for both HBV and HCV sero-markers. As compared to the international figures of DOPPS study population of North America and Europe (HBV 3.0% and HCV 13.5%),^{7,8} the prevalence of viral

hepatitis (especially HCV), is significantly higher in our patient population.

Seroprevalence of HBV in Pakistani ESRD population is reported to range from 10.2 % to 14.6%.^{11,15,16} Thus, the prevalence of HBV of 3.3% in our hemodialysis population is significantly less than that mentioned by other authors from Pakistan. Such a high prevalence of HBV in some centers can be attributed to the selective referral of HBV positive patients for hemodialysis, as not all centers entertain HBV positive patients. Since in our study multiple centers across the province were included, the effect of selective referral of HBV positive patients to centers offering dedicated HBV positive machines is unlikely to affect our results.

The prevalence of HCV ranges from 23.7% to 68% in Pakistani ESRD patients.^{12,13,16} In a study by Khan et al Anti HCV antibodies were detected in 29.2% of their hemodialysis patients. In addition, 5.9% of patients who were initially negative for anti HCV antibodies were found to be HCV positive by PCR testing. Thus the total prevalence was in order of 35.1%.¹⁷ In another study, Zarkhoon et al found 23.7% of their hemodialysis dependent population to be anti-HCV positive.¹⁸ Thus in comparison the prevalence of HCV of 17.7% in our hemodialysis dependent population is less than that mentioned by other authors from Pakistan.

Studies of the general healthy Pakistani population yield the prevalence of HBV from 1.7 to 5.5%, and that of HCV from 2.52% to 5.4%.^{16,19} Azam et al concluded that the overall country wide prevalence of HBV was 4.5% and HCV was 3.2% in healthy population. Khyber Pakhtunkhwa (KPK) (former NWFP) had lower prevalence values as compared to the other provinces, 2.7% for HBV and 1.4% for HCV.²⁰ Other Studies primarily focusing on the local population of KPK have yielded similar conclusions. For HBV the prevalence ranges from 1.9-3.0% and for HCV this ranges from 2.2-3.19%.^{21,22} This can be one reason why in our hemodialysis patients the prevalence of viral hepatitis is less than other studies from other regions of Pakistan.

This leads to an interesting conclusion that the seroprevalence of HBV in our hemodialysis dependent patients is only slightly higher as compared to that of the general population in Pakistan while the prevalence of HCV in our dialysis dependent patients is significantly higher as compared to the general healthy population of Pakistan.

Majority of the centers reported regular 3 monthly screening of their patients for viral hepatitis which reflects the level of their concern. Kidney Disease Improving Global Outcome (KDIGO) guidelines²³ recommend initial testing for viral hepatitis serology with EIA (Enzyme Immunoassay) in low prevalence areas and nucleic acid test (NAT) in high prevalence areas. The same guidelines recommend 6-12 monthly monitoring of hemodialysis dependent patients using

the same test recommendations. Majority of our centers reported using immune-chromatography (ICT) based technique to screen and monitor patients for viral hepatitis infection. This is clearly not in compliance with the recommended guidelines. Our dialysis patients should be considered a high risk, high prevalence group. Therefore viral testing at our centers should ideally be NAT based instead of EIA or ICT based.

The care of dialysis machine involves cleaning of the external surfaces and internal machine circuits. The external cleaning and disinfection involves cleaning of all the surfaces with a detergent followed by disinfection with an intermediate level disinfectant such as Bleach or chlorine. It is recommended that this process should be performed after each and every dialysis cycle. This is because viruses and bacteria can live on machine surfaces for variable periods of time, notably HBV that can survive for up to one week in dried blood. The pressure transducer filters should be changed after each treatment cycle. Guidelines also recommend measures of internal machine disinfection. There is general consensus that routine disinfection of the machine internal pathways is not mandatory after each treatment as with single-pass machines the risk of transmission of infection is minimal. However in case there is a blood leak from the hemodialyser it is recommended that the machine should be disinfected before reuse. The internal machine pressure transducer port should also be disinfected if found to be contaminated. The United States Center for Disease Control Recommendations for Preventing Transmission of Infections among Chronic Hemodialysis Patients recommends that for single pass machines the rinsing and disinfection should be done once every day.

Indian guidelines recommend heat rinsing after every dialysis session, Citric Acid based chemical disinfection every day and Bleach based disinfection every month. In our study only one center reported surface disinfection after each and every dialysis session. Majority of centers were performing surface disinfection after each shift or once a day, which is clearly insufficient. This clearly shows the lack of education and the room for improvement in our dialysis practices. Regarding the internal disinfection, our centers reported that they were rinsing the machines after each dialysis cycle and were disinfecting their machines every shift or every day which suggests adequate internal machine disinfection practices.

Majority of centers claimed the application of staff protection and infection control measures such as, hand hygiene, use of masks, gloves, gowns, proper disinfection of patient contact surfaces and proper handling of waste materials and spills. Only about half (55.4%) dialysis technicians were vaccinated against Hepatitis B infection. This can be taken as an indirect marker of lack of safety measures of the dialysis staff. None of our centers reported Re-use of hemodialysers.

Although when appropriately handled, the dialyzer re-use has not been shown to be involved in the transmission of blood borne viruses and it is a cost effective measure; this practice is seldom performed in our dialysis centers.

CONCLUSION

We conclude that viral hepatitis is common in our local hemodialysis dependent patient population. The prevalence of HBV is only slightly higher than that of general population while the prevalence of HCV is significantly higher than that for our general population. When comparing to the international figures, our dialysis centers have a higher prevalence of both viral Hepatitis. We conclude that inadequate general infection control measures especially inadequate Surface disinfection can prove to be important risk factors for transmission of viral hepatitis among our hemodialysis patients.

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Diagnostic Accuracy of Lung Ultrasound in Diagnosis of Pediatric Pneumonia

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ABSTRACT

Objective: This study was designed to assess the accuracy of lung ultrasound (LUS) in the diagnosis of pneumonia in children in comparison to chest X-ray.

Study Design: Randomized controlled trial study

Place and Duration of Study: This study was conducted at the Pediatrics Medicine Ward, King Edward Medical University/Mayo Hospital, Lahore from August 2016 to February 2017.

Materials and Methods: A total of 282 patients fulfilling the inclusion criteria were enrolled and underwent clinical examination, chest radiograph (AP view, interpreted by a Paediatric radiologist blinded to the sonography results), lung ultrasound (by a pre-specified hospital radiologist) and blood sample analysis in the first 24 hours after admission. The accuracy of US in diagnosing pneumonia (i.e. its sensitivity, specificity, and positive and negative predictive values) was compared with that of chest radiographs

Results: A total of 48 patients had radiographically confirmed community acquired pneumonia (CAP). The sensitivity, specificity, and positive and negative predictive values of LUS in comparison with chest radiograph (CR) were respectively 95.5%, 90.0%, 99.6%, 42.8%.

Conclusion: LUS identified a significantly higher number of cases indicating that it's also a sensitive tool in comparison of chest radiography in the diagnosis of pneumonia in children although its effectiveness in determining the type of lung involvement requires further evaluation.

Key Words: Radiograph, Pneumonia, Ultrasonography, Lung, Worldwide, Predictive Values.

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INTRODUCTION

Pneumonia is a leading cause of death in children, having considerable impact on children mortality and morbidity globally¹. Community acquire pneumonia (CAP) is responsible for 150-160 million new cases each year and 1.1million die with this condition¹. Majority of these cases occur in developing countries like Pakistan. Studies show that 18% of total under five deaths worldwide are caused by Pneumonia².

As pneumonia is one of the major causes of lower respiratory infections in children, its diagnosis remains a challenge in resource limited settings³. Signs and symptoms of pneumonia vary depending on a child's age and the etiology of infection.⁴⁻⁷

Moreover, presenting signs and symptoms have poor diagnostic specificity, which may further complicate the diagnosis. The American Academy of Pediatrics recommends the use of chest radiographs (CRs) cautiously for different reasons. First, ionizing radiation in young children may have potential late adverse effects.⁸⁻¹⁰ Second, the lack of findings on CR does not rule out the diagnosis if there is a strong suspicion of pneumonia³. Finally, although a chest computed tomography (CT) scan has a higher diagnostic yield; it's never been used because of radiation hazard and also requires cooperative patient, sedation and in our setup availability and cost issue¹¹ Other disadvantages of both techniques as a tool for the diagnosis of pneumonia, especially in resource-poor settings, include availability and lack of portability. Even though CR is available, there can be a considerable time delay for between ordering and reporting of chestx-ray. Recently there is an increase in trend of using Lung ultrasound for the diagnosis of pneumonia because of its feasibility and accuracy in diagnosis and at the same time minimum radiation exposure. Advances in ultrasound technology have made lung ultrasound (LUS) an attractive option for the diagnosis of pneumonia. Moreover, it is safe, portable, inexpensive, and relatively easy to teach. With the current lack of worldwide diagnostic criteria, the diagnosis is usually made on clinical manifestations and findings from chest

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radiographs. Chest ultrasonography has recently been applied to the detection of pulmonary diseases. However, few evidenced based data have been published showing its effectiveness in detecting pneumonia in children. This study was designed to assess diagnostic accuracy of lung ultrasound (LUS) in diagnosis of pneumonia in children using chest X-ray as gold standard.

MATERIALS AND METHODS

This randomized controlled trial study was conducted at Pediatrics Medicine Ward, King Edward Medical University/Mayo Hospital, Lahore, from August 3, 2016 to February 3, 2017. 282 patients fulfilling the inclusion criteria were recruited. All patients underwent clinical examination, chest radiograph (AP view), lung ultrasound and blood sample analysis in the first 24 hours after admission. Chest radiograph was performed with commercially available X-ray machines. Chest radiographs were interpreted by a pediatric radiologist blinded to the sonography results. Lung ultrasound was carried out by pre-specified hospital radiologist.

Suspected Pneumonia was defined as presence of fever (>100 OF), cough, difficult breathing, fast breathing (respiratory rate > 30/mint), lower chest in-drawings or chest pain in a previously healthy child. Pneumonia on CXR was defined by presence of area of opacity on CXR. Pneumonia on LUS was defined by presence of sub pleural echo-poor or tissue-like structures on lung ultrasound

DATA ANALYSIS PROCEDURE:

Results were analyzed by SPSS version 23.0. Quantitative variables like age, weight and duration of illness were presented as Mean±S.D. Qualitative variables like gender, previous antibiotic treatment and pneumonia on lung ultrasound and chest X- Ray were presented as frequency and percentages. A 2x2 contingency was generated to calculate sensitivity, specificity, PPV, NPV and accuracy of lung ultrasound in diagnosis of pneumonia by taking chest X-ray as gold standard. Data were stratified for age, sex, weight, duration of illness and previous antibiotic treatment (during last 1 week) to address the modifier effect. Post stratification, 2x2 tables were computed to calculate sensitivity, specificity, PPV, NPV and accuracy of lung ultrasound taking chest X-ray as gold standard.

RESULTS

In this randomized controlled trial study 282 patients with clinical features of pneumonia were enrolled. Analysis of data on socio demographic variables of patients revealed that out of 282 participants, 60.3% were male and rest of the participant were female. Age range in this study was from 6 months to 12 years with mean age of 6.5±2.4 years. Majority of the patients 105(37.2%) were >6 years of age group. While 79(28.0%) and 98(34.8%) patients were between 6

months-2 years and 2-6 years of age groups respectively. Majority of the patients 105(37.2%) were >25 kg of weight group. While 79(28.0%) and 98(34.8%) patients were between 7-15 kg and 16-25 kg of weight groups respectively.

Majority of the patients 100(35.5%) were >10 days of duration of illness group. While 100(35.5%) and 82(29.1%) patients were between 3-6 days and 7-10 days of duration of illness groups respectively. Majority of the patients 225(79.8%) did not have history of antibiotic treatment. 273(96.8%) patients were diagnosed on Lung Ultrasound and 260(92.2%) on Chest X-ray. Sensitivity (Se), specificity (Sp), positive predictive value (PPV), negative predictive value (NPV), accuracy and prevalence of lung ultrasonography (US) vs. chest radiography (CR) in diagnosing pneumonia was 95.5%, 90.0%, 99.6%, 42.8%, 95.3% and 96.4% respectively.

Table No.1: Demographic Profile of the Patients Frequency Distribution of Gender, Age and Weight

		Frequency
Gender	Male, n (%)	170 (60.3)
	Female	112 (39.7)
Age	6 months - 2 years	79 (28.0)
	2-6 years	98 (34.8)
	>6 years	105 (37.2)
Weight	7-15 kg	79 (28.0)
	16-25 kg	98 (34.8)
	>25 kg	105 (37.2)

35.5% of patient's duration of illness was 3 to 6 days whereas more than 10 days' duration of illness was observed in 35.5% of patients as well.

Table No.2: Frequency of Distribution of Pneumonia on Lung Ultrasound and Chest X-Ray

		Frequency
Pneumonia on Lung Ultrasound	Yes	273 (96.8)
	No	9 (3.2)
Pneumonia on Chest X-ray	Yes	260 (92.2)
	No	22 (7.8)

96.8% of patients were having pneumonia on Lung Ultrasound while 92.2% of patients were diagnosed on chest X-ray.

Table No.3: Pneumonia on Chest and Lung

Pneumonia on Chest X-ray	Pneumonia on Lung Ultrasound		Total	Sn 95.5% Sp 90.0% PPV 99.6% NPV 42.8% Accuracy 95.3% Prevalence 96.3%
	Yes	No		
Yes	260	1	261	
No	12	9	21	

Table No.4: Stratification with Respect to Age Groups of Lung Ultrasound Vs. Chest X-Ray in Diagnosing Pneumonia

Age Groups	Pneumonia on Chest X-ray	Pneumonia on Lung Ultrasound		Total	
		Yes	No		
6 months - 2 years	Yes	75	1	76	Sn=98.6%, Sp=66.6%, NPV=66.6%, PPV=98.6%, DA=97.4%
	No	1	2	3	
2-6 years	Yes	90	0	90	Sn=95.7%, Sp=100.0%, NPV=50.0%, PPV=100.0%, DA=95.9%
	No	4	4	8	
>6 years	Yes	95	0	95	Sn=93.1%, Sp=100.0%, NPV=30%, PPV=100.0%, DA=93.3%
	No	7	3	10	

DISCUSSION

The diagnosis of pneumonia, once thought to be accomplished by physical examination, history-taking, and specific findings on auscultation, has recently relied more on imaging. Chest radiography has been widely used for the diagnosis of pneumonia because of its convenience and ease of access. However, some studies have shown significant variability in the interpretation of chest radiographs² as well as the risk of the development of cancer after radiation exposure in early life³. Although the lung is not an ideal target for ultrasonography, once fluid or solid material has accumulated in the lung it can more easily be visualized on an ultrasound scan⁴. Some studies have focused on the use of LUS in the diagnosis and follow up of community-acquired pneumonia in adults. Reissig et al reported the first prospective study of the diagnosis of community-acquired pneumonia using LUS with an excellent sensitivity of 94% and specificity of 98%^{5,6}. In our study, the detection of pneumonia using LUS was better (96.8%) than with chest radiography (92.2%). In a prospective study published by Urbanowska et al LUS had a sensitivity of 93.4% and PPV of 95.3% in identification of lung involvement⁶. A meta-analysis including 8 prospective studies performed in neonates and pediatric population and enrolling 765 children showed that LUS had an overall sensitivity of 95% (95%CI: 94-97), positive likelihood ratio of 15.3 and negative likelihood ratio of 0.06 for the presence of pneumonia as diagnosed based on clinical criteria and radiographic findings. Esposito et al. in Milan, Italy in a cohort of 103 patients showed sensitivity and specificity of 97.9% (48/49) and 94.5% (55/58) for

LUS compared with 92.1% (47/52) and 94.5% (52/55) for chest radiograph respectively, CXR was gold standard in this study.⁷ Chieh HO et al. in Taiwan showed that LUS was sensitive in detecting consolidation was found to be useful for follow up of consolidation avoiding the unnecessary radiation exposure associated with chest radiograph.⁷ Various other studies found similar results in favor of LUS⁸⁻¹⁰. There are no local studies conducted in this regard so far. In a study done by Shah et al, Sensitivity and specificity of LUS showed as 86% and 89% respectively¹⁰.

LUS is also a useful tool in the follow up of patients with pneumonia and it could be used to estimate the pneumonia size semi quantitatively^{5,11,12}. However, the true pneumonia size estimated by LUS was always underestimated as a result of distal multiple amplification artifacts or air inclusions. Not only can the size of pneumonia be measured by LUS, but a decreased air bronchogram and the volume of pleural effusion compared with baseline can also indicate remission of the disease¹¹. For these reasons, we can monitor the progress of the disease in patients and guide our treatment by repeating LUS within a few days¹¹. The major strength of this study is that an unexplored variable was measured and prospective nature of the study justifies the linear temporal relationship necessary for causation. A standardized questionnaire and ultrasound system were used.

CONCLUSION

This study concludes and provides evidences that for the diagnosis of pediatric pneumonia, lung ultrasound appears more effective than chest x-ray. It is also useful in following up the progress of pneumonia. LUS can be used as a complementary tool to chest radiography in the diagnosis of pneumonia in children.

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Determine the Outcomes of Bailout Thrombectomy in Patients Undergoing Primary Percutaneous Coronary Intervention

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ABSTRACT

Objective: To determine the clinical outcomes of patients who received bailout thrombectomy for primary percutaneous coronary intervention.

Study Design: Observational / cross-sectional study.

Place and Duration of Study: This study was conducted at the Department of Cardiology, Bolan Medical Complex Hospital Quetta from July 2018 to December 2018.

Materials and Methods: Two hundred patients of both genders undergoing primary percutaneous coronary intervention were analyzed in this study. All patients were divided into two groups. Group A comprised 100 patients and received PPCI with bailout thrombectomy and Group B comprised 100 patients and received primary percutaneous coronary intervention alone. Outcomes such as mortality, re-infarction, heart failure, cardiogenic shock, renal impairment, excess bleeding, post procedure stroke and hospital stay were examined and compare between both groups.

Results: In Group A, there were 53% males and 47% females with mean age 56.45±10.88 years. In Group B 55% were males and 45% were females with mean age 58.35±9.23 years. In Groups A there were more diabetic patients 45% than Group B 32% (p-value 0.005), Group B had more smokers 60%. There was a significant difference between group A and B regarding family history of coronary artery disease 35% vs 20% (p=0.003). In Group A, 3% patients were died and in Group B 2% patients were died with no significant difference. Group A patients had more renal impairment 9% vs 5% and stroke 3% vs 1% than Group B. Hospital stay was high in Group A patients 7.12±2.05 vs 5.34±1.02 days.

Conclusion: Patients received bailout thrombectomy for percutaneous coronary intervention had high rate of comorbidities. There was no significant difference in term of mortality between both groups. However, patients with bailout thrombectomy had more renal impairment and post-procedure stroke.

Key Words: ST-segment elevated myocardial infarction, Bailout thrombectomy, PPCI, Outcomes

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INTRODUCTION

Globally, acute myocardial infarction is one of the leading causes of morbidity and mortality in cardiac patients and acute coronary artery thrombosis is the major cause of ST-segment elevated myocardial

infarction.¹In these patients aspiration thrombectomy for PPCI considered a useful management.^{1,2} Aspiration thrombectomy is mostly not useful procedure in patients who presented in the early hours after the event occur. Many of studies reported that aspiration thrombectomy had major adverse outcomes in patients presented in early hours.³ Patients presented late after the event occur the procedure aspiration thrombectomy considered a procedure of choice with better outcomes.^{3,4}

After the acute myocardial infarction myocardial blush grade and TIMI flow is a main predictor of mortality and morbidity. Routine aspiration thrombectomy during percutaneous coronary intervention in STEMI patients is associated to high rate of stroke.⁴⁻⁶Therefore, routine aspiration thrombus is considered not useful procedure in patients with ST-segment elevation.⁷ Aspiration thrombus is very effective with very low rate of mortality and cardiovascular morbidity in patients having TIMI thrombus grade>3. Thus, in this condition bailout thrombectomy considered an effective and useful procedure. Many of studies demonstrated that bailout

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thrombectomy for percutaneous coronary intervention had low mortality rate in patients having thrombus grade >3.⁷⁻⁹

MATERIALS AND METHODS

This cross-sectional study was conducted at Department of Cardiology, Bolan Medical Complex Hospital Quetta from 1st July 2018 to 31st December 2018. Two hundred patients of both genders with ages above 35 years presented with acute ST-segment elevated myocardial infarction undergoing percutaneous coronary intervention were included. Patients detailed demographic including, age, gender, residence, comorbidities such as diabetes mellitus, hypertension, smoking history and hypercholesterolemia, history of liver disease and renal disease were examined after taking informed written consent. Patients who were presented late after 24 hours with STEMI, those who required CABG and those with no consent were excluded. All the patients were divided in to two groups. Group A contains 100 patients and received PPCI with bailout thrombectomy and Group B consist of 100 patients and received primary percutaneous coronary intervention alone. Outcomes such as mortality, re-infarction, heart failure, cardiogenic shock, renal impairment, excess bleeding, post-procedure stroke and hospital stay were examined and compare between both groups. Data was analyzed by SPSS 20.0. Student t-test and chi-square test was used to compare the outcomes between both groups. Frequencies and percentages was obtained to analyze the values in tabulation form. P-value <0.05 was set as statistically significant.

RESULTS

In Group A there were 53% males and 47% females with mean age 56.45±10.88 years. In Group B 55% were males and 45% were females with mean age 58.35±9.23 years. There were 52% and 45% patients in Group A and B had rural residency while 48% and 55% patients in Group A and B had urban residency. In Group A 45% patients had diabetes mellitus while in Group B 32% had diabetes mellitus. Hypertension found in 35% in Group A and 32% in Group B. Hypercholesterolemia found in 60% and 59% in Group A and B. There were more smokers 60% in Group B than 38% in Group A patients. Liver disease found in 10% and 21% patients in Group A and B. History of renal disease found in 22% and 10% patients in Group A and B. There were no significant difference regarding previous history of coronary artery disease, myocardial infarction and percutaneous coronary intervention ($p=>0.05$). There was a significant difference between group A and B regarding family history of coronary artery disease 35% vs 20% ($p=0.003$) (Table 1). According to the clinical presentation we found 12% in Group A and 8% patients in Group B had cardiogenic

shock. 18% and 15% in Group A and B had Killip class >2 heart failure, 35% patients in Group A had early presentation within 12 hours while 65% patients had late presentation 12 to 24 hours. In Group B 33% patients had early and 67% patients had late presentation. No significant difference between both groups. 54% and 59% patients had anterior myocardial infarction and 36% and 27% patients had inferior myocardial infarction in Group A and B (Table 2).

Table No.1: Demographic information of the patients

Variable	Group A	Group B	P value
Age (years)	56.45±10.88	58.35±9.23	0.062
Gender			
Male	53 (53%)	55 (55%)	>0.05
Female	47 (47%)	45 (45%)	>0.05
Residence			
Rural	52 (52%)	45 (45%)	>0.05
Urban	48 (48%)	55 (55%)	>0.05
Comorbidities			
Diabetes	45 (45%)	32 (32%)	<0.05
Hypertension	35 (35%)	32 (32%)	>0.05
Hypercholesterol emia	60 (60%)	59 (59%)	>0.05
History of Smoking	38 (38%)	60 (60%)	0.001
History of CLD	10 (10%)	21 (21%)	0.024
History of renal disease	22 (22%)	10 (10%)	0.021
Cardiac Factors			
History of CAD	8 (8%)	7 (7%)	>0.05
History MI	9 (9%)	8 (8%)	>0.05
History of PCI	10 (10%)	11 (11%)	>0.05
Family history of CAD			
Yes	35 (35%)	20 (20%)	0.003
No	65 (65%)	80 (80%)	-

Table No.2: Clinical findings between both groups

Variables	Group A	Group B	P-value
Cardiogenic Shock	12 (12%)	8 (8%)	0.031
Class>2 HF	18 (18%)	15 (15%)	0.049
Early Presentation	35 (35%)	33 (33%)	>0.05
Late Presentation	65 (65%)	67 (67%)	>0.05
Myocardial Infarction			
Anterior	54 (54%)	59 (59%)	0.046
Inferior	36 (36%)	27 (27%)	0.033

In Group A 3% patients were died and in Group B 2% patients were died with no significant difference. Group A patients had more renal impairment 9% vs 5% and stroke 3% vs 1% than Group B. In Group A and B 5% and 4% patients had NYHA class IV heart failure. In Group A 3% patients found to have excess bleeding and in Group B 2% patients had excess bleeding. Re-

infarction found in 4% and 2% patients in Group A and B. Hospital stay was high in Group A patients 7.12 ± 2.05 vs 5.34 ± 1.02 days (Table 3)

Table No.3: Outcomes of procedure between both groups

Outcome	Group A	Group B	P-value
Died	3 (3%)	2 (2%)	>0.05
Renal Imp	9 (9%)	5 (5%)	0.04
Stroke	3 (3%)	1 (1%)	0.048
HF	5 (5%)	4 (4%)	>0.05
Excess Bleeding	3 (3%)	2 (2%)	>0.05
Re-infarction	4 (4%)	2 (2%)	0.049
Hospital stay (days)	7.12 ± 2.05	5.34 ± 1.02	0.02

DISCUSSION

Acute myocardial infarction is one of the most common cardiac disorders. In USA about 0.6 million people found to have myocardial infarction categorized as STEMI.¹⁰ Every year 0.12 million people have undergo percutaneous coronary intervention.¹¹ Present study was conducted aimed to examine the outcomes of percutaneous coronary intervention with bailout thrombectomy in patients presented with ST-segment elevated myocardial infarction. In this study we analyzed 200 patients whom were undergoing PPCI. We divided patients into two groups Group A and B. Group A consist of those patients who received bailout thrombectomy for PCI and Group B received PCI alone. We found that there were no significant difference regarding gender and age wise distribution between both groups. These results were similar to some other studies.^{12,13}

In present study we found that in Group A 45% patients had diabetes mellitus while in Group B 32% had diabetes mellitus. Hypertension found in 35% in Group A and 32% in Group B. Hypercholesterolemia found in 60% and 59% in Group A and B. There were more smokers 60% in Group B than 38% in Group A patients. These results were comparable to some other studies.^{14,15} In this study we found a significant difference between group A and B regarding family history of coronary artery disease 35% versus 20% ($p=0.003$). A study conducted by Alsaïdy¹⁶ reported no difference in term of family history of coronary artery disease.

In present study Group A patients had more cardiogenic shock and killip class >2 heart failure than the patients treated PCI alone. These results were similar to other study in which patients who received bailout thrombectomy for PPCI had increase rate of cardiogenic shock.¹⁷

In our study we found In Group A 3% patients were died and in Group B 2% patients were died with no significant difference. These results were similar to some other studies in which no major difference was

found in term of mortality between patients who received aspiration thrombectomy and patients who received PCI alone.¹⁸ We found that group A patients had more renal impairment 9% vs 5% and stroke 3% vs 1% than Group B. In Group A and B 5% and 4% patients had NYHA class IV heart failure. In Group A 3% patients found to have excess bleeding and in Group B 2% patients had excess bleeding. Re-infarction found in 4% and 2% patients in Group A and B. Hospital stay was high in Group A patients 7.12 ± 2.05 vs 5.34 ± 1.02 days. These results were comparable to international literature.¹⁹

CONCLUSION

Patients received bailout thrombectomy for percutaneous coronary intervention had high rate of comorbidities. There was no significant difference in term of mortality between both groups. However, patients with bailout thrombectomy had more renal impairment and post-procedure stroke. More patients had major bleeding and length of hospital stay was also high in patients who received bailout thrombectomy.

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Evaluation of Complications of Root Canal Treatment Performed by BDS Fresh Graduates

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ABSTRACT

Objective: This current case actually aimed at radiographic assessment of quality of RCT along with procedural and technical errors evaluation by free BDS fresh graduates during era of 2015 to 2018 at Dental OPD of different hospitals.

Study Design: Observational study.

Place and Duration of Study: This study was conducted at the Department of Oral Medicine, Avicenna Dental College Lahore from March 2017 to March 2019.

Materials and Methods: A chart was recorded to register record of RCT quality and its outcomes in 280 patients handled by fresh graduates. This case was performed at dental OPD of different hospitals, in which the root canal treatment outcome quality and shortcomings by BDS fresh graduates was judged.

Results: The results were recorded based on root canal obturation, its good adoption to root canal walls and obturated apex radiodensity ≤ 2 mm as compared to apex from radiograph of respected tooth. The root obturation that was not up to standard measurements were ended in root canal failures such as ledge formation, canal transportation, furcal perforation, instrument separation, strip formation, formation of voids and over and under filling of obturated material. It was estimated in case study that 87 patients (31.1%) had inadequate RCT whereas 193 (68.9%) patients were treated successfully by fresh graduates without any procedural defects.

Conclusion: It was finally concluded that RCT performed by an undergraduate student in 68 percent cases was adequate and without any technical and procedural errors, where as in 31.1 percent RCT was inadequate. The technical and procedural errors were mostly in molars and procedure that was not done adequately was obturation of root canal (under filling). The fresh graduates and final year students had same technical and procedural errors with no prominent differences.

Key Words: technical quality, dental, endodontics, procedural errors, education, dental graduates

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INTRODUCTION

In dentistry, there is significant importance of RCT with respect to tooth health and care¹. The quality from both technical and procedural aspect performed by fresh graduates & students has been demonstrated radiographically at Jordan, dental teaching centre². The dental students in turkey also performed RCT with

radiographic evidences. From studies that had done RCT in past, we came to know the fact that there was about >90% success rate if conditions were all controlled carefully^{3,4}. There was retrospective study performed to calculate success outcome regarding RCT in relation with 2000 cases done by endodontist, who was specialist in this field. There was decline in RCT success rate if case were allotted to general dentists by 40–65%⁵. The general public patients of Turkey were evaluated and their radiographic RCT view was assessed for quality and outcome. The decline in RCT success rate by general dentists was due to lack of proper educational program regarding RCT and self-confidence regarding procedures⁶. A study of endodontic treatment carried out in dental practice within the UK⁷. So, it is need of time to make efforts in dental educational training from both practical and theoretical aspects to improve the success rate of RCT in patients^{8,9}.

The technical errors in RCT can be accessed by radiograph easily and most commonly^{10,11}. The RCT of Japanese patients was accessed radio graphically especially the peri apical view. The judgment of canal

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obturation is very important from both procedural and technical aspect for successful RCT prognosis⁹. The quality of RCT accessed radio graphically done by fresh graduates & student.¹² In France regarding teaching centre indistry, the root canal fillings were accessed technically done by free BDS fresh graduates & students. There were involvements of many technical factors that decide the prognosis of RCT like distance of obturation material from apex, voids in obturated canal and final taper of obturated material in canal¹³. The RCT quality done by fresh graduates during dental training¹⁴. In Jordan, university, RCT on posterior was performed by fresh graduates & final year student by hand and rotary and its quality was judged. The ideal radiographic obturation include absence of voids, uniform obturated material filling and smooth taper of obturated material from coronal to apical end¹⁵. The shortening of 1mm of working length along with presence of apical periodontitis cause failure of RCT with success 14%¹⁶. The prognosis of RCT success was also effected by under and overfilling of obturation material¹⁷. The assessment on basis of apical periodontitis and RCT prognosis in population of Belarusian was charted. The other factors involve regarding RCT failure and poor prognosis were formation of ledge, fracture of instrument in canal, perforations especially apical one^{4,18}.

Several studies have reported the adequacy of RCT performed by undergraduate students as varying between 33% and 70%^{13,19}. Assessment of treatment quality and frequency of procedural errors will help improve educational programs and enhance health services¹⁴. Technical quality of root canal treatment of posterior teeth after rotary or hand preparation by fresh graduate final year students²⁰. Technical quality of root canal therapies performed by novice dental students in preclinical practice.

The endodontic course is offered to dental students in their third year of Bachelor of Dental Surgery. The whole endodontic course is divided between 30% training on extracted tooth and 70% on theory. Moreover, in fourth year (one semester) students were offered clinical course regarding RCT on patients that consists of 30% clinical and 70 theoretical. Both single and multi-rooted teeth were offered to students for complete practice. Each student was allotted with 3-6 numbers of cases that include either one or two molar, one or two premolar, and one or two incisors. The root canal treatment becomes the most important element of dental care course in final year and that must be performed under supervision of specialists.

MATERIALS AND METHODS

Between the time span March 2017 to March 2019, the RCT treatment was done by fresh graduate and final year students on 310 patients. The fourth year students did 131 patients and fresh graduates did 110 patient. A

chart was made based on RCT treatment outcome on patients.

The technique used in root canal obturation was step-back instrumentation technique with the help of 0.02 tapered stainless-steel k files. 2.5% sodium hypochlorite was used for irrigation and to wash rootcanals. The technique that was adopted for obturation of root canals was the lateral condensation. The bisecting-angle technique was used to have clear radiographic view of affected tooth.

2.2. Evaluation of complications of RCT

The assessment of RCT with respect to technical and procedural errors was done by different qualified endodontists with >7 years of experience in operative dentistry. There was appointment of few endodontists in case of disagreement. The endodontists set basic criteria for assessment of RCT like adequate and inadequate RCT. The adequate RCT include good root canal obturation with ≤ 2 mm canal obturation from the apex shown in radiograph along with smooth adoption and inadequate RCT include any kind of procedural and technical error that led to failure of RCT.

The complications regarding RCT performance were listed as errors that happened during access cavity formation, root canal instrumentation and canal obturation. In case of access cavity preparation, the most common error and mistake was furcal perforation that was detected by radiograph in case of multi rooted teeth. In case of instrumentation, ledges transportation, strip perforation, root perforation and instrument separation was most common. The ledge formation was detected radio graphically when root canal obturation deviates from its original canal route (especially happened in case of curved canal). when the obturated material radio graphically undesirably deviates from its original natural path, transportation said to occur. When obturated material undesirably identified in the distal and mesial root of mandibular molars or buccal root of maxillary molars in any root of other teeth strip perforation said to occur. If the obturated material extruded undesirably in the root area, root perforation said to occur. When radio opaque instrument segment found in root or peri apical region radio graphically. Instrument separation said to occur. The most common errors in obturation were voids, overfilling and underfilling. The voids could be detected in radiograph and can be seen visually seen in radiographs of roots. When root canal obturation material extended beyond apex radio graphically, overfilling said to take place and when root canal obturation was ≤ 2 mm then under filling said to occur.

2.3. Statistical analysis

IBM SPSS Statistics for Windows v20 (IBM Corp., Armonk, NY) was used to access and examine the case date statistically. $P < 0.05$ was marked as statistical significance. Statistically significant differences were calculated by using the chi-square tests regarding

technical and procedural error frequency among different too.

RESULTS

The technical quality of root canal obturation was accessed and recorded for 280 teeth. In all 310 cases, the root canal in teeth was performed by an free BDS graduate student during year March 2017 to 2019, at different OPDs. The distribution of root canal treated teeth according to academic level is shown by table 1 Table 1. At academic level, distribution of teeth are shown in table as

It was estimated that in 193 (68.9%) RCT patients ,root canal was successful with no technical and procedural errors and regarded as adequate ,whereas in 87 (31.1%), RCT treated tooth were ended in failed RCT and regarded as inadequate due to technical and procedural errors. There was success rate of 90 (68.7%) teeth and failure of 41 (31.3%) teeth by fourth year students and success rate of 103 (69.1%) teeth with failure of 46 (30.9%) teeth by final year with respect to RCT treatment.

Table 1. At academic level, the assessment of technical quality of treated teeth are shown in following table as

Table No.1: 3.2. Iatrogenic errors

Tooth type	Fourth year	Fresh Graduates	All students & Fresh Graduates
Upper incisor	29 (22.1%)	49 (32.9%)	78 (27.9%)
Lower incisor	7 (5.3%)	12 (8.1%)	19 (6.8%)
Upper premolar	19 (14.5%)	26 (17.4%)	45 (16.1%)
Lower premolar	17 (13.0%)	17 (11.4%)	34 (12.1%)
Upper molar	17 (13.0%)	15 (10.1%)	32 (11.4%)
Lower molar	42 (32.1%)	30 (20.1%)	72 (25.7%)
Total	131 (100)	149 (100%)	280 (100%)

The total frequency of procedural and technical errors was calculated as 31.1%. The procedural and technical errors in root canal treated teeth were mostly under filling of root canal, over filling of root canal, voids in obturation, broken instruments, apical perforation and root canal transportation with frequencies 49.9%; 24.1%; 12.6%; 9.2%; 2.3%; and 2.3%, respectively . Figure 1 shows the procedural error frequencies in all treated teeth.

3.3. Effect of academic level on frequency and type of procedural errors

The different patients were treated by Fresh Graduates and final year with 30.9% and 31.1% frequencies. The

most common error detected by fresh graduates and final year was under filling of root canal obturation with frequencies (51.2%) and (47.8%), respectively. The least frequent procedural error done was transportation and apical perforation by fresh graduates and final year students with frequencies 2.4% and 2.2%, respectively. The errors regarding lower incisors RCT treatment, fresh graduate did fewer errors than final year students. In both group of students of fourth and final year, there was no as such procedural error differences overall ($p > 0.05$) .The procedural errors and its frequencies done by fourth and final years students can be presented in tabular form.

3.4. Effect of tooth type on frequency and type of procedural errors

It was estimated from case study that maxillary incisors had the lowest technical and procedural error with respect to RCT (19.2%), whereas mandibular molars had highest (43.1%) as compare to other teeth maxillary molars with highest frequency ($p < 0.05$) of overfilling of canal obturation. In other teeth, technical errors frequency was same.

DISCUSSION

During the study, a dental study was conducted related to RCT success rate, its quality and complications due to failure by an undergraduate student. These results were recorded based on radiographic evidences especially periapical radiographs. Radiographs that showed root vision obstruction of tooth due to anatomical tooth structure or superimposition by other tooth were not included. This was done in order to get clear radiographic results with no doubts. The assessment of RCT quality from both procedural and technical aspect was done on basis of guidelines practised in Europe⁹. The root canal assessment was made radio graphically, performed by dental students of fourth and final year²¹. In a dental clinic RCT, assessment was made from technical aspect by undergraduate students. In the present report, about 68.9% were regarded as adequate RCT, without technical and procedural error. The outcome of this case somehow differs from the outcome of other reports where 13% to 60.4% of RCT were regarded as adequate²². In Pakistan, technical aspect of RCT by fresh graduates & students were assessed²³. The difference of opinion among different BDS colleges was thought due to difference in method, educational training, evolution criteria and number of patients treated. In current studies, about 31.1% of RCT cases were labelled as inadequate. This inadequacy might be because of procedural and technical errors in treatment. With respect to performance, the fresh Graduates and final year students were same as far as RCT success rate was considered. This thing clearly indicates that RCT success rate is not affected by academic grades. In Greece, the same results were filed by khabbaz⁹.

In the current scenario, the records showed that final year students were able to perform successful RCT in case of lower incisors as compare to fresh graduates. This outcome was due to large number of patients with lower incisors defected have been treated by final year students than fourth year students. Another thought might be inexperience of fresh graduates in treating lower incisors as compared to fourth year students at preclinical training.

The incidence of RCT failure in maxillary incisors were lower (19.2%). There was similarity of results in other case study also with this²¹. There was procedural and technical errors in RCT done by undergraduate students²⁴. The RCT was performed by BDS graduates on single rooted teeth and its quality was judged. The success rate of RCT in maxillary incisors was due to its anatomy and location (easy to access). Moreover, it was thought that success rate of RCT in maxillary incisors was due to repeated practice at preclinical levels. Lower molars exhibited the most procedural errors (43.1%). Other studies also showed similar results of inadequate RCT with respect to lower molars with large number of procedural errors.^{9,25} There was dental study conducted between success RCT outcome by rotary and hand instrumentation technique. This failure of RCT in mandibular molar is might be due to its complex anatomy or inadequate training at preclinical stage. So it is a need of time that experts should train students at best with respect to RCT of lower molars.

In the current scenario, the most common error was under filling of obturation (49.4%). This mistake by students was due to faulty measurement of working length (just radiographic alone) without the use of electronic apex locator that could help them in determining correct working length. From many retrospective studies, we came to know that electronic apex locators had success rate of 97%²⁶. The shaping and cleaning of canals was done by two basics techniques i.e. step-back technique (with the help of stainless steel k-files) and secondly, lateral condensation technique. The application of technique by k files from apical to coronal part could lead to injury and damage to original anatomy of root canal and mishaps like ledges, root canal transportation and blocking that could lead to inadequate cleaning and shaping the root canal and ultimately under filling of root canal²⁸. There was comparison made between step back RCT technique and 8-step method done by senior dentist. A case study was also carried out to note the prognosis of RCT by Ni-Ti rotary and between hand stainless steel files. The rotary is new technology in the world of dentistry and produce better prognosis of RCT success rate as compare to hand instrumentation because of its ability to maintain original curves of root canals of teeth²⁹. The computer tomography was used to made comparison between rotary and k file RCT. There was poor prognosis of RCT performed by

stainless steel k files as compare to canals obturated by Ni-Ti rotary because hand stainless steel instrumentation lead to more technical and procedural errors²⁵.

In the current scenario, the maxillary molars were most wrongly filled (overfilled) as compare to rest of teeth in mouth. Moreover, in contrast, other studies have reported the quality of root canal obturation of maxillary teeth to be better than that of mandibular teeth¹. Radiographic technical quality of root canal treatment performed by dental students at the Dental Teaching Center in Lahore. It is thought that, teeth were overfilled because of negligence in control of k files usage during cleaning n shaping that resulted in missing the apical stop. So, it is very important and need of present age that availability of specialists should be there for guidance to students at clinical and pre-clinical levels. More over training timings should be increased to improve technical and procedural RCT elements. So, it is very important to re access the quality of RCT by fresh graduates repeatedly in order to modify dental educational system and trainings at preclinical and clinical level.

CONCLUSION

In this report, it was finally concluded that RCT performed by an undergraduate student in 68percent cases was adequate and without any technical and procedural errors, where as in 31.1 percent RCT was inadequate. The technical and procedural errors were mostly in molars and procedure that was not done adequately was obturation of root canal (under filling). The fresh graduates and final year students had same technical and procedural errors with no prominent differences. So, suggestion is made to enhance and upgrade the dental study program at dental college. Moreover, their dental studies evaluation should be done at regular intervals in order to access the need of improvement in dental discipline at clinical n preclinical levels.

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Involved in Children Having Hematuria

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ABSTRACT

Objective: To find out pattern of presentation as well as factors involved in children with hematuria.

Study Design: Cross sectional study.

Place and Duration of Study: This multicentre center study was conducted at Children Hospital, Chandka Medical College, Larkana, Department of Paediatrics of Pir Syed Abdul Qadir Shah Jeelani Institute of Medical Sciences, Gambat, and Department of Pediatrics of Ghulam Muhammad Mahar Medical College and Hospital, Sukkur from Jan 2019 to June 2019.

Materials and Methods: A total of 152 children, aged 1-15 years, reporting in out-patient department or emergency department, having hematuria (> 5 red blood cells per high power field in centrifuged urine following a positive dipstick test) were enrolled in this study. Demographic data like age, gender, sign and symptoms, along with risk factors, clinical features and laboratory investigations were recorded on a predesigned proforma. Mean and standard deviation was calculated for quantitative variables while frequency and percentages were calculated for qualitative variables.

Results: Out of a total of 152 children, 87 (57.2%) were male and 65 (42.8%) female. Most children, 66 (43.4%) were between 1 and 5 years of age while 49 (32.2%) between 6 to 10 years and 37 (24.3%) between 11 to 15 years. Most common presentation of children with hematuria were recorded as fever in 89 (58.6%) followed by red or cola color urine 66 (43.4%) and hypertension in 57 (37.5%). Post streptococcal glomerulonephritis was noted to be the commonest finding as 63 (41.3%) children had that whereas urinary tract infection 36 (23.7%), renal stone (11.2%) and vesico ureteric reflux were some of the other most common conditions.

Conclusion: Age group of 1 to 5 years and male gender seem to be more common among children having hematuria. Fever as well as red / cola color urine seemed to be the commonest presentation. Post streptococcal glomerulonephritis and UTI were the commonest factors found.

Key Words: Fever, hematuria, hypertension, urinary tract infection.

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INTRODUCTION

Hematuria is considered a common problem amongst children and described as > 5 red blood cells (RBCs) per high power field in sediment from 10ml of fresh voided and centrifuged urine.¹ The prevalence of

hematuria is presented as less than 1 to 14% with differences among different communities.²

Hematuria can be distinguished as macroscopic or microscopic haematuria. Many children having isolated microscopic hematuria do not need urgent investigations. Blood found in urine, can have origin from any part of urinary tract while gross as well as microscopic haematuria can indicate major underlying etiology.^{3,4}

Urine analysis done by dipstick is an important initial medical assessment. It has been estimated that about 50% of the patients having hematuria possess some sort of underlying defect and 10% having microscopic hematuria have been noted to contain urologic malignancy.⁵

Hematuria can be symptomatic as well as asymptomatic, transient or persistent, isolated or linked with proteinuria or some other urinary tract disorders. In comparison to gross hematuria, asymptomatic microscopic hematuria seems to be 10 times more common.⁶ Hematuria along with proteinuria is rare but their presence at the same time points major renal abnormality. Red urine is not always indicative of

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blood coming in the urine as beetroot as well as blackberries can cause redness to blood color, whereas, drugs like rifampacin and medical states like hemoglobinuria and myoglobinuria can also be the reason of red color urine.^{7,8}

Hematuria is considered a frequent finding in primary as well as tertiary care settings. American Academy of Pediatrics (AAP) removed routine urine analysis from their recommendations, but still, paediatricians use screening of urine as a part of their practice.^{1,9} Not all presenting with hematuria have underlying renal abnormalities but persistent hematuria requires further assessment depending upon the history and initial evaluation. AAP has not endorsed annual assessment of urine using dipstick analysis in paediatric population but many countries including Japan, Taiwan and Korea recommend regular routine screening among paediatric population.¹⁰⁻¹⁵

Laboratory investigations assessing haematuria usually depend upon history and physical examination. Investigations like urinalysis, blood urea nitrogen, serum creatinine, hematological and coagulation profiles, urinary calcium excretion, serological testing, urine culture, radiological studies and renal biopsy help identifying underlying etiology of hematuria.¹⁴ This study was planned to find out pattern of presentation as well as factors involved in children with hematuria. The findings of this study will help paediatricians and general practitioners in early identification of this common problem amongst pediatric age group.

MATERIALS AND METHODS

This was a cross sectional study from Jan 2019 to June 2019. Three centers were the venues for this study including Children Hospital, Chandka Medical College, Larkana, Department of Paediatrics of Pir Syed Abdul Qadir Shah Jeelani Institute of Medical Sciences, Gambat, and Department of Pediatrics of Ghulam Muhammad Mahar Medical College and Hospital, Sukkur.

A total of 152 children, aged 1-15 years, reporting in out-patient department or emergency department, having hematuria (> 5 red blood cells per high power field in centrifuged urine following a positive dipstick test)⁴ were enrolled in this study. All those children using rifampicin or food like beetroot, berries and food dyes were not included. Children on renal dialysis and using anti-coagulation therapies were also not included as well. Informed consent was taken from parents or guardians of all the study participants. Approval from institutional ethical and research committees were sought for this study.

Demographic data like age, gender, sign and symptoms, along with risk factors, clinical features and laboratory investigations were recorded on a predesigned proforma. SPSS version 21.0 was used for data analysis. Mean and standard deviation was calculated

for quantitative variables while frequency and percentages were calculated for qualitative variables.

RESULTS

Out of a total of 152 children, 87 (57.2%) were male and 65 (42.8%) female. Overall, mean age of the children studied was recorded to be 7.43 years with standard deviation of 3.39 years. Most children, 66 (43.4%) were between 1 and 5 years of age while 49 (32.2%) between 6 to 10 years and 37 (24.3%) between 11 to 15 years. There were 97 (63.8%) children who belonged to urban areas whereas 55 (36.2%) from rural areas.

Table No.1: Distribution of Gender, Age and Area of Residence Among Children With Hematuria

Study Variables	Number (%)	
Gender	Male	87 (57.2%)
	Female	65 (42.8%)
Age	1-5	66 (43.4%)
	6-10	49 (32.2%)
	11-15	37 (24.3%)
Area of Residence	Urban	97 (63.8%)
	Rural	55 (36.2%)

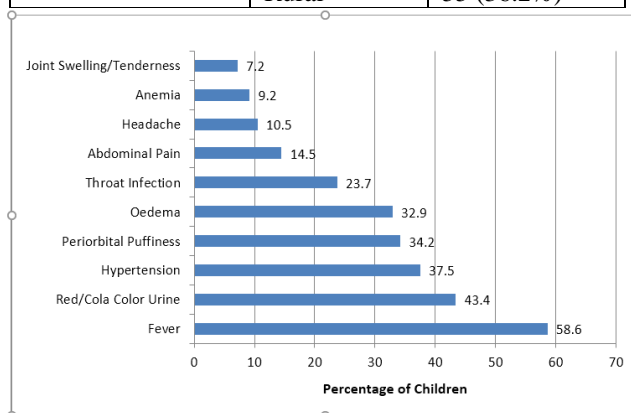


Figure No.1: Sign and Symptoms amongst children having Hematuria (Some sign and symptoms were overlapped)

Table No.2: Factors Associated With Hematuria Among Children

Clinical Condition	Number of Children (%)
Post Streptococcal Glomerulonephritis	63 (41.3%)
Urinary Tract Infection	36 (23.7%)
Renal Stone	17 (11.2%)
Vesico Ureteric Reflux	14 (9.2%)
Systemic Lupus Erythematosus	11 (7.2%)
Chronic Renal Failure	7 (4.6%)
Henoch Schonelon Purpura	5 (3.3%)
Atypical Nephrotic Syndrome	5 (3.3%)

Most common presentation of children with hematuria were recorded as fever in 89 (58.6%) followed by red or cola color urine 66 (43.4%) and hypertension in 57 (37.5%). Figure No.1 shows spectrum of presentation in children reporting with hematuria.

Table No.2 shows number having factors associated with hematuria. Post streptococcal glomerulonephritis was noted to be the commonest finding as 63 (41.3%) children had that whereas urinary tract infection 36 (23.7%), renal stone (17 (11.2%) and vesico ureteric reflux were some of the other most common conditions.

DISCUSSION

In children having microscopic or gross hematuria, initial visits of to clinicians with up to date knowledge about epidemiology and factors involved, can certainly lead to better management. It has also been advocated that early diagnosis of hematuria can prevent extra investigations as well as interventions.¹⁵

In the current work, most children, 87 (57.2%) were male and 65 (42.8%) female. Overall, mean age of the children studied was recorded to be 7.43 years with standard deviation of 3.39 years. Most children, 66 (43.4%) were between 1 and 5 years of age while 49 (32.2%) between 6 to 10 years and 37 (24.3%) between 11 to 15 years. A study conducted by Ahmed S et al from Lahore⁴ noted the mean of children having hematuria as 7.64±4.45 years which is quite close to which we noted. In the same study, the researchers noted an overall male predominance amongst children as male to female ratio of 1.2:1. A study conducted by Orta N et al² also noted the mean age of children with hematuria as 7.7±6.1 years which is again close to our findings. They also noted that age less than 5 years was the most common (40%) group amongst children. Gupta S and colleagues¹⁶ also got age 2 to 6 years as the most common age group amongst children.

In the present study, we found that 94 (61.8%) children were having microscopic hematuria where detection was based on dipstick and confirmation was done by analyzing urine sediment. Korean School Screening Program revealed that 50% of the children had microscopic hematuria.¹⁷

In the present work, most common presentation of children with hematuria were recorded as fever in 89 (58.6%) followed by red or cola color urine 66 (43.4%) and hypertension in 57 (37.5%). Ahmed S et al⁴ also noted fever to be the commonest complaint, noted in 54.7% children with hematuria whereas red or cola color urine was noted in 41.3% of the children. We noted abdominal pain in 22 (14.5%) children. Similar findings have already been reported in the past where abdominal pain was noted in 12% of children having hematuria⁴ whereas Vachvanichsanong P et al¹⁸ also reported 11.5% children having abdominal pain along with hematuria. A study from Korea¹⁹ revealed 17.5%

of the school going children with urinary abnormalities to have hematuria as well as proteinuria.

We noted that 23.7% of children having hematuria were seen to have urinary tract infection (UTI). UTI is quite common in children with hematuria especially in children with age between 1 to 5 years. Another local study⁴ noted 22.6% children between 1 to 5 years to be having UTI while similar findings were also recorded by Patel HP et al²⁰ where 19% of the children having hematuria had UTI. Other common findings in the present study were renal stone 17 (11.2%) and vesico ureteric reflux amongst children with hematuria. Our findings regarding vesico uteteric reflux were quite similar to other studies where authors reported vesico uteteric reflux in 8%⁴ and 6.4%²⁰ children. We had noted renal stone in 11.2% of children but other researchers²¹ have noted renal stones to be present as high as 20% children with hematuria. In another local study⁴ evaluating significance of presence of different factors with regards to hematuria among children, no significant difference has been recorded.

CONCLUSION

Age group of 1 to 5 years and male gender seem to be more common among children having hematuria. Fever as well as red / cola color urine seemed to be the commonest presentation. Post streptococcal glomerulonephritis and UTI were the commonest factors found.

Author's Contribution:

Concept & Design of Study:	Mumtaz Ali Bharo
Drafting:	Asif Ali Khuhro
Data Analysis:	Bakhtiar Ahmed Bhanbhro, Hafiz Muhammad Anwar ul Haq
Revisiting Critically:	Mumtaz Ali Bharo
Final Approval of version:	Mumtaz Ali Bharo

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

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Myopathies Associated with Statins Use in MI Patients

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Javeria Saqib¹

ABSTRACT

Objective: To determine the spectrum of myopathies in patients of MI after taking statins.

Study Design: Observational / case-control study.

Place and Duration of Study: This study was conducted at the Ayub Medical Complex, Abbottabad. It was conducted from Dec 2013 to May 2014.

Materials and Methods: The study involved 100 known MI patients on statins of different ages and 100 control subjects. Their history regarding duration, dose, and muscle pain was taken and blood was collected for serum CPK. A relationship between duration of statin used and muscle symptoms were studied.

Results: chi-square test gives 10.4904 which is significant. The p-value is .0012. This result is significant at $p < .05$. There is a positive association of CPK levels and muscle pain with odd ratio of 20.9. which shows a positive association and 95% confidence interval shows a significant association with 9.7-41.4, $p < 0.000$ which is highly significant.

Conclusion: The study concluded that long term unchecked therapy of statin can cause severe damage to the body muscle even the heart muscles. So there should be proper follow up after 2-3 months to protect the patients from fatal myopathic effects.

Key Words: Myocardial infarction, Statins, Myopathies and Serum CPK levels.

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INTRODUCTION

Myocardial infarction (MI), also known as a heart attack occurs when blood flow decreases or stops to a part of the heart causing damage to the heart muscle¹. It is explained as a threat that leads to severe tensions in one's whole life and it is also a serious family stress especially for the couples². According to WHO (2011) 14 million people die every year³. Risk of Myocardial Infarction Study (PROMIS) was conducted, in Pakistan a country with a population of 175 million only 1,000 patients and same number of controls had been assessed in all available epidemiological studies of CHD⁴. WHO's (World Health Organization) criteria of myocardial infarction is as follows; Characteristic chest pain (usually more than 30 minutes) and diagnostic electrocardiogram (ECG) changes. Rise and subsequent fall of serial levels of cardiac markers.

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Chest pain may travel into shoulder, arm, back, and neck or jaw often on left side⁵.

In western countries, MI is commonly seen in elderly men of the age of forty and atherosclerosis is the major underlying cause⁶. Atherosclerosis is a state in which plaque builds up within the arteries and it is made of cholesterol, fatty substances, cellular waste products, calcium and fibrin (a clotting material in the blood)⁷. In long term management with all others, statins are very important. Recent statistics demonstrate increasing statin use in patients with elevated atherosclerotic cardiovascular risk⁸. Statins are the most effective medicines in the prevention of atherosclerosis and thereafter myocardial infarction, these reduces the risk of both morbidity and mortality by effectively lowering LDL level and these are the best selling medicine in controlling cholesterol in blood⁹. Although statins are very good, but the associated myopathies are the most prevalent and important adverse event. About 72% all adverse events are being muscle related., and the most common one is skeletal muscle toxicity¹⁰. There are several factors that predispose patients to muscle-related adverse effects. These include advanced age (>80 years), female sex, Asian ethnicity, low body mass index¹¹. All statins have the capacity to develop muscle toxicity but severity varies widely among statins¹². Statin induced myopathy is a vast term including disorders ranging from myalgia to lethal rhabdomyolysis now known as (SAMS)¹³. Rhabdomyolysis is a well-documented side effect of statin therapy¹⁴. It is characterized by muscle necrosis

and the release of intracellular muscle constituents into the circulation. Creatine kinase (CK) levels are typically markedly elevated, and muscle pain and myoglobinuria may be present¹⁵. To evaluate the statin adverse effects CPK levels are measured. Patient management through evaluation of CPK levels physician often measure serum CPK levels as a clue for severity of statin-induced muscle toxicity. Creatine phosphokinase (CPK) is an enzyme also known as creatinine kinase or phospho-creatin kinase. This enzyme basically catalyses the alteration of creatinine and use of Adenosinetriphosphate (ATP) to phosphocreatine and ADP.¹⁶ The frequency of statin myopathy is reported more frequently in clinical practices, since RCTs are not explicitly designed to assess myopathy and the patient population studied does not reflect the same population. Indeed, observational evidence estimates that skeletal muscle myopathies occur in 10-15% of patients^{17,18,19}. All statins have been implicated in causing muscle side effects, but at differencing frequencies. The in vitro level order for statin cytotoxicity has been reported to be more in cerivastatin than in simvastatin acid, fluvastatin, atorvastatin, lovastatin acid, pitavastatin, rosuvastatin, pravastatin²⁰. Myopathy related with statin usage can begin as early as one week into therapy but onset also can be late for several years. On average, myopathy is reported to occur 6 months after starting therapy²¹. Muscle complaints from statins are dose dependent, of diffuse origin²² and often result in the structural damage to muscle fibres which can persist even after discontinuation of therapy²³. To combat severe adverse events patient more hospitalizations which could lead further expenses on drugs. Increasing the burden of healthcare expenditures and the drug interaction could increase the risk of muscle disorders or increased CPK levels ten folds²⁴. Asian are more sensitive in its clinical response to statins than is the Western population, and for this reason dose of statin for Japanese are relatively low compared with those prescribed in the USA¹⁶. In hospital serum CPK levels can predict the severity of statin-induced myotoxicity but the link between symptoms and CPK level is not very clear. Though the explanation of CPK level is complex and hence there is not a compromise on the explanation of statin myopathy by The American College of Cardiology²⁵, FDA.) At present, the different studies supports three diagnostic ways: Initial myopathy (CPK above 3-fold the ULN, less than 10-fold the ULN), Myopathy (CPK above 10-fold the ULN, less than 50-fold the ULN), and Rhabdomyolysis (CPK above 50-fold the ULN)²⁶ CPK levels are not routinely measured.

MATERIALS AND METHODS

The purpose of present study was to assess the spectrum of statin induced myopathies in Pakistani

population. The study was conducted in the Department of Biochemistry Hazara University Mansehra and Ayub Teaching Hospital. Samples were collected from patients visiting outpatient department of ATH Abbottabad. It was an observational study (case/control). The study include 200 subject divided in to two groups. Study group consists of 100 patient of MI on statins between the age of 25 and 80 yrs. Control Group consist of 100 age and gender matched non MI patients. Convinent sample technique was used on 100 known MI patients satisfying the criteria of WHO for myocardial infarction and controls were 100 age and gender matched having no heart disease like MI. Cases included were Patients of myocardial infarction on statins between 25 to 80 yrs of age of either gender. Age and gender matched subjects having no heart disease (MI) were selected as Controls. Exclusion criteria for Cases Recent i/m injection: Patient should not receive Intra muscular injection before the performance of CPK because any prick or injury of musle cans raise CPK, exercise can raise the CPK level, Muscular trauma: Any injury to the muscle can raise the CPK level and Prolong immobilization can raise the CPK level. Controls excluded were Patients of Myocardial infarction, patient of any muscular disease, Recent i/m injection: Patient should not receive Intra muscular injection before the performance of CPK because any prick or injury of muscle cans raise CPK, Any heavy exercise can raise the CPK level, any injury to the muscle can raise the CPK level and prolong immobilization can raise the CPK. After taking informed consent, the purpose of the study and its procedure was explained to the patients. Data was collected on predesigned Performa containing name, age, sex, occupation, medical and, drug history and history of muscle pain. Blood was collected from controls and cases both male and female by using standard aseptic technique. And then perform the CPK test on the sample. Data was entered into computer, analysed by using SPSS version 21 and mean \pm SD significance odd ratios and confidence interval (CI) were calculated. After taking informed consent, the purpose of the study and its procedure was explained to the patients. Data was collected on predesigned Performa containing name, age, sex, occupation, medical and, drug history and history of muscle pain. Blood was collected from controls and cases both male and female by using standard aseptic technique. And then perform the CPK test on the sample. Data was entered into computer analyzed by using SPSS version and mean \pm SD significance odd ratios and confidence interval (CI) were calculated.

RESULTS

A total of 200 participants, 100 cases and 100 controls were studied for myopathies and CPK levels. Chi Square for the group having muscle pain with raised

CPK levels was 34.2 and p value was found highly significant ($P < 0.005$) as shown in table 1. The odd ratios were taken shown in table 2. These showed a positive association of CPK levels with muscle pain and 95% confidence interval showed a significant association, which strengthen the results, p-value showed a very highly significant result.

History of muscle pain was of different grades (mild to severe) are shown in Figure 1. The frequency distribution of muscle pain was 25% with no pain, 44% mild pain, 17% moderate and 14% patient on statins showed severe muscular pain. We also studied the different levels of CPK in muscle pain like normal and raised CPK level in patient of myocardial infarction who are taking statins (lipid lowering drugs). In first group these were 69% with raised CPK and 6% with normal CPK having muscle symptoms. In second group 9% with raised CPK and 16% with normal having no muscle pain shown in Figure 2.

Table No.1: Chi Square for the group having muscle pain with raised CPK.

	Test statistic(chi sq)	p-value	Result
CPK and muscle pain	34.2	0.000	Very highly significant

Table 1: Shows the Chi Square for the group having muscle pain with raised CPK levels that was 34.2 and p value was 0.000 which was found highly significant $P < 0.05$.

Table No.2: Positive association of CPK levels and muscle pain.

Statistics	Values	Results
Odd ratio	20.9	Positive association
95% Confidence interval	9.7-41.4	significant
p-value	0.000	Very highly significant

Table 2: Shows a positive association of CPK levels and muscle pain. The odd ratio of 20.9, which shows a positive association, and 95% confidence interval shows a significant association with value 9.7-41.4, $p < 0.000$ which is very highly significant.

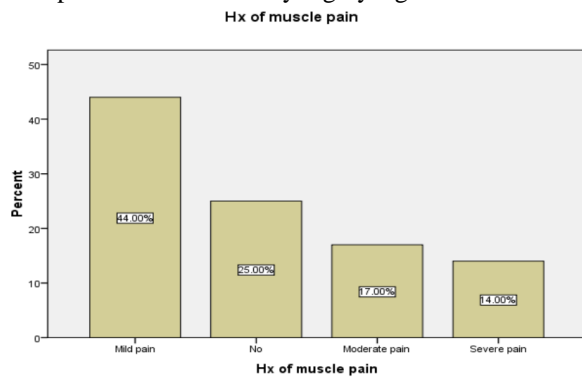


Figure No.1: Frequency distribution of muscle pain

Figure.1 Shows the frequency distribution of muscle pain was 25% with no pain, 44.00% mild pain, 17.00% moderate and 14.00% severe.

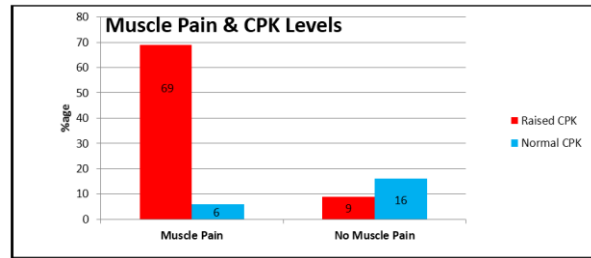


Figure No.2: Muscle pain and CPK level

Figure 2 shows the comparison of muscle pain with normal and raised CPK level in patient of myocardial infarction who are taking statins (lipid lowering drugs). In first group there were 69% with raised CPK and 6% with normal CPK having muscle symptoms. In second group 9% with raised CPK and 16% with normal having no muscle pain.

DISCUSSION

Myocardial infarction is a very important topic of discussion all over the world as it is causing physical, psychological and financial harm to the humans. Even though awareness is increasing day by day but there are some factors which need a proper and strict follow up, but unluckily some things are not properly monitored by the health care provider and patients both that are causing serious issues. The incidence of muscle symptoms associated with statins was estimated in the observational PRIMO study in patients receiving high dose statins. Myopathy related with statin usage can begin as early as one week into therapy but onset also can be late for several years. On average, myopathy is reported to occur 6 months after starting therapy²⁷. In a study by ISIS on non-Pakistani population (14,000 cases of acute myocardial infarction (MI), 16,000 controls: 95% white British²⁸, the value of large case-control studies of CHD in relation to genetic and lifestyle factors has been raised.

The present study has pointed out similar issues of muscle damaging by long term use of drugs called "statins". No doubt these are very very effective in preventing atherosclerosis, a main culprit of MI but their long term use can cause muscle damage ranging from myopathies, to severe "rhabdomyolysis". In this study association of these drugs with myopathies was studied on the basis of elevated serum CPK levels. We find a significant rise in its level and associated muscle pain like symptoms. The result of our study was consistent with an earlier study by^{29,30}. One can suspect statin-associated myopathy when a statin-treated patient reports an unexplained, generalized muscle pain, tenderness, or weakness. Importantly,

about 5.6% in women older than 65 years presents with these symptoms³¹. Another study strengthen my study by saying that statin carry distinct risk factors of muscle pain stiffness, weakness etc³². An other study by Karen was similar with this study which proves that, patients with statin-associated myopathies becomes c pain free when they stop taking statin therapy .Hence it proves the myopathic effects of statins³³. In my study 95% confidence interval shows a significant association with value 9.7-41.4.p<0.000 which is very highly significant when we compare the statins induced high CPK levels similar to the study by Gaist³⁴ which explained that the comparative risk of muscle damage is of very significance.in addition, Thompson et al indicated that less serious side effect like muscle pain and weakness exist among patients using statins rather than rhabdomyolysis³⁵.

CONCLUSION

The study concluded that long term unchecked therapy of statin can cause severe damage to the body muscle even the heart muscles. So there should be proper follow up after 2-3 months to protect the patients from fatal myopathic effects.

Author's Contribution:

Concept & Design of Study: Madeeha Jadoon
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Seropositivity of Rheumatoid Factor in Patients with Rheumatoid Arthritis

Shabana Qabulio¹, Fouzia Shaikh¹, Ahmed Iqbal Mirza² and Muhammad Ali³

ABSTRACT

Objective: To determine the frequency of positive rheumatoid factor and its association with demographic and clinical characteristics in rheumatoid arthritis patients.

Study Design:

Place and Duration of Study: This study was conducted at the Department of Rheumatology, Ziauddin Hospital, Karachi from June 2018 to May 2019.

Materials and Methods: Patients who fulfill American College of Rheumatology (ACR) classification criteria 2010 were included in the study. The rheumatoid factor status of patients was acquired by qualitative latex agglutination test. The appearance of a detectable agglutination was considered to be a positive indicator of RF. Increased levels of ESR defined as ≥ 15 mm/hr in male and ≥ 20 mm/hr in female patients was also studied. All data were analyzed by SPSS v23.0. As the data was qualitative in nature, chi-square test was used to detect significant difference. The p-value ≤ 0.05 was statistically taken as significant.

Results: RF was moderately higher as positive 66(75.0%). The most important result of our study was the significant correlation of RF sero-positivity with severity of symptoms specifically early morning stiffness ($p=0.000$) and Joint swelling ($p=0.005$).

Conclusion: Positive Rheumatoid factor with high serum values can be correlated with early morning stiffness and joint swelling.

Key Words: Autoimmune Disease, Rheumatoid Arthritis, Erythrocyte Sedimentation Rate Rheumatoid Factor.

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INTRODUCTION

Rheumatoid joint pain is a constant immune system illness wherein the articular side effects is the most prominent symptom. The condition influences a huge number of individuals around the world, with an incidence going from 0.5%-1% among general individuals.¹⁻³ Hazard factors for rheumatoid joint pain incorporate hereditary factors, sex, age, smoking, hormonal variables and ethnic elements.⁴⁻⁵ It has been proposed that HLA-DRB1 shared epitope alleles are associated with anti-citrullinated protein antibodies (ACPA) in three Asian populations, namely the Malay, Chinese and Indian ethnicities from Malaysia,⁶ which suggests that in the pathogenesis of RA genetic susceptibility factors play a vital role.⁷

RA manifestations can involve any of the proximal inter-phalangeal (PIP) joints, meta-carpophalangeal (MCP) joints and meta-tarsophalangeal (MTP) joints, and the joints in the wrist and knee as well.⁸ The long joints incorporate as shoulder, elbow, knee and lower legs, and the little joints incorporate the MCP, PIP, MTP, thumb inter-phalangeal joints and wrist.⁹ An introduction as clinically of rheumatoid arthritis differs, in spite of the fact that a guileful beginning of pain joined by swelling symmetrically of the little joint is the most well-known indication.¹⁰

Rheumatoid factor (RF) are the primary auto-antibodies to be found in the serum of patients of Rheumatoid Arthritis.¹¹ RF is a specific autoantibody directed towards the IgG molecule.¹² The RF related to IgM are the major rheumatoid factor species found in Rheumatoid Joint pain in the beginning periods of the disease.¹³⁻¹⁴ Moreover, Rheumatoid Factor could be recognized in healthy individuals quite a while before the beginning of Rheumatoid Arthritis clinically.¹⁵⁻¹⁶ Rheumatoid Factor has additionally been found in a few different ailments, like systemic lupus erythematosus, blended connective tissues illness and essential Sjögren's disorder, just as in non-immune system conditions, for example, incessant contaminations and older age,^{13, 17} that demonstrates, Rheumatoid Factor can be a result of non-explicit resistant actuation.¹⁸

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MATERIALS AND METHODS

This study was conducted at Rheumatology Department, Ziauddin Hospital, Karachi from June 2018 to May 2019. Patients who fulfill American College of Rheumatology (ACR) classification criteria 2010 were included in the study.⁹

The basic demographic data was recorded as, age of Rheumatoid Arthritis, sex, serologically biomarkers, like (ESR), CRP and clinical side effects like stiffness at morning, swelling in joints and patterns of joint effected by Rheumatoid Arthritis. Joint association here involves as swollen painful joints distinguished through the examinations by rheumatologists.

The rheumatoid factor status of patients was acquired by qualitative latex agglutination. The appearance of a detectable agglutination was considered to be a positive indicator of RF. Increased ESR levels were defined as ≥ 15 mm/hr in male and ≥ 20 mm/hr in female patients.

Data were analysed by SPSS v23.0. To detect significant difference, chi-square test was used as the data was qualitative in nature. The p-value ≤ 0.05 was statistically taken as significant. Relative descriptive statistics were also presented in the tables.

RESULTS

The average age of patients was 35.5 ± 3.6 years. Mean ESR was 42.6 ± 4.7 mm/hr. There were 11(12.5%) male and 77(87.5%) females. The numbers of small joints were 74(84.0%) and large joints affected by RA were 69(78.0%).

Table No.1: Frequency distribution of Gender, Age

Gender(n=88)	Age	Frequency
Male(n=11)	>40	10
	<40	01
Female(n=77)	>40	47
	<40	30

Table No.2: Frequency distribution of ACR criteria

Characteristics	Male(11)	Female(77)
Morning Stiffness	10	59
Joint Swelling	11	67
RF (+ve)	10	56

Table No.3: Frequency distribution of Pattern of joint involvement

Pattern of joint involvement	Frequency(88)	Percent%
Wrist	33	37.5
Elbow	10	11.4
Knee	11	12.5
Shoulder	10	11.4
Hand	69	78.4
Ankle	4	4.5
Small Joints	74	84.1
Large Joints	19	21.6

The clinical symptoms recorded were joint swelling 39(39.0%) and morning stiffness 56(56.0%). The most frequently involved joints were the hand 28(28.0%), knee 10(10.0%), wrist 14(14.0%), ankle 5(5.0%), shoulder 9(9.0%) and elbow 12(12.0%). In terms of the immunological investigation, RF was moderately higher as positive 66(75.0%).

No significant differences founded between the RF sero-positivity in terms of the correlation with gender. The most important result of our study was the significant correlation of RF sero-positivity with morning stiffness ($p=0.000$) and Joint swelling ($p=0.005$).

Table No.4: Stratification of Rheumatoid Factor with respect to Morning stiffness, Joint swelling and ESR

Characteristics	Rheumatoid Factor		p-value
	Positive	Negative	
Morning Stiffness	64	05	0.000
Joint Swelling	62	04	0.005
ESR	66	22	0.668

DISCUSSION

Data concerning the demographic and clinical characteristics were presented In current study, as well as their association with RF, among RA patients. In this study female patients were in majority, which is similar to findings from other parts of the world, including the China, Japan, USA, United Kingdom, Malaysia and India.¹⁹⁻²⁴

The deregulation of hormone estrogen may defines why females are most affected in RA than men, however androgens might have suppressive role in the progression of the disease.²⁵

In current study, (87.5%) RA patients were female, which is similar with other Malaysian cohorts of RA patients²⁶⁻²⁸ that showed an identical percentage of female patients (83.8–91.3%). In current study, 66(75.0%) tested positive for RF using the latex agglutination methodology, while another study involving Malaysian RA patients reported a higher proportion of patients (85.0%) testing positive for RF using the ELISA kit methodology.²⁷

This indicates that methods employing distinct principles (e.g. agglutination versus ELISA) to assay RF could, at least partially, contribute to differential RF detection. In terms of the ESR values, our study demonstrated mean ESR: 47.6 ± 4.7 mm/hr, which is similar to the ESR value obtained from other local RA patients with a mean of 51.6 ± 5.2 mm/hour²⁹.

It has been seen that the majority of cases experiences agony, swelling and tightness in various joints. The clinical findings of synovitis were more severe at morning in and around the joints was a typical feature of Rheumatoid Arthritis.⁸ In spite of the fact that there is no single research center test used for diagnosis of

Rheumatoid Arthritis, the most common finding of RA is the increased level of systemic inflammatory marker, like ESR that is most frequently advised test to monitor disease activity in patients with rheumatoid Arthritis.⁴

CONCLUSION

A positive Rheumatoid factor seems to be associated with presence symptoms. However other sensitive diagnostic techniques may produce better outcome of the above findings.

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Depression among Mothers in Antenatal Period and its Causes; a Study Conducted on Primigravida Mothers

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ABSTRACT

Objective: To determine frequency of antenatal depression among primigravida mothers in antenatal period and causes of this depression.

Study Design: Observational / cross sectional study

Place and Duration of Study: This study was conducted at the M. Islam Teaching Hospital Gujranwala, a tertiary care hospital from January 2019 to June 2019.

Materials and Methods: We studied total 400 cases. An inclusion and exclusion criteria was designed for including patients in the study. Primigravida patients reported in Gyne & Obs OPD of study institution during study period, mothers having signs and symptoms of depression in antenatal period and depression diagnosed by psychiatrist as well having no co-morbidity were included in this study. Those mothers having any other co-morbidity as a cause of depression, conceiving second or third time were not included in the study. Patients for depression were evaluated on the basis of ICD-10 symptom checklist. SPSS version 16 was used to analyze data. Percentage, frequencies, means and P-value were calculated. Graphs and tables were used to express results. Written consent was obtained from all cases in the study group and permission was taken from ethical committee of the study institution as well.

Results: Four hundred 400 primigravida mothers were included in this study. Out of them 41.2% were diagnosed for depression including 49.7% mothers having mild, 35.2% with moderate and 15.2% having severe depression. Age range of cases was 15-40 years with mean age 24.5±5 year. Causes of depression among cases in study group were evaluated as low socioeconomic status in 54.5% mothers, lack of social support from husband in 18.8%, due to physical stress of pregnancy in 6.7%, unintended pregnancy in 6.1%, domestic violence in 9.1%, previous history of psychiatric illness and smoking was found as a cause of depression in 1.8% mothers. Single causative factor of depression was found in 69.7% and more than one causative factor were found in 30.3% cases. Educational status was also an important factor determining rate of depression among mothers. Out of 165 cases having depression, 34.5% were educated and 65.5% were uneducated mothers.

Conclusion: Depression is much common among primary gravida mothers and most common causes are low socioeconomic status, illiteracy, no social support from partner and domestic violence. It is more common in young mothers as compared to mature aged mothers.

Key Words: Depression, Antenatal period, primigravida mothers, psychological stress

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INTRODUCTION

Depression among mothers in prenatal period may cause negative outcomes and even developmental disorders in infants. Most common cause of depression among mothers is hormonal imbalance.^{1,2}

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Period of parenthood is naturally very stressful for mothers. After difficult experience in birth one out of four mothers suffers from depression. Demographic factors are also very important in determining depression among mothers such as maternal age and body mass index which causes stressful delivery which often leads to cesarean section and causing increased mental stress and depression.^{3,4} Other factors include any disease already present, tiredness due to lack of rest during pregnancy, financial status, burden of job on working women, behavior of partner, family behavior and personal relationship status. Outcomes of maternal depression in pregnancy may lead to preterm birth, low birth weight, miscarriage and fetal growth retardation. Depression can occur in any stage of pregnancy in first, second or third trimester. It can be prevented by medical or psychological therapy. Postpartum depression is more common. Severity of depression is different in various modes of delivery such as more in

cesarean section than spontaneous vaginal or vaginal assisted delivery.⁵ In Asia 30.7% women suffer from depression in prenatal period and 63.3% in postnatal period.^{6,7} In developed countries incidence of maternal depression is much low as compared to developing and underdeveloped countries because of availability of good health services and early detection of problem and immediate management, increased number of skilled health professionals and high literacy rate of female population which make them health conscious themselves. In Pakistan there is low literacy rate especially among female population which is a major factor determining depression. In our society mental depression is frequently neglected and is not diagnosed early until unless disease is advanced or negative outcomes appear but in that case as well it is frequently misdiagnosed in underdeveloped areas. High illiteracy rate, old wrong customs, male dominance society and limited approach of health professionals to the mothers in our society due to culture or misbelieves and lack of trust its incidence is increasing with the passage of time.

MATERIALS AND METHODS

This is a cross sectional study of observational type conducted in out-patient door of Gynecology and obstetrics of study institution. Study was started in January 2019 and completed after six months duration in June 2019. A performa was used in which all relevant data was documented such as age, residency, occupation or housewife, number of parity and gravida, ICD-10 symptoms checklist was used to diagnose the disease. Help of a consultant psychiatrist was also taken to diagnose depression among mothers reporting in OPD having pregnancy. An inclusion and exclusion criteria was formed according to which only those females were included which were primigravida, pregnancy confirmed by urine pregnancy test or level of blood B-HCG, having signs and symptoms of depression. Mothers who have been conceived before, having no symptom or sign of depression according to ICD-10 symptom checklist, having previous history of psychological issue or consulted with psychiatrist, taking antipsychotics, having gestational hypertension or gestational diabetes mellitus were not included in this study. Mothers diagnosed for antenatal depression were evaluated for contributing cause of depression. Proper history was taken from each patient in study group about partner support, socioeconomic status, and domestic violence and did she want pregnancy or having pressure of partner or family. Approval was taken from ethical committee of the study institution for conducting study. Informed consent was taken from all cases in the study group and privacy of data was made sure. All collected data was analyzed using SPSS software version 20. Frequency, means and percentages were calculated and results were presented in tabular

and graphical form. Confidence interval was 95% and margin of error was 5%.

RESULTS

Total 400 primigravida mothers were included in this study falling on inclusion criteria. Out of them only 165(41.2%) were diagnosed for having antenatal depression. Age range of cases in study group was 15-38 years with mean age of 24.5±4 years. There were 55(33.3%) cases between 15-20 years age, 47(28.5%) between 21-25 years, 24(14.5%) between 26-30 years, 20(12.1%) between 31-35 years and 19(11.5%) having age above 35 years (Table-1).

Causative factors evaluated among 165 mothers out of 400 cases having depression include low socioeconomic status in 90(54.65%) cases, no social support from partner in 31(18.8%) cases, previous history of any psychological issue reported in 5(3%), unintended pregnancy was a cause of depression in 10(6.1%) cases, domestic violence in 15(9.1%) cases, physical stress in 11(6.7%) and smoking was reported in only 3(1.8%) cases as a contributory factor of antenatal depression. In 115(69.7%) cases single causative factor was found while in 50(30.3%) cases there were multiple factors causing depression (Table-2).

In our study uneducated mothers were more in proportion than educated mothers as educated were 57(34.5%) and uneducated were 108(65.5%) (Figure-1).

Table No.1: Age distribution among cases in study group (n=400)

Age of patients (Years)	Number of patients (n=400)	Percentage	Patients having Depression (N=165)	Percentage
15-20	72	18%	55	33.3%
21-25	95	23.7%	47	28.5%
26-30	134	33.5%	24	14.5%
31-35	60	15%	20	12.1%
Above 35	39	9.7%	19	11.5%

Table No.2: Causative factors of antenatal depression among mothers in study group (n=165)

Causative factors of depression	Frequency	Percentage
Low socioeconomic status	90	54.5%
No social support from partner	31	18.8%
Past history of psychiatric issue	5	3%
Unintended pregnancy	10	6.1%
Domestic Violence	15	9.1%
Physical stress	11	6.7%
Smoking	3	1.8%
Total	165	100%

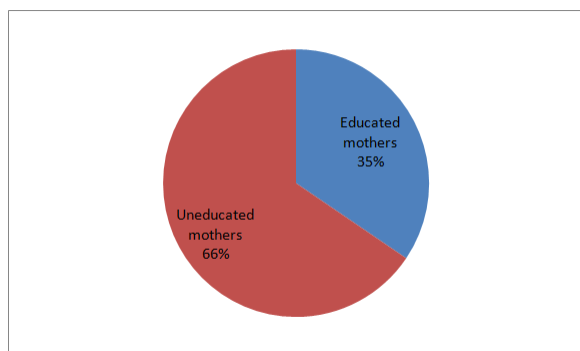


Figure- No.1: Frequency of educated and non-educated mothers among females having depression in study group (n=165)

DISCUSSION

Hormonal imbalance in pregnancy and physiological stress and many other personal factors may cause depression among mothers which can lead to harmful outcomes in mother and especially in infants in their form of low birth weight, preterm delivery and congenital abnormalities etc. Psychological depression in pregnancy can lead to abortion.^{8,9} Many studies reported that low socioeconomic status causes depression and poor fetal outcomes in poor societies. In Pakistan many studies have reported correlation of maternal depression and retarded fetal growth.^{10,11} Developed countries have made proper system in health departments to detect this problem early and manage promptly to ensure safe mother and child.¹² Antenatal depression causes morbidities among mothers even after delivery of child.¹³ A study reported that chances of antenatal depression is more in young mothers mostly around 16 years of age as compared to others with increased age.¹⁴ Another study conducted on pregnant mothers above 18 years age concluded rate of depression 39% and out of them 60% were having low socioeconomic status.¹⁵ There are many other factors as well causing depression such as most important one is non cooperative partner and lack of socio economical support from husband. A study conducted on young mothers having age 15-18 years concluded that cause of depression among 20.4% depressed mothers lack of support from partner and in 23% females there was history of previous psychiatric issue.¹⁶ Early detection of problem and quick management can avoid preterm birth and low birth weight of newborns. It was seen that females from poor socioeconomic status areas were more prone to gain antenatal depression once they are exposed to it due to insufficient diet and unsafe environment around them.¹⁷ There are many ways by which depression causes poor birth outcomes such as release of stress hormones cortisol, epinephrine and nor-epinephrin due to abnormal stimulation of hypothalamic pituitary adrenocortical axis. These

changes cause decreased oxygen perfusion of placenta which leads to preterm birth and underweight baby.^{18,19} Lack of proper healthcare facilities and difficult to avail them in remote areas often cause these symptoms neglected.²⁰ Pregnancy is a suitable period of time in which depression can be diagnosed in women having pre existing signs and symptoms. In Pakistan religious myths and social misbeliefs enhance anxiety among mothers. Education status is a very important factor determining depression among mothers. In our study 41.2% mothers were having depression and these results are comparable to the study conducted by Kim HG et al who reported 30.7% women having depression.²¹

CONCLUSION

In our study depression was present in 41.2% mothers with most common cause was low socioeconomic status and no social support from partner. Majority of mothers with depression were below 20 years of age. Illiteracy was a major factor causing depression among mothers contributing 65.5% in our study. Early detection of problem and immediate management can reduce fetal complications.

Author's Contribution:

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

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Hemostatic Abnormalities in Ischaemic Stroke Patients

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ABSTRACT

Objective: To evaluate hemostatic markers, D. Dimers, PT and APTT in ischaemic stroke patients.

Study Design: Observational study.

Place and Duration of Study: This study was conducted at the Medical Department of Mardan Medical Complex (Medical Teaching Institute) and Pathology Department of Bacha Khan Medical College, Mardan, from November, 2018 to July, 2019.

Materials and Methods: Hundred patients of stroke and fifty healthy individuals were included in this study. All patients and healthy individuals were subjected to hemostatic markers i.e. D. Dimers, PT and APTT.

Results: In this study total of 65 patients with stroke showed elevated D. Dimers levels. Eighteen out of 100 i.e. 18% had D. Dimers level in the range of 199-500 ng/ml. Fifteen patients had D. Dimers in the range of 501-1000 ng/ml and 32 out of 100 i.e. 32% of the stroke patients showed D. Dimers levels in the range of 1001-2000 ng/ml. Thirty five patients had D. dimers in the normal range. Activated partial prothrombin time (APTT) in 8 patients was found to be shortened. Mean APTT was 33 +.562 seconds. Similarly prothrombin time (PT) in 6 patients was found to be shortened than normal. Mean PT value was 11 + .265 seconds. This study showed that D. Dimers were significantly elevated and PT and APTT were significantly shortened in stroke patients. P value for D. Dimer was P<.00265 and for PT and APTT, P value was <.00326.

Conclusion: This study concluded that stroke patients with infarction are associated with significant hemostatic abnormalities which reflect changes in hemostasis and thrombosis. Findings of elevated D. Dimers and shortened PT and APTT in patients with infarction will reduce morbidity and mortality in such patients if properly identified and managed in time.

Key Words: D. Dimer, PT, APTT, Stroke Patients.

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INTRODUCTION

Stroke is a syndrome characterized by the initiation of acute neurological disorder lasting for at least 24 hours. It reflects the focal disturbance in brain circulation^{1, 7, 8}. If the disorder lasts for less than 24 hours, it is referred as Transient Ischemic Attack (TIA)². The neurons of the affected area die due to obstruction of the arteries and so there is no supply of oxygen and nutrients to the involved area³. There are two main types of stroke, ischemic and hemorrhagic, accounting for approximately 85% and 15% respectively⁴.

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Stroke is the world's third leading cause of mortality and morbidity with high incidence in the population⁵.

It has been reported by the American Heart Association that on average, every 40 seconds someone in the United States has a stroke⁽⁶⁾. Various studies have been conducted which demonstrated that hemostatic disturbances are common in stroke patients⁷ and that stroke is a thrombo-inflammatory disease⁸. The pathophysiological mechanism of this phenomenon is multifactorial. Stroke is associated with significant coagulation abnormalities. There is evidence of increased thrombin generation and fibrin turn over, altered fibrinolytic activity and disturbed endothelial dysfunction^{9,10}.

D. dimer is a useful marker and elevated level easily identify thrombus formation in such patients before going into expensive, time consuming investigations. Elevated level can give immediate information to the clinician regarding thrombotic status of the patient. Similarly shortened PT and APTT also help in the prediction of ischaemic stroke.

MATERIALS AND METHODS

This study was conducted in Pathology Department of Bacha Khan Medical College, Mardan and Medical

Department at Mardan Medical Complex (MTI), Mardan, from November, 2018 to July, 2019.

A total 100 patients of ischaemic stroke were included in the study and 50 patients were taken as a control group. Sixty patients (60%) were males and 40% were females. Age was from 50-70 years. Patients with history of venous thrombosis, septicemia, malignancy and infection were excluded from the study. For D. Dimer 1.8 cc of blood was taken in a tube containing 0.2 cc of sodium citrate. The same procedure was adopted for PT and APTT. These samples were then centrifuged. For D. dimers plasma was analyzed by Hittech machine Architect C 400 using Quantia D. Dimer reagent.

For PT 200 ul of soluplastin (PT reagent) was added to 100 ul of patients serum white 100 ul of APTT reagent along with 100 ul of calcium chloride was added to 100 ul of patients serum for measurement of APTT. The tests were performed on K.C 4 (Anelung) machine.

D. dimer is formed as plasmin mediated proteolytic degradation product of cross linked fibrin clots. D. dimer fragments increase in any condition where clot formation and subsequent fibrinolysis occurs. Measurement of D. dimer identify both clot formation and degradation and also determine the severity of hypercoagulable state as hypercoagulable state is more prone to thrombosis. The normal value of D. dimers in our study was 140-198 ng/ml.

Prothrombin Time and APTT are also hemostatic investigations which determine the activity of both the extrinsic and intrinsic pathways. Normal value of PT and APTT in our study was 12 second and less than 35 seconds respectively. These investigations were also performed according to standard procedure. Its high level identify that there is coagulation factor deficiency or there is consumption of the coagulation factors. Its low level signify a hypercoagulate state and activated hemostatic mechanism.

All the data was subjected to statistical analysis by using Chi.square Test and T. Test. Level of significance was set at P value less than .002.

RESULTS

In our study hundred cases of stroke with infarction were included. In all these patients infarction was confirmed by C.T or MRI. They were both adult males and females. Age range was 50 to 70 years. All patients were subjected to hemostatic markers i.e. D. Dimers, PT and APTT. Fifty healthy individuals were taken as control group. Their D. dimers, PT and APTT were also performed.

Sixty five patients of ischaemic stroke showed elevated D. dimer levels. Eighteen of them i.e 18% had D. dimers level in the range of 199-500 ng/ml. Fifteen percent had D. dimers level in the range of 501-1000 ng/ml while in 32% of the patients it was in the range of 1001-2000 ng/ml. This study of stroke patients with

infarction showed that D. dimers are significantly elevated in such patients as compared to control group. P. value is less than .00265.

Similarly PT and APTT of these patients were also performed. In eight patients out of hundred mean value of APTT was 33+.562 seconds which was significantly shortened than control group. Six patients showed shortened PT with mean value of 11 + .265 seconds, significantly lower than control group. P value of APTT and PT was less than 0.00326.

Prothrombin time (PT) and APTT were performed by manual and coagulation analyzer method for accurate results.

Table No.1: Frequency of Hemostatic Markers in Stroke Patients.

S.No.	Hemostatic Marker	
1.	Raised D. dimer	65%
2.	Shortened PT	5%
3.	Shortened APTT	8%

Mean Values of Hemostatic Markers in Stroke Patients.

Table No.2: Hemostatic marker observations in patients with mean value of control subjects

Hemostatic Marker	No. of Patients	Observed Value	Mean Value of Control Subjects
D. dimer level	18	199 – 500 ng/ml	140-198 ng/ml
	15	501 – 1000 ng/ml	
	32	1001– 2000 ng/ml	
	35	140 – 198 ng/ml	
APTT	8	33 + .562	33.5–35 seconds
PT	6	11 + .265	11.3 – 12 seconds

P value for D. dimer P< .00265

P value for APTT & PT P< .00326

DISCUSSION

Stroke is a major health problem worldwide resulting in high rates of morbidity and mortality¹¹. Thrombosis is a key mechanism for many acute strokes and is associated with severe coagulation and fibrinolysis¹². D. dimer is a frinogen degradation product that reflects thrombus formation and breakdown and its elevated level shows prothrombotic tendency in the patient and is an independent risk factor for ischemic stroke^{13,14}.

In the present study we evaluated hemostatic marker, D. dimer, PT and APTT in stroke patients as stroke patients are associated with coagulation abnormalities. In the present study 65% of the stroke patients showed elevated D. dimer levels. Eighteen patients had D. dimer level in the range of 199-500 ng/ml. Fifteen patients had D. dimer level in the range of 501-1000 ng/ml and 32 patients had D. dimer level in the range 1001-2000 ng/ml. Thirty five patients had D. dimer level in the normal range.

Similar studies have been conducted which have shown positive association of D. dimer levels in stroke patients. Usman et al in his study identified that stroke patients are associated with elevated D. dimer level¹⁵. The study of Sazonova et al also shows similar correlation to our study. They have also reported that raised D. dimer level are found in stroke patients¹⁶. A lot of other studies have been conducted on this issue, the results showed that elevated D. Dimer levels are found in stroke patients which strongly signify thrombotic tendency^{17,18}.

In the present study PT and APTT of the stroke patients were also performed. Eight patients showed shortened APTT while Six patients presented with shortened PT. Mean PT and APTT was 11+. 265 seconds and 33+. 562 seconds respectively as compared to control group. Different authors have studied PT and APTT in stroke patients. Some reported shortened PT and APTT while others reported the results to be prolonged. Some authors have reported no change in the results. Sari Kaya et al reported in their study that no change in PT and APTT occurs in patients with ischaemic stroke¹⁹. Similarly Selyopranoto et al concluded no change in PT and APTT in ischaemic stroke patient as compared to control group²⁰. However Gaston et al in their study reported shortened PT and APTT in ischaemic stroke²¹. Similarly Kuowy et al reported in their study that shortened APTT occurs in stroke patients²².

A large number of studies have demonstrated that hemostatic disturbances play major role in the pathogenesis of stroke but the exact mechanism is unknown or multifactorial²³. Firstly elevated D. dimer levels may reflect the ongoing thrombus formation within cerebral vessels and hence act as a marker of systemic hypercoagulability²⁴. Secondly thrombi formed in hypercoagulable state and D. dimer levels may be resistant to fibrinolytic system²⁵. Thirdly D. Dimer levels act as marker of acute phase reactants as there is evidence that D. dimer may stimulate the inflammatory response D. dimer stimulate monocyte synthesis and release pro-inflammatory cytokines IL-6^{26,27}. This increase inflammatory response further contribute to ischaemic stroke and as progression.

D. dimer is a circulating peptide degradation product of cross linked fibrin so higher levels of D. dimer indicate more systemic fibrin formation and degradation of fibrin clot⁽²⁸⁾ and so elevated D. dimer is a marker of coagulation and fibrinolytic system²⁹.

The present study revealed that stroke is associated with hemostatic abnormalities as indicated by elevated D. dimer levels and shortened APTT and PT. This hemostatic activation may be an important contributor to progressing ischemic stroke⁹.

CONCLUSION

The study concluded that hemostatic markers are significantly elevated in ischaemic stroke. Patients

elevated D. dimer is a useful marker for the clinician to identify stroke patients at risk of thrombosis. Its low level excludes thrombus formation while elevated level immediately guides the clinician that stroke patient has thrombo-embolic phenomenon which can be further confirmed by other supportive investigations like C.T or MRI brain. Shortened PT and APTT are also associated with ischaemic infarction.

Author's Contribution:

Concept & Design of Study:	Naveed Khan
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Data Analysis:	Shah Zeb, Muhammad Amjad
Revisiting Critically:	Naveed Khan, Murad Ali
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Dramatic Effect of Common Salt (Cooking/Table Salt) to Manage Umbilical Granuloma in Neonates and Infants

Umbilical
Granuloma in
Neonates and
Infants

Mohyuddin Kakar¹, Khushal Khan², Mobeen-ur-Rehman Khan³ and Ahmad Shah²

ABSTRACT

Objective: To evaluate the dramatic effects of table salt on umbilical granuloma in neonates and infants.

Study Design: Experimental descriptive study

Place and Duration of Study: This study was conducted at the Department of Paediatric Surgery, Sandman Provincial Teaching Hospital Quetta from July 2018 to December 2018.

Materials and Methods: A total of 46 patient's neonates and infants from 3 weeks of age to 4 months (16 weeks) of age. Both male and female included. Patients with rectal polyp, omphalomesenteric duct and urachal remnants were excluded. The parents of patients especially mothers are instructed to clean the umbilicus of baby with cotton swab soaked with normal saline let it dry and then apply a chunk of salt sprinkled over the granuloma. Pad the umbilicus with a piece of gauze and adhesive dressing (sunny plast) remove the dressing after 20 to 30m re-clean the umbilicus. This procedure should be done thrice a day for consecutive 3 days.

Results: There were 44 cured completely with a dramatic effect of common salt which is about 95.6%, while two patients had no response or poor response which is about 4.3%. These two patients with no response were diagnosed after surgical excision and histopathology as rectal polyps.

Conclusion: The common salt method is simple to use, perfect cure, dramatic, cost effective and safe.

Key Words: Umbilical granuloma, Common salt, Infants, Neonates

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INTRODUCTION

Umbilical granuloma is reported as the most frequent disorder originating from umbilicus in newborns.¹ It is commonly seen as small 1 to 10mm in size, soft febrile, non tender, pale pink/red coloured lesions at the base of umbilicus on physical examination.² Normally after delivery spontaneous separation of cord begins and it is completed about 7-15 days. After separation of cord the granuloma became apparent.³ After cord separation there may be incomplete epithelization of granuloma tissue over the umbilicus. This normal granulation tissue normally resolves within 2-3 weeks, if it does not resolve and over growths this will lead to umbilical granuloma, it contains no feelings and nerves.⁴

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The exact etiopathogenetic of the umbilical granuloma is unknown. An inflammatory process and non-hygienic care is suggestive factor for granuloma formation.⁵ The presence of infection in the umbilical is directly associated to the delay in cord separation.⁶

Al-Sony et al⁷ suggested that proximal cord clamping, and antiseptic is very simple and effective method that reduces umbilical infection and consequently preventing granuloma formation.

At present there are multiple options for the management of umbilical granuloma like 75% silver nitrate stick method, electric cautery, double ligation, cryotherapy, surgical excision, doxycycline, copper sulphate powder and common salt application method. All above method and procedures are effective and important but each have own advantages disadvantages, cost-effectiveness, surgical skill and equipment requirement.

In history Schmitt⁸, 1975 illustrated the little effect of common salt on umbilical granuloma in his short note; this examination gives idea to the future researcher to manage the umbilical granuloma.

MATERIALS AND METHODS

This clinical trial was conducted in the Department of Paediatric Surgery Sandeman Teaching Hospital Quetta from 1st June 2018 to 31st December 2018.

In this study we put a total of 46 babies both male and female with age ranging from 3 weeks to 4 months. Patients with clinically evident granuloma are treated in outpatient department and also at home. In each case the first time procedure is performed in front of the mother by cleaning the umbilicus with cotton pad wet with normal saline, lead them dry for a while and then a pinch of salt sprinkled on granuloma packed with small gauze and covered with adhesive (sunny plast). The mothers are instructed to remove dressing after 30m re clean the button belly of baby and repeat this procedure thrice a day for consecutive three days. They were also keep in confidence that after first dressing you may found a drop of dark blood on umbilicus but doesn't worry clean that because this occurs only initially and mild. The patients are followed after one and three weeks to evaluate the effect of common salt on granuloma. The effect was graded according to response observed like; dramatic response; when complete regression of granuloma, no discharge, umbilicus clean and epithelized and no response/poor response. Computer statistical software SPSS 20.0 was used to analyze the data.

RESULTS

The mean age of the patients was 1.84 ± 1.01 months. There were 24 (52.2%) males and 22 (47.8%) were females (Table 1). There were 44 (95.6%) children have dramatic response while 2 (4.4%) have poor response/ no response (Table 2).

Table No.1: Demographic information of the patients (n=46)

Variable	No.	%
Age (months)		
<2	33	71.7
2-4	13	28.3
Gender		
Male	24	52.2
Female	22	47.8

Table No.2: Frequency of response (n=46)

Response	No.	%
Dramatic response	44	95.6
Poor response/no response	2	4.4

DISCUSSION

The curative mechanism of salt is because of high concentration of Na ions which drains water from the cells and results shrinkage and damage of granuloma. However this effect is not so powerful to damage the normal surrounding tissue. Therefore in such situation common salt is effective for the management of umbilical granuloma.

Umbilical granuloma is commonly found disorder in neonates and infants. It may causes life threatening

infections such as omphalitis and necrotizing fasciitis it is not treated on time.⁹ Therefore it should be appropriately managed after establishing diagnosis.

Delayed separation of cord is the major cause of formation of granuloma and persistent inflammation .consequently, application of topical antibiotic and elimination of the friction of a wet diaper may allow the granuloma to epithelized.¹⁰ There are different modalities for the management of umbilical granuloma, though each have their own advantages and disadvantages.¹¹

Electrocautry and cryotherapy is also used in limited cases.¹² These procedures are again costly, skilled related, foul smelling and discoloration of skin is the side effect. Loten et al¹³ suggested double ligation method where a thread is used, its again a skilled related having a complication of bleeding, needs of anesthesia and can be applied only used in pediculated granulomas not sessile ones.

Surgical excision is another method which can be done by a skilled surgeon, needs anesthesia and equipment. This is not practicable in routine use but it is the better treatment modality for larger granuloma.¹⁴

Recently topical clobetasol propionate in 109 patients with umbilical granuloma is suggested as effective as silver nitrate.¹⁵ However Aydin et al¹⁶ reported topical clobtasol propionate was very effective in children with ages above 12 years.

We selected 46 patients in our study having a age ranges from 3 weeks to 4 months .the male to female ratio which is almost same in literature but in our study male was slightly more like Annapurna and Ramu.¹⁶ In our study 44 patients cured completely which is about 95.6% while in remaining 2 patients there was no or poor response which is about 4.4%. Two children having no or poor response patient are latter on treated with excision method and histopathology shows that a umbilical polyp. Though our study shows 95.6% dramatic and 5.5% no response but as the no response ones are diagnosed to umbilical polyp so the actual result can be taken as 100%.

CONCLUSION

Common salt application method is simple to use, dramatically effective, without any relapse and complications and more ever can be used by doctors, nurses and parents.

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Frequency of Common Bile Duct Stones Detected on ERCP in Patients Presenting with Obstructive Jaundice & Having Normal CBD on Ultrasound Abdomen

Frequency of
Common Bile
Duct Stones
Detected on
ERCP

Muhammad Tanweer Khalid, Shahid Karim, Hamid Ali, Muhammad Usman Khalid,
Faizan Ahmed and Ghulam Mujtaba

ABSTRACT

Objective: To determine the frequency of Common stones in Bile Duct detected on Endoscopic Retrograde Cholangiopancreatography (ERCP) in patients presenting with obstructive jaundice & Having Normal CBD on ultrasound Abdomen.

Study Design: Cross sectional study.

Place and Duration of Study: This study was conducted at the department of Gastroenterology, Liaquat National Hospital, Karachi from July to December 2016.

Materials and Methods: Total 162 patients with obstructive jaundice of 2-4 weeks duration and normal ultrasound abdomen were included. Before ERCP, patients were clinically evaluated. Outcome variable was the presence of CBD stone in ERCP. Descriptive statistics of the collected data were computed. Stratification was done. For post stratification, Chi-square test was applied. Confidence interval was kept to be 95% and the level of significance was kept to be 5%.

Results: Number of male respondents was 106 and the female respondents were 56. Average age was 35.69±11.30 years. Mean duration of jaundice was 2.94±0.81 weeks. The CBD stone was 32.7% detected in ERCP. Significant association of age was observed with CBD stone in ERCP.

Conclusion: ERCP is the gold-standard for the diagnosis and evaluation of morphological changes in the pancreas. In the common stones of bile duct, for treatment, ERCP is the preferred modality.

Key Words: Common stones of Bile Duct, ERCP, obstructive jaundice, Normal ultrasound Abdomen

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INTRODUCTION

Blockage in any duct in which the bile is flows to gall bladder from liver or to small intestine from gall bladder; obstructive jaundice is caused because of this blockage. This can be because of extrahepatic or intrahepatic reasons. Extrahepatic reasons are divided into the extra-ductal and intra-ductal reasons. Neoplasm, biliary stricture, choledocholithiasis, parasites and primary sclerosing cholangitis cause intra-ductal obstruction.

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Biliary channels` external compression neoplasm, pancreatitis or stones of cystic duct with succeeding distention of gallbladder cause extra-ductal obstruction.¹⁻²

Choledocholithiasis or common stones of bile duct are the public cause of cholangitis and obstructive jaundice³. In about 10 to 20% of patients, choledocholithiasis is developed with the stones of gallbladder, whereas, about 3 to 10% patients underwent cholecystectomy would have common stones of bile duct (CBD)⁴.

Cholangitis can be caused by CBD stones, acute pancreatitis, obstructive jaundice and sepsis. Thus, for the clinical decision making, accurate diagnosis of choledocholithiasis. Endoscopic Retrograde Cholangiopancreatography (ERCP) for therapeutic and diagnostic procedure for CBD stones. Whereas, it is offensive and several complications may be caused i.e. acute pancreatitis (1.3-6.7%), bleeding (0.3-2%), duodenal perforation (0.1-1%), biliary tract infection (0.6-5%).⁵ With cholangiography alone, the sensitivity of ERCP is indicated to be 89-93% when successive sphincterotomy and balloon or basket were utilized as the standard criterion for duct sweeping⁶. Recognized

clinical abnormalities and those which are related to biochemistry and ultrasonography the basis of criteria for ERCP⁷. By the use of these criteria, the studies have shown the stones of bile duct may be identified positively at ERCP in 10-60 percent of cases but even then variations are documented.⁸

This study aims to elucidate the current frequency of CBD stones detection on ERCP among patients with obstructive jaundice. As there is very limited international & local data is available on the frequency of Common stones of Bile Duct detected on ERCP in patients presenting with obstructive jaundice & having Normal CBD on ultrasound Abdomen.

With the present era of cost efficient and time saving medical practice, the study will help in formulating a protocol regarding use of ERCP in investigating obstructive jaundice in our local population and will help in providing shorter hospital stays, reduced medical costs and faster decision making for patient care and also help rationalize the need for ERCP in such patients as other diagnostic modalities like MRCP or Endoscopic Ultra sound are upcoming as alternative to ERCP.

MATERIALS AND METHODS

All the patients of obstructive jaundice as defined in operational definition and fulfilling selection criteria were enrolled in the study. Informed consent was obtained from all the patients after explanation of the study protocol. Before the ERCP, clinical evaluation of patients was conducted by the fellows of gastroenterology at the time of their presentation. ERCP was performed in all patients by gastroenterologist of Department of Gastroenterology, Liaquat National Hospital, Karachi. The equipment used For ERCP would include:

For screening, Fluoroscopy-A TOSHIBA was used and taking hard copy plain films. Duodenoscopy - An Evis Olympus JF type 230 duodenovideoscope. Outcome variable was the presence of CBD stone identified by gastroenterologist during ERCP. All the results were catered in the preapproved Performa. Confounding variables and biases were controlled by strictly following inclusion and exclusion criteria

Data Analysis

The collected data was analyzed in the statistical package for social sciences (SPSS) version 22.0 Descriptive statistics were included mean±standard deviation (SD) of continuous data, like age and duration of obstructive jaundice. Frequencies and percentages were calculated from the categorical data, like gender (male or female), CBD stones (presence or absence). The data were presented in the form of tables and histograms. Effect modifiers were controlled by stratification of age in groups and duration of jaundice by chi square test. Confidence interval was kept to be 95% and the level of significance was kept to be 5%.

RESULTS

Total 162 patients of either gender, age more than 18 years and less than 60 years with obstructive jaundice of 2-4 weeks duration and normal ultrasound abdomen were included in the study to determine the frequency of Common Bile Duct stones detected on ERCP. Descriptive statistics were calculated. Stratification was done to see the effect of modifiers on outcome. Post stratification chi square test was applied considering $p \leq 0.05$ as significant.

Number of male patients was 106 and female patients were 56. In table-1, the frequency distribution is presented.

The mean age of study subjects was 35.69 ± 11.30 years. The distribution of age is presented in Graph-1. The descriptive statistics of age is presented in Table-1.

The mean duration of jaundice was 2.94 ± 0.81 weeks. The descriptive statistics of duration of jaundice is presented in Table-1.

The final outcome of study showed that CBD stone was 32.7% detected in ERCP even have the normal ultrasound. In table 1, the frequency distribution is presented.

Table No. 1: Frequency Distribution of Gender, Cbd Stone in Ercp & Descriptive Statsttiics of Age & Duration of Jaundice (n=162)

Gender	Frequency (n)	% age
Male	106	65.4%
Female	56	34.6%
Total	162	100%
CBD stones in ERCP		
YES	53	32.7%
NO	109	67.3%
TOTAL	162	
Variable	Mean & standard deviation	
Age (years)	35.69 ± 11.30	
Duration of jaundice (weeks)	2.94 ± 0.81	

Table No.2: Frequency and Association of Cbd Stone in Ercp According to Age (years) (n=53)

	CBD IN ERCP			P-value
	YES (n=53)	NO (n=109)	TOTAL	
≤ 35 years (n=88)	5	83	88	0.001
> 35 years (n=74)	48	26	74	
TOTAL	53	109	162	

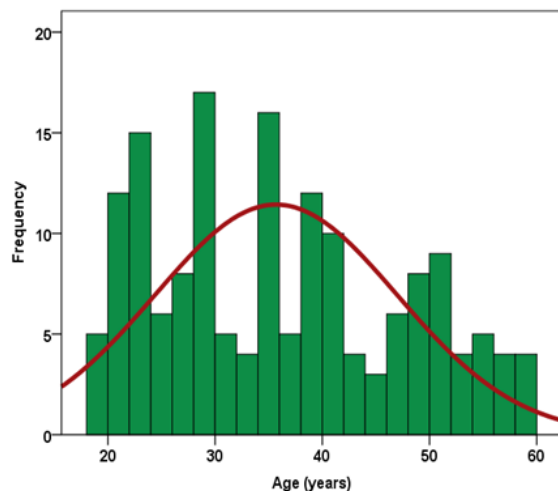
The stratification according to age, duration of jaundice was done to observe the effect of these modifiers on CBD stone in ERCP. Post stratification association of

outcome was observed with modifiers by the use of chi square test.

The results showed that significant association of age with CBD stone in ERCP (P=0.001). No significant association of duration of jaundice was observed with CBD stone in ERCP (P=0.924). The results are presented in detail in Table-2, and Table-3.

Table No.3: Frequency and Association of Cbd Stone in Ercp According to Duration of Jaundice (weeks) (n=53)

	CBD IN ERCP			P-value
	YES (n=53)	NO (n=109)	TOTAL	
2 weeks (n=58)	18	40	58	0.924
3 weeks (n=55)	19	36	55	
4 weeks (n=49)	16	33	49	
TOTAL	53	109	162	



Graph No.1: Histogram Presenting Distribution of Age (years) (n=162)

DISCUSSION

For abdominal surgery, Symptomatic gallstone disease is quite common sign. 500,000 cholecystectomies are estimated to be performed on yearly basis in the United States. Rarely, the gallstones are only the sign for the surgery but it is believed to be carried by 10% of the adult population.

Moreover, the population up to one-third having the age greater than 70 years would have gallstones. Formation of gallstone is a multifactorial process but undoubtedly it is related to the history of the family, pregnancy, diabetes mellitus, obesity, hemolytic disease and significant weight loss⁵.

35% patients with suffering from gallstones would at last become indicative and cholecystectomy would be required¹⁰. Common symptoms for surgical treatment

for cholelithiasis are incorporated with biliary acute cholecystitis, gallstone pancreatitis, colic and various other choledocholithiasis` presentations i.e. cholangitis and bile duct obstruction⁵.

Other related signs e.g. patients of hemolytic anemia experiencing splenectomy with gallstones, patients at high risk before the treatment phase for bone marrow transplant. Cholecystectomy is no more performed routinely for asymptomatic gallstones in those patients who are undergoing aortic surgery or bariatric surgery. Stones of Common bile duct (CBD) may be diagnosed preoperatively, intraoperatively or postoperatively. Those patients who are with signs attributable to cholelithiasis, the standard preoperative workup is carried out for them; the workup is included with the tests of liver function and the ultrasound of abdomen⁵. Combined with the clinical examination and the history, these tests organize the entire workup for many patients. Presence of choledocholithiasis may be suggested by the abnormalities in these tests. The occurrence of Choledocholithiasis may be found in patients with cholecystectomy⁹ or in some series, the occurrence goes to 14.7%.

This is included with various patients deprived of classic preoperative outcomes indicative of choledocholithiasis. It is believed of these asymptomatic patients that around 15% will ultimately become symptomatic and interventional treatment will be required for them⁵.

Since the initiation of timely laparoscopic cholecystectomy, the debate about the utilization of intraoperative bile duct assessment has been continued, with cholangiography or intraoperative ultrasonography primarily. This deliberation endures to some level, with most of the surgeons either selectively or timely conduct the intraoperative evaluation of the bile duct. Only preoperative assessment tools are relied by a smaller subset, this include, endoscopic retrograde cholangiopancreatography (ERCP), magnetic resonance cholangiopancreatography (MRCP) as a accompaniment to tedious investigation of laboratory and imaging. The most prevalent involvement for stones of common bile duct (CBD) is ERCP⁵.

EUS's sensitivity changes from 95%, whereas, specificity is in between 95–98%¹⁰. TUS is significantly less sensitive than EUS in the detection of stones of CBD. EUS sensitivity is comparable to the diagnostic ERCP, whereas, its major benefit is a significantly reduced morbidity in the comparison of ERCP¹¹. Specifically, in the identification of patients it may be beneficial; who would have an advantage from early interference.¹²

Latest authoritative meta-analysis which was incorporated with 67 published controlled trials indicates that MRCP possesses very good sensitivity i.e. 95% and the specificity i.e. 97% for the demonstration of CBDS¹⁴. It was reported by Verma et

al. that there was no any significant differences in EUS and MRCP in the rate of detection of CBDS¹⁵. Lower spatial resolution, potential for claustrophobia, unit availability and inability in the evaluation of patients who are with pacemakers or ferromagnetic implants are counted to be some of the major disadvantages of MRCP in the comparison of ERCP¹³.

CBD stones generally migrate after their origination in the gallbladder. Thus, consequent cholecystectomy would be beneficial in preventing the recurrence of CBD stone. However, in the considerable number of patients with cholecystectomy, recurrence of CBD stone is observed yet. Bile duct stones are considered to be recurrent which are indicated 6 months or greater after endoscopic retrograde cholangiopancreatography (ERCP)¹⁴.

Karki et al¹⁵ have reported 63% patients with CBD stones on ERCP amongst a total of 88 patients with obstructive jaundice. Vidhul et al has reported presence of cbd stones in 42% of patients with elevated liver function values²⁰. Siddique et al¹⁶ found CBD stones were the commonest benign cause but they were just 35% of total.

Similarly Verma et al¹⁷ have reported only 29.1% patients with CBD stones with Obstructive jaundice but in this study, only 15 ERCPs were performed. So it is quite clear that there are variable results in the studies regarding prevalence of CBD stones detected by ERCP. A recently published outcome analysis from Nepal shows overall prevalence of 72.81% CBD stones in patients with different presentation and second common presentation was obstructive jaundice.¹⁸ Another Indonesian study conducted on obstructive jaundice patients shows 51% CBD stone prevalence. Magalhães J et al²⁰ has shown prevalence of 66.8% cbd stone on ercp; main predictor of cbd stone in this study was abnormal liver function tests.²⁰ Slott et al has showed less accuracy of ultrasonography in detecting CBD stone.²¹

The rate of recurrence (4% to 24%) CBD stone has been reported. For recurrent bile duct stones, the risk factors after EST were suggested previously for the dilation of common bile duct, Gall Bladder (GB) stone, biliary stricture, periampullary diverticulum, angulation of the CBD, previous open cholecystectomy, and lithotripsy.²²

CONCLUSION

ERCP is counted to be the gold-standard for the diagnosis and the evaluation of morphological changes in the pancreas. In common bile duct stones, ERCP is the preferred modality for treatment.

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

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To Evaluate the Causes of Primary Infertility on Diagnostic Laparoscopy

Causes of
Primary
InfertilitySarwat Noreen¹, Roeda Shams², Muhammad Alam³ and Nuzhat Amin¹

ABSTRACT

Objective: To find out frequent pelvic pathologies in primary infertility on diagnostic laparoscopy.

Study Design: Observational study.

Place and Duration of Study: This study was conducted at the Health Care Centre Mardan from November 2015 to October 2016.

Materials and Methods: Total of 65 patients with primary infertility was selected. Patients with previous abdominal surgeries and medical comorbidities were excluded. After thorough gynecological examination, necessary investigations were done. Laparoscopy was done on day 10 of menstrual cycle calculated from last menstrual period (LMP) through sub umbilical incision. Data was collected in terms of age, duration of infertility.

Results: Majority of patients were in age group of 26-33 [64%]. Mean age was 28 years (range 18-40). About 41 percent of patients had active marital life of 5-7 years duration. 53 percent had normal findings on laparoscopy. Among the various pathologies most commonly observed was block tube contributing to about 23%. Out of which 9.2% had blocked tubes without adhesions and 13% had blocked tubes with adhesions. Next frequent pathology was PCOS contributing to about 7 (10.8%). Uterine pathologies like fibroid, anomalies were seen in 6.7% and endometriosis in 2.7%.

Conclusion: The most frequent pathology seen in primary infertile patients in diagnostic laparoscopy is tubal blockage.

Key Words: Primary infertility, Diagnostic Laparoscopy, Pathology

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INTRODUCTION

Infertility defined as failure of couple to achieve a successful pregnancy after twelve months or more of regular unprotected intercourse is major cause of disruption of family life.¹ Worldwide subfertility is observed in 60 to 80 million couples and 10-15% married couples are considered infertile. The prevalence of infertility in industrial countries is 20%,² while in Pakistan 21.9% of infertility cases are observed (3.5% primary and 18.4% secondary infertility).³ 90% causes are curable and only 10% are complicated.⁴ Leading causes of infertility includes tubal disease, ovulatory disorder, uterine or cervical factors, endometriosis and male factor infertility.^{5,6}

Hysterosalpingography, the traditional method to evaluate the tubal patency, is largely replaced by laparoscopy, saline intra uterine infusion (SIS) and HYCOSY. Diagnostic laparoscopy is safe and cost effective in the initial management of infertility.⁷ The advantage of laparoscopy over hysterosalpingography is that it not only allows direct visualization of the exterior of uterus and tubes, but also helpful in treatment of selected cases there and then.⁸

MATERIALS AND METHODS

This observational study was done in Health Care Centre Mardan from 1st November 2015 to 31st October 2016. All patients who presented with primary infertility were included in study. After thorough history and examination, baseline hormonal assay (FSH, LH, serum prolactin) and husband semen analysis were carried out. Patients were admitted on day 10 of menstrual cycle and informed consent was taken. Patients with male factor infertility, with previous laparoscopy, non-compliant with the procedure, previous multiple surgeries and patients who were not fit for general anesthesia were excluded from the study. Patients were kept Nil by mouth for 8 hours before the procedure. Laparoscopy was performed under general anesthesia. Laparoscope was introduced through sub umbilical incision and CO₂ insufflation done up to 10-14 mmHg. Thorough assessment of the uterus, tubes, ovaries and pouch of Douglas were done.

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Tubal patency was checked using Methylene blue dye findings were recorded. Patients were discharge in the evening when completely conscious, mobile and passed urine. The data was analyzed using SPSS- 20.

RESULTS

Majority of patients were in 26-33 age group (64%). Sixteen (24.6%) patients were in 18-25 age group and only 7 (10.8%) in 34-40 years (Table1). Duration of infertility was 5-7 years in 27 (41.5%) patients, 2-4 years in 12 (18.5%), 8-9 years in 11 (16.9%) and 11-15 years in 10 (15.4%) patients (Table 2). In 35 patients (53.8%) no pelvic pathology was seen. The most frequent pelvic pathology observed was tubal blockage seen in 23% of patients (13.8% with adhesions and 9.2% without surrounding adhesions) followed by PCOS in 7(10.6%). Frequency of endometriosis and uterine pathology (bicornuate in one patient and fibroids in three patients) was equal in 4 (6.2%)] (Table3).

Table No.1: Frequency of age (n=65)

Age (years)	No.	%
18 – 25	16	24.6
26-33	42	64.6
34-40	7	10.8

Table No.2: Frequency of duration of infertility

Duration of infertility (years)	No.	%
0 -2	3	4.6
3-4	12	18.5
5-7	27	41.5
8-10	11	16.9
11-15	10	15.4
Missing	2	3.1

Table No.3: Frequency of causes of infertility

Cause of Infertility	No.	%
Normal	35	53.8
Blocked tube	6	9.2
Adhesion with block tube	9	13.8
Endometriosis	4	6.2
Uterine pathology	4	6.2
PCOS	7	10.8

DISCUSSION

Laparoscopy is a gold standard investigation for evaluating pelvic pathology in work up of infertile couple. Treatment of Infertility is a challenge for gynecologist as many pathological and social issues are involved with it, due to these issues the management is multidisciplinary approach. About 40% of infertile couples fails to seek treatment, illustrating lack of education and awareness.⁹

In our study majority of patients were in age range of 26-33 years [n=42 (64%)] which is contrary to study done by Haider et al¹⁰, where about 55% of patients

belong to age range of 18-25. About 10% of patients belong to age range of 34-41 years. Female age is considered to be an important determinant in both spontaneous as well as assisted conception and age less than 35 years is considered to be good prognostic factor for fertility.¹¹

Young couples are referred for investigation of infertility after 12 months of failed conception but, for age more than 35 years NICE recommends early intervention.¹² The mean age at which women present with infertility is rising, probably due to delayed marriage and childbearing. In present study mean age was 28 years, similar age group was found in study conducted by Aziz et al.¹³

Regarding causes of infertility tubal occlusion was the most common cause of infertility total 6 cases (9.2%) were of tubal occlusion without adhesions, while 9 cases (13.8%) were tubal occlusion with adhesion contributing to about 23% to the total pathologies. Which is comparable to the study done by Panchal et al¹⁵, where about 21.9% primary infertility was due to tubal occlusion. In developing countries, pelvic inflammatory disease (PID) is the most common cause of tubal pathology. A single episode of PID causes 10% of future tubal factors infertility. Second most common cause was PCOS seen in 7 (10.6 %). Similar result were noted by study conducted by Ara et al¹⁰, 4 cases were of endometriosis (6.2%), comparable results noted by study conducted by Aruna Reddy et al¹⁶ in laparoscopic evaluation of female factors infertility. Laparoscopy is the gold standard both for diagnosis and treatment of endometriosis. Four cases (6.2%) were of uterine pathology like bicornuate uterus (1) and fibroids (3).

CONCLUSION

Tubal occlusion is most common cause of infertility, which mostly results from pelvic inflammatory disease. So, pelvic inflammatory disease needs to be recognized and treated promptly and laparoscopy should be performed as primary investigation in work up of infertile couple.

Author's Contribution:

Concept & Design of Study: Sarwat Noreen
 Drafting: Roeda Shams
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 Revisiting Critically: Sarwat Noreen, Roeda Shams
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Variation in QTc Interval and QT Dispersion Before and After Dialysis among Patients on Thrice Weekly Hemodialysis - Multi Centered Study

Shahid Anwar¹, Alvina Zanib² and Shehzad Tawab³

Variation in QTc Interval and QT Before and After Dialysis

ABSTRACT

Objective: In this study, we intended to measure variation in QT, QTc interval and dispersion before and after hemodialysis in patients of ESRD on MHD. We also tried to check its relationship with various biochemical parameters.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Dialysis centers of SughraShafi Hospital, Narowal and Sir Ganga Ram hospital, Lahore during July 2019.

Materials and Methods: Sixty eight patients of ESRD booked for thrice weekly MHD were enrolled in this study. Baseline characteristics of the all patients recorded. Measurement of QT, QTc and QTD are made on 12 leads ECGs during pre and post dialysis period and compared with the values of serum electrolytes and other dialysis related variables recorded at the time of ECG.

Results: Male to female ratio was 1.9:1, with mean age of 47 years. QTc and QTD were prolonged in 100% and 53% of patients pre-dialysis and prolonged further among 75% and 66% of patients during post dialysis respectively. Serum potassium, magnesium levels, LVH, and serum bicarbonate appeared to be the main determinants of QTD pre and post dialysis.

Conclusion: This study showed that QTcmax and QT dispersion are elevated in hemodialysis patients, and rose further during post-dialysis period. Significant association seen with changes in serum potassium, magnesium, changes in acid-base status and presence of LVH.

Key Words: ESRD: end stage renal disease, MHD: maintenance hemodialysis, QTD: QT dispersion, QTc, corrected QT interval, LVH: left ventricular hypertrophy, ECG: electrocardiography.

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INTRODUCTION

It is true that patients on maintenance dialysis are still having increase risk of death in spite of significant improvement in techniques of dialysis. In United States, the annual mortality rate among dialysis patients in the year of 2008 was 200 deaths per 1000 patient-years¹. Major cause of death among these patients was related to the underlying cardiac diseases, accounting for 40% of all cause mortality¹.

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Another study showed that 50% of the patients suffering from end stage renal disease died due to cardiovascular event². Arrhythmias and sudden cardiac arrest (SCA) are the most common cardiac events according to the United States Renal Data System (USRDS) database¹. In hemodialysis patients, arrhythmias lead to almost 64% of deaths³ while coronary artery diseases (CAD) accounted for almost 20% of deaths. These mortality figures are considerably higher compared to normal population.

What is causing sudden death among dialysis patients is still unknown. However, multiple causes leading to irregularities between myocardial depolarization and repolarization have been identified⁴. It has been proposed that, QT dispersion can directly measure the changes in myocardial repolarization⁵. QT dispersion measured on 12 lead electrocardiogram by subtracting duration of shortest QT interval from longest QT interval. A QT dispersion above 80 ms is considered as abnormal and it reflects that repolarization process in myocardial tissue is not in synchrony⁶. Abnormal QT dispersion can predispose to life threatening arrhythmias and sudden cardiac death^{7,8}. It has been

studied that QT interval can be affected by multiple factors involved in active dialysis session e.g, coronary artery disease, left ventricular hypertrophy^{9,10}, rapid electrolyte shift, hyperkalemia, and increase dialysis vintage¹¹⁻¹⁵.

Fewer previous studies are available showing the variable effect of changing electrolyte concentration on QTc and QTD during hemodialysis^{16,17} but none of the local study is available up to date. Furthermore, assessment of QT interval can provide us with a simple, easy to perform, cheap and fast test to diagnose changes in myocardial action potential. The main objective was to assess changes in QT, corrected QT (QTc) interval and QT, QTc interval dispersion pre and post hemodialysis in patients on MHD. We also tried to check relationship between various biochemical parameters with changes in QT interval.

MATERIALS AND METHODS

Seventy one patients with ESRD undergoing regular HD three times a week, 3-4 hours per session from dialysis centers of Sughra Shafi Hospital, Narowal and Sir Ganga Ram hospital, Lahore, were enrolled in this cross sectional study during July 2019.

Inclusion criteria: The subjects were patients with end stage renal disease on maintenance hemodialysis three times per week above 15 year of age.

Exclusion Criteria: Patients having ECGs with Un-measurable T waves, Atrial fibrillation, Bundle branch block, Pacemaker and Patients taking drugs that affect the QT interval e.g quinidine, procainamide, digoxin, tricyclic & tetracyclic antidepressant were excluded from study.

Data collection procedure:

Patients were enrolled in this study after getting informed written consent. All data regarding their age, gender, cause of end stage renal disease, associated comorbidities, and duration of renal replacement therapy was recorded. Vital signs and ECG was recorded before and after dialysis along with serum electrolytes including serum sodium, potassium, calcium, magnesium, bicarbonate levels. Furthermore serum creatinine and urea levels were checked both pre and post dialysis. Ultrafiltration volume was assessed, and the ultrafiltration rate was calculated. Patient were weighed before and after dialysis. Dialysis of all patients was done with the same dialysate, constituting Na/Ca/K/Mg/Cl/acetate/Hco3- 138/1.25/2.0/0.75/107.5/5.0/35.0 mmol/l, glucose 5.5mmol/l, total osmolarity 294.5mosm/l.

Patient underwent 12 lead electrocardiograms immediately before and after single hemodialysis session under similar conditions. Position of Chest leads was fixed by marking with marker to avoid position change. All ECGs were coded and analyzed manually by first observer. Later on these findings were

confirmed by a second blind observer, an experienced cardiologist, to confirm changes. The QT interval was labelled as the distance between start of Q wave to end of T wave. The end of T wave was marked by a tangent intersecting to limb of T wave with the isoelectric line. In case if U wave was seen then QT interval was measured till the notch between T and U wave. If in any lead end of T wave is not clear, that was excluded from study. Mean value of QT was calculated from three successive QT readings. The Bazett's formula was applied to the maximum QT interval value to get corrected QT for heart rate. The QT dispersion was calculated by the difference between maximum and minimum QT interval in same ECG. Later on corrected QT dispersion was calculated. Abnormal value for QTc interval and QT dispersion were considered if found greater than 440ms and 65ms respectively.

Statistical analysis:

Data analysis was done with the help of SPSS 21. All categorical variables were presented in frequencies and percentage form. All quantitative variables described in mean and standard deviation form. Paired t-test was used for paired samples (pre and post-dialysis) to determine statistical significance. Pearson's test was used to look for correlations between variables. Significant differences in proportions were assessed by the chi-square test. P values <0.05 was considered significant.

RESULTS

We studied 71 patients enrolled in dialysis center of Sir Ganga Ram Hospital, Lahore. Three of them were excluded from study and rest of 68 patient's data was entered for analysis. The major characteristics of patients are shown in table # 1A and 1B. The mean values of serum markers before and after dialysis are shown in table # 2. The mean QT interval duration and QTD values, before and after dialysis, are shown in table #3. Both the QTc interval duration and QTD showed marked variability after hemodialysis. In all patients QTc was found abnormal (>440ms) even in pre-hemodialysis period and increased further in post-hemodialysis period in 51 patients and decreased in 14 patients and remain almost unchanged in 3 patients.

QTD was found abnormal (>65ms) in 36 patients and normal in 32 patients pre-hemodialysis, while post hemodialysis it was abnormal in 51 patients and remain normal in 17 patients. QTD increased post-hemodialysis in 45 patients and decreased in 14 patients and remain almost unchanged in 9 patients. Table # 4 is showing percentage of patients having prolonged QTD in post dialysis period from different categories.

Serum potassium, magnesium levels and presence of LVH appeared to be the main determinants of QTD duration pre-dialysis, while serum bicarbonate was appeared to be the main determinants of QTD duration post-dialysis. While no relationship was observed with

age, gender, mean body weight, blood pressure, changes in serum calcium, albumin, sodium, creatinine, urea and blood sugar level, or with presence or absence of hypertension, diabetes, IHD, or with any specific medications.

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Table No.1A: Baseline characteristics of patients

Characteristics	Frequency (percentage)
Male	44 (64)
Female	24 (36)
Known IHD	16 (23.5)
Hypertension	61(89.7)
Diabetics	32(47)
Current smoker	5(7.4)
Past smoker	18(26.4)

Table No.1B: Baseline characteristics of patients

Characteristics	Frequency (percentage ± SD)
Age (years)	47.2 (13.3)
BMI	24.6 (6.9)
Duration of RRT(years)	4 (2.3)
Ultrafiltration volume(ml)	2406.8 (666.5)

Table No.2: The result of measured variable before and after hemodialysis

	Before hemodialysis (Mean ± SD)	After hemodialysis (Mean + SD)
Serum sodium(meq/L)	141.4 (6.5)	142.7 (5.9)
Serum potassium(meq/L)	5.0 (0.9)	3.6 (1.0)
Serum magnesium(meq/L)	2.1 (0.6)	1.6 (0.4)
Serum calcium(mg/dl)	8.0 (1.0)	8.6 (0.6)
Serum Bicarbonate(mg/dl)	12.6 (4.6)	17.7 (3.5)
Serum urea(mg/dl)	108.9 (29.6)	37.8 (15.4)
Serum Creatinine (mg/dl)	8.2 (2.4)	3.3 (1.2)
Blood sugar level(mg/dl)	157.3 (82.1)	139.7 (51.6)
Serum Albumin(g/dl)	3.9 (0.43)	4.3 (0.5)
Blood pressure (mmHg)		
Systolic	153.9 (21)	144.5 (22.8)
Diastolic	77.9 (12)	73.7 (13.8)
Heart rate (beats/min)	83.4 (13.3)	87.8 (14)
Weight (Kg)	68.4 (19.5)	66.1 (19.3)

Table No.3: Mean values of QTc interval duration and QTD before and after hemodialysis (msec)

	Before hemodialysis	After hemodialysis
QTc interval max	538.7 (49.1)	574.2 (62)
QTD	77.03 (40.7)	107.5 (53.1)
QTcD	89.3 (44.2)	126.5 (56.7)

Table No.4: Percentage of patients having Post dialysis prolonged QTD

Diabetic	35.5%
Non-diabetic	39.7%
Hypertensive	67.6%
Non-hypertensive	7.4%
IHD	19.1%
Non-IHD	55.4%
LVH by Framingham criteria	39.7%
Non-LVH	35.3%

DISCUSSION

This study showed that QTc and QTc dispersion are higher in hemodialysis patients, and rose significantly in post-dialysis period. Similar results are seen in different previous studies^{18,19}. On the other hand, a study done by Covic et al demonstrated that hemodialysis lead to the prolongation of corrected QT interval but no effect seen on corrected QTD in patients with end stage renal disease¹⁷. Such higher levels of QT

dispersion are seen following acute myocardial infarction when patients are at highest risk of potentially fatal ventricular arrhythmias²⁰. Therefore, these results suggest that patients on dialysis are at higher risk of ventricular arrhythmias, especially in the immediate post-dialysis period. Holter monitoring has also documented increased incidence of ventricular arrhythmias among hemodialysis patients²¹.

As we already know that, the QT interval is influenced by changes in serum electrolytes, cations and anions. So, we attempted to check the effect of these variables on changes in QTc dispersion. In our study, serum potassium and magnesium were main determinants of QTD interval in pre-dialysis period with p-value of <0.05. On the other hand, serum bicarbonate was an independent predictor of the QT dispersion during immediate post-dialysis period. However, rest of the plasma variable didn't show any significant relationship with QTc dispersion. However, in previous studies inverse relationship seen between QTc dispersion and serum potassium and serum calcium levels, but no correlation found with serum magnesium levels and serum bicarbonate levels^{17,22,23,24}. This can be due to the fact that the serum bicarbonate level could be influenced by the bicarbonate-based dialysate fluid in our study. So, additional studies are therefore needed with direct measurement of PH and varied composition of bicarbonate in dialysate, to determine this association in more detail.

Another factor which was found significant determinant of increased QT dispersion was presence of LVH by voltage criteria. There is high prevalence of LVH in dialysis dependent patient as seen in previous studies^{10,25} and confirmed in this study by voltage criteria.

The main limitations in our study were small sample size and varying composition of bicarbonate based dialysate solution. Therefore, further studies are needed with larger sample size and standardized dialysate solution to mask its effect on results.

CONCLUSION

This study showed that QTcmax and QT dispersion are elevated in hemodialysis patients, and rose further during post-dialysis period. We found significant association with changes in serum potassium and magnesium, changes in acid-base status and presence of LVH. As this elevated QTc dispersion is linked to increase risk of malignant ventricular arrhythmia, therefore, In future, QT dispersion may prove a novel target for monitoring of hemodialysis patients to reduce mortality and risk of sudden death.

Author's Contribution:

Concept & Design of Study: Shahid Anwar
 Drafting: Alvina Zanib
 Data Analysis: Shehzad Tawab

Revisiting Critically: Shahid Anwar, Alvina Zanib
 Final Approval of version: Shahid Anwar

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

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Examine the Predictor of Mortality in Cirrhotic Patients with Acute Kidney Injury

Abad ur Rehman Awan¹, Ali Saqlain Haider¹ and Syed Waseem Ahmad Mujtaba²

ABSTRACT

Objective: To analyze the predictors that were involved in-hospital mortality associated to acute kidney injury with cirrhosis.

Study Design: Prospective study

Place and Duration of Study: This study was conducted at the Department of Nephrology, Shaikh Zayed Hospital Lahore from 1st July 2018 to 31st December 2018.

Materials and Methods: A total of 100 cirrhotic patients of both genders with acute kidney injury were included. Patient's ages were 25 to 70 years. Patients demographic including age, sex, co-morbidities, etiology of cirrhosis and stages of acute kidney injury were recorded after taking written consent. In-hospital mortality according to the types of acute kidney injury and outcomes were analyzed.

Results: There were 88% males and 12% were females with mean age 42.6 ± 8.22 years. 20% patients had acute kidney injury stage I, 25% patients had stage II and 55% patients had stage III. 40% patients had acute tubular necrosis acute kidney injury type, 44% patients had hepatorenal syndrome and 16% patients had pre-renal azotemia. In-hospital mortality was 47%, in which 22% had hepatorenal syndrome type of acute kidney injury, 20% patients had acute tubular necrosis type. Mortality rate was high in acute kidney injury stage III patients and who required hemodialysis ($p=0.001$).

Conclusion: In-hospital mortality was high in acute kidney injury patients with cirrhosis. Patients with hepatorenal syndrome and acute tubular necrosis had high mortality as compared to pre-renal azotemia. Severity of acute kidney injury was the major predictor of in-hospital mortality.

Key Words: Acute kidney injury, Liver cirrhosis, Mortality

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INTRODUCTION

Worldwide, acute kidney injury considered most common disorder with high rate of morbidity and mortality in patients with cirrhosis of liver.¹⁻³ This malignant and life threatening disorder had different etiologies such as glomerulonephritis, drugs toxicity and ascites but the most common types of AKI are pre-renal azotemia, acute tubular necrosis and hepatorenal syndrome. Many of studies demonstrated hepatorenal syndrome and acute tubular necrosis are the most common classification of acute kidney injury in cirrhotic patients.^{3,4}

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Acute kidney injury patients seen to have very low survival rate and many of factors associated with high mortality rate.⁵⁻⁷ Serum creatinine, MELD score are the prominent measures for examine renal function in patients with liver cirrhosis.⁸⁻¹⁰

There are many causes of acute kidney injury in cirrhotic patients but hepatorenal syndrome is the leading cause in these patients and is directly associated with in-hospital mortality. Many of studies demonstrated that the severity of acute kidney injury is directly associated to high mortality rate.¹¹

Many of studies illustrated patients with HRS type of AKI has high risk of mortality among all types of acute kidney injury with very low survival rate.¹²

MATERIALS AND METHODS

This prospective/observational study was conducted at Department OF Nephrology Shaikh Zayed Hospital, Lahore from 1st July 2018 to 31st December 2018. A total of 100 cirrhotic patients of both genders with acute kidney injury were included. Patient's ages were 25 to 70 years. Patients demographic including age, sex, co-morbidities, etiology of cirrhosis and stages of acute kidney injury were recorded after taking written consent. Acute kidney injury stages were accessed according to the new 2015 Ascites Cub Criteria. Patients with pre-existing chronic kidney disease were

excluded. All patients were categorized according to the types of acute kidney injury. Mortality and factors associated to in-hospital mortality were examined. All the data was analyzed by SPSS 20. Mean±SD was applied. P-value <0.05 was considered as significant.

RESULTS

Out of 100 patients, 88% were males and 12% were females with mean age 42.6±8.22 years. Comorbidities such as diabetes mellitus, chronic liver disease, cardiovascular disease and hypertension found in 12%, 10%, 8% and 10% patients. According to the etiology of cirrhosis 30% patients had hepatitis C, 50% patients had B & C and 20% patients had alcohol consumption. 20% patients had AKI stage I, 25% patients had stage II and 55% patients had stage III. 40% patients had acute tubular necrosis AKI type, 44% patients had hepatorenal syndrome and 16% patients had pre-renal azotemia. At enrollment mean serum creatinine was 2.2±1.32 mg/dl and mean serum urea 90.36±37.76 mg/dl. Mean peak serum creatinine 3.56±1.42 mg/dl (Table 1).

Table No.1: Demographic information of all the patients

Variable	No.	%
Mean age (years)	42.6±8.22	
Gender		
Male	88	88.0
Female	12	12.0
Comorbidities		
Diabetes	12	12.0
CLD	10	10.0
Cardiovascular disease	8	8.0
Hypertension	10	10.0
Etiology of Cirrhosis		
Hepatitis C	30	30.0
Hepatitis B& C	50	50.0
Alcohol	20	20.0
AKI stages		
I	20	20.0
II	25	25.0
III	55	55.0
AKI type		
PRA	16	16.0
HRS	44	44.0
ATN	40	40.0
Laboratory values		
Mean serum creatinine (admission)	2.2±1.32mg/dl	
Mean serum urea	90.36±37.76mg/dl	
Mean peak creatinine	3.56±1.42mg/dl	

In-hospital mortality was 47%, in which 22% had HRS type of AKI, 20% patients had ATN type and 5% patients had pre-renal azotemia. According to the stages of AKI 6% patients were died of stage I, 12% patients

with stage II were died and 29% patients belongs to stage III were died. Severity of AKI is significantly associated to higher mortality (p=0.001) [Table 2]. According to the metabolic parameters as a predictor of mortality, we found out of 47 died patients 43 patients had peak serum creatinine >3mg/dl and 40 patients had peak serum urea >100mg/dl. 40 patients required hemodialysis in which 30 patients were died and 10 patients survived (Table 3).

Table No.2: In-hospital mortality associated to types and stages of AKI

Variable	Died	Survivor	P value
Mortality	47 (47%)	53 (63%)	-
Types of AKI			
HRS	22 (22%)	22 (22%)	0.001
ATN	20 (20%)	20 (20%)	
Pre-renal A	5 (5%)	11 (11%)	
Stages of AKI			
I	6 (6%)	14 (14%)	<0.001
II	12 (12%)	13 (13%)	
III	29 (29%)	26 (26%)	

Table No.3: Metabolic Parameters and hemodialysis as a predictor for mortality

Metabolic parameters	Died	Survivor	P value
Peak serum creatinine >3mg/dl			
Yes	43	10	0.001
No	4	43	
Peak serum urea >100 mg/dl			
Yes	40	12	0.001
No	7	41	
Required Hemodialysis			
Yes	30	10	0.001
No	17	43	

DISCUSSION

Cirrhotic patients with acute kidney injury had a high rate of mortality. Worldwide prevalence of acute kidney injury in liver cirrhosis patients accounted 20-50% and mortality rate varies 10 to 60%.¹³ Many of factors associated to high rate of mortality in acute kidney injury with liver cirrhosis and several studies have been conducted to examine the predictor of mortality in patients with AKI with liver cirrhosis.^{14,15} We also conducted this study to examine the predictors of in-hospital mortality in acute kidney injury patients with cirrhosis of liver. We prospectively analyzed 100 cirrhotic patients of acute kidney injury. In this study majority of patients 88% were males as compared to females with mean age 42.6±8.22 years. These results were similar to many other studies in which male patients population was high as compared to females and majority of patients were ages above 35 years.^{16,17} In present study diabetes mellitus was the most frequent comorbidity found in 12% patients followed by chronic

liver disease and hypertension. Several studies illustrated diabetes mellitus and hypertension were the most frequent comorbidities in AKI patients with liver cirrhosis.¹⁸ In our study 20% patients had AKI stage I, 25% patients had stage II and 55% patients had stage III. We found 40% patients had acute tubular necrosis AKI type, 44% patients had hepatorenal syndrome and 16% patients had pre-renal azotemia. These results were similar to some other studies in which majority of patients had AKI stage III and most of the patients had hepatorenal syndrome and acute tubular necrosis.^{19,20}

In present study mortality was 47%, in which 22% had HRS type of AKI, 20% patients had ATN type and 5% patients had pre-renal azotemia. We found that patients with hepatorenal syndrome and acute tubular necrosis had poor survival as compared to pre-renal azotemia patients. According to the stages of AKI 6% patients were died of stage I, 12% patients with stage II were died and 29% patients belongs to stage III were died. Severity of AKI is significantly associated to higher mortality ($p=0.001$). These results showed similarity to many other studies in which patients with AKI type hepatorenal syndrome and acute tubular necrosis had a high rate of mortality as compared to pre-renal azotemia.^{19,21} We found that patients with AKI stage III had poor survival rate and these results were similar to many other studies in which increase in severity of AKI is significantly associated to high rate of mortality.^{22,23}

In present study according to the metabolic parameters as a predictor of mortality, we found out of 47 died patients 43 patients had peak serum creatinine $>3\text{mg/dl}$ and 40 patients had peak serum urea $>100\text{mg/dl}$. 40 patients required hemodialysis in which 30 patients were died and 10 patients survived. A study conducted by Bhattacharya et al²⁴ reported that peak serum creatinine and those who required hemodialysis and severity of AKI and hepatorenal syndrome were the most important predictors of in-hospital mortality.

CONCLUSION

Acute kidney injury in patients with liver cirrhosis had a poor survival rate in all over the world. We concluded that in-hospital mortality was high in acute kidney injury patients with cirrhosis. Patients with hepatorenal syndrome and acute tubular necrosis had high mortality as compared to pre-renal azotemia. Severity of AKI and hemodialysis were the major predictors of in-hospital mortality.

Author's Contribution:

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Data Analysis:	Syed Waseem Ahmad Mujtaba
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Early Acute Kidney Injury: Examine the Prevalence, Risk Factors and Outcomes in Non-Surgical Patients

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ABSTRACT

Objective: To examine the prevalence of early acute kidney injury, risk factors and outcomes of life threatening disorder.

Study Design: Retrospective/Observational study.

Place and Duration of Study: This study was conducted at the Department of Nephrology, Shaikh Zayed Hospital Lahore from October 2018 to March 2019.

Materials and Methods: Total 200 patients of both genders with ages above 20 years were included. Patients demographic such as age, sex, residence were recorded after taking informed consent. Incidence of early acute kidney injury was examined during first 5 days of hospitalization. Acute kidney injury patients were screened according to Kidney Disease Improved Global Outcomes (KDIGO) guidelines. Risk factors associated to acute kidney injury were analyzed. Outcome in term of mortality was examined.

Results: There were 120 (60%) male patients and 80 (40%) were females with mean age 38.15 ± 12.45 years. Forty (20%) patients were diagnosed to had acute kidney injury in which majority of patients 30 (75%) patients were male. Twelve (30%) patients had AKI stage I, 15 (37.5%) patients had stage II and 13 (32.5%) had AKI stage III. Pre-hospital nephrotoxic use, delay hospitalization, sepsis, age and low education were the associated risk factors of AKI ($p < 0.05$). Ten (5%) patients died in which 9 had AKI.

Conclusion: Prevalence of early acute kidney injury is high in hospitalized patients. Nephrotoxic use, sepsis, delay hospitalization and older age were the associated risk factors. Mortality rate is also high in patients with acute kidney injury.

Key Words: Acute Kidney Injury, Prevalence, Risk factors, Mortality

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INTRODUCTION

Globally, acute kidney injury is considered one of the most common life threatening disorders with high morbidity, mortality.¹⁻³ Early and accurate diagnosis is very helpful measures to reduce the morbidity and mortality associated to acute kidney injury. Molecular markers of early kidney damage would be ideal⁴, but unluckily these tools are not available for routine clinical use. In this scenario measurement of serum creatinine by Acute kidney injury network (AKIN) and KDIGO (Kidney disease improve global outcomes) are the essential tool for diagnosing acute kidney injury.^{5,6}

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The incidence rate of acute kidney injury in hospitalized patients is 5-30% with high mortality and morbidity rate. It could be reduce if early diagnosis and risk factors associated to acute kidney injury were identified. It is very important to indentify the risk factors of AKI for better treatment and to decrease the mortality rate in hospitalized patients. Many of risk factors documented in development of acute kidney injury in hospitalized patients such as age, gender, comorbidities, pre-hospital nephrotoxic use, chronic kidney disease and sepsis, infections etc. If these risk factors are identified on early hospitalization than it could be very helpful to provide better treatment and to reduce the mortality and morbidity.^{7,8} Many of previous studies reported these factors are directly associated in development of early acute kidney injury.^{9,10}

MATERIALS AND METHODS

This retrospective/observational study was conducted at Department of Nephrology, Shaikh Zayed Hospital Lahore from 1st October 2018 to 31st March 2019. Total 200 patients of both genders with ages above 20 years were included. Patients demographic such as age, sex, residence, education were recorded after taking informed consent. Patients less than 20 years and those

with history of chronic kidney disease were excluded. At admission comorbidities such as diabetes mellitus, hypertension, infection, cardiovascular disease, chronic pulmonary disease and history of cirrhosis were examined. At enrollment prevalence of acute kidney injury were examined by serum creatinine according to the Acute Kidney Injury Network (AKIN) and Kidney Disease Improve Global Outcome (KDIGO) criteria. Patients were categorized in to stage I, II and III. Risk factors associated to acute kidney injury were analyzed. Outcomes such as mortality and need for hemodialysis was examined. All the data was analyzed by SPSS 20.0. Chi-square test was applied to examine the outcomes between acute kidney injury patients and non AKI patients. P-value <0.05 was considered as significant.

RESULTS

There were 120 (60%) male patients and 80 (40%) female patients with mean age was 38.15 ± 12.45 years (Table 1). From all the patients, 40 (20%) patients found to have acute kidney injury while 160 (80%) with non-AKI (Table 2). In AKI patients, majority of patients were males 30 (75%) while 10 (25%) were females with mean age 52.36 ± 10.75 years. 25 (62.5%) patients had rural residence while 15 (37.5%) patients had urban residence. Most of the patients 24 (60%) were illiterate. The median serum creatinine level was 0.09 mg/dl, The most common comorbidity in AKI patients was diabetes mellitus found in 16 (40%) patients followed by chronic liver disease 11 (27.5%) patients, cardiovascular disease found in 10 (25%) and hypertension in 8 (20%). Some of the patients had combine morbidities. 12 (30%) patients had KDIGO stage I, 15 (37.5%) patients had stage II and 13 (32.5%) had KDIGO stage III (Table 3).

Table No.1: Overall mean age and gender-wise distribution

Variable	No.	%
Mean age (years)	38.15±12.45	
Gender		
Male	120	60.0
Female	80	40.0

Table No.2: Prevalence of Acute kidney injury

Acute kidney injury	No.	%
Yes	40	20.0
No	160	80.0

The most common risk factor for acute kidney injury was age ($p=0.001$), pre-hospital nephrotoxic drugs use found in 20 (50%) with $p=0.002$, delay hospitalization 15 (37.5%) patients, sepsis in 12 (30%) and no education in 11 (27.5%) patients. Mostly patients had two or more risk factors associated to acute kidney injury (Table 4). Ten (5%) patients were died in which 9 were AKI patients and 1 patient was non-AKI ($p=0.001$). Four (2%) required hemodialysis all were

AKI, Need of ICU admission in 15 patients in which 12 were AKI (Table 5)

Table No.3: Characteristics of all the AKI patients (n=40)

Characteristics	No.	%
Mean Age (years)	52.36±10.75	
Gender		
Male	30	75.0
Female	10	25.0
Residence		
Rural	25	62.5
Urban	15	37.5
Education		
Literate	16	40.0
Illiterate	24	60.0
Comorbidities		
Diabetes	16	40.0
CLD	11	27.5
Cardiovascular disease	10	25.0
Hypertension	8	20.0
AKI Stages		
I	12	30.0
II	15	37.5
III	13	32.5

Table No.4: Associated risk factors

Risk factors	Non-AKI (n=160)	AKI (n=40)	P-value
Age	39.85±12.46	52.36±10.75	0.001
Pre-hospital nephrotoxic drugs use	35 (21.88)	20 (50)	0.001
Delay hospitalization	26 (16.25)	15 (37.5)	0.02
Sepsis	22 (13.75)	12 (30%)	0.01
No education	25 (15.63)	11 (27.5)	0.02

Table No.5: Outcomes among all the patients

Risk factors	Non-AKI (n=160)	AKI (n=40)	P-value
Died	1 (0.63)	9 (22.5)	0.001
ICU admission	3 (1.88)	12 (30%)	0.001
Required Hemodialysis	0 (0)	4 (10%)	<0.001

DISCUSSION

Globally, incidence of early acute kidney injury in hospitalized patients is quite high and ranges 5-30%.^{11,12} Many of risk factors involved in development of acute kidney injury in which age, gender, socioeconomic status, education, diabetes mellitus, use of herbal medicine, chronic kidney disease stage 3,4, sepsis and delay hospitalization are the most frequent risk factors and documented in many of studies regarding acute kidney injury.^{13,14} Present study was

conducted aimed to examine the incidence and risk factors of early acute kidney injury in hospitalized patients. In this regard 200 patients were met the inclusion criteria. In our study the incidence rate of acute kidney injury was 20%. A study conducted by Javier Enrique Cely et al¹⁵ reported incidence of early acute kidney in hospitalized patients was 16% from 400 patients. Some other studies reported 5 to 7% incidence rate of early acute kidney injury in hospitalized patients.^{16,17}

In present study majority of patients who developed early acute kidney injury were males 75% with mean age 52.36 ± 10.75 years. There was significant difference regarding age between patients of AKI and non-AKI $p=0.001$. These results were similar to many other studies in which male patient population was high as compared to females and majority of patients were ages above 45 years.^{18,19} In this study we found 25 (62.5%) patients had rural residence while 15 (37.5%) patients had urban residence. Most of the patients 24 (60%) were illiterate. The median serum creatinine level was 0.09 mg/dl, The most common comorbidity in AKI patients was diabetes mellitus found in 16 (40%) patients followed by chronic liver disease 11 (27.5%) patients, cardiovascular disease found in 10 (25%) and hypertension in 8 (20%). Javier et al¹⁵ reported history of diabetes mellitus and AHT were the most common comorbidities among AKI patients. Another study by Nie et al²⁰ regarding incidence of AKI among hospitalized patients reported hypertension, diabetes and cardiovascular disease were the most common comorbidities.

In our study the most important risk factor for acute kidney injury was age ($p=0.001$), patients with older age had a high risk of developing acute kidney injury among hospitalized patients. Pre-hospital nephrotoxic drugs use found in 20 (50%) with $p=0.002$, delay hospitalization 15 (37.5%) patients, sepsis in 12 (30%) and no education in 11 (27.5%) patients. Mostly patients had two or more risk factors associated to acute kidney injury. Many of studies demonstrated age, pre-hospital nephrotoxic use and sepsis were the most common risk factor of developing early acute kidney injury.^{21,22} In this study 12 (30%) patients had KDIGO stage I, 15 (37.5%) patients had stage II and 13 (32.5%) had KDIGO stage III. These results vary in different studies. Some of studies reported mostly patients with KDIGO stage I and some studies reported most of patients were of stages II and III.^{23,24} These results varies may be due to environmental change and due to the severe conditions of hospitalized patients.

In present study 10 (5%) patients were died in which 9 were AKI patients ($p=0.001$). 4 (2%) required hemodialysis all were AKI, Need of ICU admission in 15 patients in which 12 were AKI. These results showed similarity to some other studies in which mortality rate and need for ICU admission among AKI

patients was high as compared to non-AKI hospitalized patients.^{25,26}

CONCLUSION

Early acute kidney injury in hospitalized patients is the most common life threatening disorder with high rate of morbidity and mortality. We concluded that prevalence of early acute kidney injury is high in hospitalized patients. Nephrotoxic use, sepsis, delay hospitalization, older age and no education were the associated risk factors. Mortality rate is also high in patients with AKI. Severity of AKI is highly associated with high mortality rate.

Author's Contribution:

Concept & Design of Study:	Ali Saqlain Haider
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Data Analysis:	Abad ur Rehman Awan
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Prevalence & Pattern of Opioid Analgesic's Prescription among Doctors of a Tertiary Care Hospital: Are We Moving Towards an Opioid Epidemic?

Muhammad Farooq¹, Sadiq Hussain², Tufail Hussain³, Sajid Razzaq³, Sultan Shah³ and Muhammad Nadeem⁴

ABSTRACT

Objective: To identify its possibility in order to warn all concerned to prevent such epidemic. Opioid epidemic has already occurred in many countries including United States of America due to similar reasons in recent years where state of emergency has been declared in October 26, 2017 to achieve opioid stewardship.

Study Design: Observational study.

Place and Duration of Study: This study was conducted at the Sheikh Khalifa Bin Zayad Alnayan Hospital (CMH) Rawalakot from October 2018 to March 2019.

Materials and Methods: Prevalence and pattern of opioid analgesic use was assessed in 72 practicing doctors (42 consultants and 30 general physicians) working in a tertiary care SKBZ hospital (CMH) Rawalakot through a performa.

Results: Almost all doctors (98.61%) stated that they prescribe opioids. Only one pediatrician stated that he did not use opioid analgesics. Most of doctors (87.50%) prescribed both injections and oral tablets. However some doctors particularly Anesthetists prescribed only injections (2.77%, nelbuphine & morphine) while few general physicians (9.72%) prescribed only oral tablets of opioid analgesics. Majority (41; 56.94%) of doctors did not counsel their patients about options, risk factors and side effects of opioid analgesics.

Conclusion: Opioid analgesics were prescribed by almost all doctors often without following proper guidelines and counseling. This trend can result in impending opioid epidemic of overuse, misuse & addiction. There is a need of physician's awareness & implementation of updated guidelines to promote reduction and judicious prescription of opioid analgesics.

Key Words: acute pain, post-operative pain, Chronic pain, narcotic analgesics, opioids, non-narcotic analgesics, non-pharmacological measures for pain control.

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INTRODUCTION

Management of pain is one of the greatest challenges for physicians. Alleviation of pain depends on the specific type of pain; nociceptive or neuropathic Pain.¹ Effective pain relief is important because it can result in psychological disturbances, disturbed sleep, anorexia, irritability, anger and depression.² Opioids produce analgesia through actions at mu, kappa & delta

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receptors at central nervous system that also respond to endogenous opioid like peptides.³ Opioids are good 2nd line analgesics for moderate to severe pain however these are not safe and can have serious side effects particularly addiction.^{4,5} Well established side effects of opioid analgesics are respiratory depression, drowsiness, sedation, confusion, nausea, vomiting, constipation, depression and risk of tolerance, physical dependence & addiction.⁶ Moreover opioids may worsen postoperative recovery and are associated with delayed wound healing, decreased immunity, increased risk of wound infection, increased morbidity, prolonged hospital stay and higher readmission rates.⁷⁻¹⁰ There is a potential risk of opioid abuse from short term opioid used for acute postoperative pain.¹¹ Estimates suggest that about 3-10% of these patients will continue to take opioids one year after surgery.¹² The euphoric effect of opioids can lead to over-dosage and misuse.¹³ Longterm use of opioid analgesics can lead to endocrinopathy mostly manifested as 'opioid associated androgen deficiency (OPIAD). This syndrome is

characterized by low levels of sex hormones particularly testosterone resulting in reduced libido, erectile dysfunction, fatigue, hot flashes and depression.¹⁴ The world is facing opioid epidemic due to increase in opioid prescriptions in response to the policy of eliminating all pain from 1991 onwards. This trend has resulted in increase in morbidity & mortality due to opioid side effects, over use, & misuse.^{15,16} It compelled many countries including USA to take measures for reduction of opioid prescriptions. On October 26, 2017, President of USA has declared opioid epidemic as public health crisis.¹³ Opioid analgesics are used in 49% cases by pain medicine specialists & in 37% cases by 3 surgeons.¹⁷ Surgeons often under appreciate the risk of developing chronic opioid use after short term use of opioids.¹⁸ Upto 10% patients who were prescribed opioids postoperatively for acute pain will continue to take it for 1 year.¹⁹

As compared to non-opioid analgesics, the benefits of opioid analgesics for pain relief and restoration of body functions are almost similar but the side effects of opioids are much more than non-opioid analgesics.¹¹ Patients should be screened to identify high risk patients, having history of substance use disorder, especially opioids, psychiatric illness, concurrent use of benzodiazepines, extremes of age, pregnancy, significant pulmonary disease, or sleep disordered breathing.²⁰ Non-pharmacological methods, when used in appropriate manner, are effective in pathologies like inflammation, edema, muscle spasm, progressive tissue damage, psychological abnormalities and function loss due to pain. These methods are cognitive-behavioral therapy, physiotherapy, psychotherapy, hot-cold treatments, relaxation-exercise, positioning, movement restriction-resting, distraction, acupuncture, hydrotherapy, transcutaneous electrical nerve stimulation (TENS) and massage.²¹

MATERIALS AND METHODS

This study was performed from October 2018 to March 2019, in Sheikh Khalifa Bin Zayad Alnayan Hospital (CMH) Rawalakot which is a tertiary care teaching hospital affiliated with Poonch Medical College. Approval from hospital medical ethical committee was also taken. Prevalence and pattern of opioid prescription was recorded among 72 practicing doctors (42 consultants and 30 general physicians). A well designed Performa was distributed to all general physicians & consultants to fill the required information. According to inclusion criteria all practicing General Physicians & consultants were included. The non-practicing doctors such as radiologists, Pathologists & administrators were excluded from the study. House job doctors were also excluded from the study. All performas were collected and data was analyzed by using SPSS-21.

RESULTS

Among 72 doctors, 71 (98.61%) stated that they prescribe opioids for acute and chronic pain. The rate of opioid prescription among doctors (table 1).

Table No.1: Prevalence of opioid prescription

S No	Type of doctor	No of doctors	%
1	Consultant Surgeons	21	29.16
2	Consultant Physicians	20	27.77
3	General physicians	30	41.66
4	Not prescribing opioid analgesics	1	1.38

Injectable opioids alone (such as nelbuphine & morphine) were used by two (2.77%) doctors particularly anesthetists. Tablets of opioid analgesics (tramadol) alone were used by 9.72% of doctors particularly general physicians..Both tablets & injections of opioid analgesics were used by 87.50% of doctors particularly by consultant physicians including cardiologists (table 2).

Table No.2: Pattern of opioid prescription

S.No		No. of doctors	%
1	Only Tablets	7	9.72
2	Only Injections	2	2.77
3	Both tablets & injections	63	87.50

Opioid analgesics were frequently prescribed by 30 (41.66%), sometimes by 18 (25%) and rarely by 23 (31.94%) of doctors (Table 3).

Table No. 3: Trend of opioid prescription

S.No		No. of doctors	% of doctors
1	Frequently	30	41.66
2	Sometimes	18	25
3	Rarely	23	31.94
4	Non	1	1.38

A significant number (41;56.94%) of the doctors stated that they did not counsel their patients about options, risks and consequences of use of opioid analgesics because of lack of time as they have to treat a lot of patients and they think that use for one time did not need it. None of the doctors identify risk factors before opioid prescription.

DISCUSSION

Over the past three decades, opioid analgesic prescriptions and their adverse consequences has increased mainly due to misinformation that opioids are highly effective and safe analgesics. Lack of knowledge

about guidelines to prescribe opioids and inaccurate belief of under treatment of pain also contributed. Now main aim is pain reduction to minimum bearable level and zero pain is considered as unrealistic expectation.²² The vast range of opioid side effects and risk of overdose due to tolerance, misuse due to euphoria and addiction due to physical dependence & euphoria explains the fact why opioids are among the most common cause of adverse drug events in the hospital. This study showed that there is a recent trend of increased use of opioid analgesics and majority of doctors (98.61%) prescribed opioid analgesics for acute and chronic pain. These results are similar to findings by Manchikanti L et al (2012) and Cramer JD et al in 2018; in USA.^{16, 23} However the only difference is that in Pakistan there were scanty Pain specialists. In a study by Bell EA (2017) it was shown that opioid prescription in adults and in pediatric patients both has increased risk of pediatric injuries, poisonings and misuse particularly by adolescents. The rate of children and adolescents hospitalization for opioid drug poisoning has increased 300 times from 1997 to 2012 in USA.²⁴ Many countries are facing epidemic of misuse of opioid prescription and USA has declared it as a public health crisis on 26-10-2017, ordering state authorities to take prompt measures to reduce opioid prescriptions. Since 1990 when zero pain strategy was adopted and opioids were falsely considered as potent safe analgesics, opioid analgesic prescriptions has increased many folds resulting to a lot of complications.²⁵

Doctors are responsible to relieve or reduce patient's pain at all costs. However increasing trend is noticed about use of opioid analgesics which can lead to opioid use disorder (OUD), opioid abuse and addiction. Opioid prescription can be reduced by doctor's awareness about recent guidelines for use of opioids. Counseling of the patients about alternate options and awareness of consequences of opioid analgesic use can help the patients to reduce the choice of opioid usage.

Non-opioid analgesic measures considered as first line treatment for any type of pain are acetaminophen, non-steroid anti-inflammatory drugs (NSAIDs), pregabalin, dexamethasone, local anesthetics, ketamine and non-drug methods. Opioid analgesics are effective for moderate to severe types of pain but due to vast range of side effects these drugs should be used as 2nd line analgesics or when non-opioid analgesic are ineffective to control pain.¹³ According to a survey report by the United Nations office on drug and crime in 2013 found that more than 6.7 million Pakistanis have used opioids in 2012 alone.²⁶ Pakistan is more prone to develop opioid epidemic due to its limited resources, poverty, low literacy rate and increasing opioid production in Afghanistan making its way to Pakistan. However it can learn lesson from America's opioid epidemic to reduce opioid prescription by active education of doctors and medical students to follow recent

guidelines to prescribe opioid analgesics. Moreover, promotion of pain management concept by multimodal methods to minimum bearable level instead of zero level and judicious use of opioids can also help to reduce use of opioid analgesics.

Adjuvant non-pharmacological measures like early patient's mobilization, physiotherapy, exercise, heat or cold therapy can also help to reduce pain to minimum bearable level.²¹

CONCLUSION

Opioid analgesics are commonly prescribed by almost all doctors often without following proper guidelines and counseling. This trend can result in impending opioid epidemic in Pakistan which can be avoided by educating doctors and medical students about opioid prescription guidelines, proper selection, counseling & monitoring of patients.

Author's Contribution:

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Data Analysis:	Sajid Razzaq, Sultan Shah, Muhammad Nadeem
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To Determine the Frequency of Biochemical Adverse Effects in Patients on Meglumine Antimoniate Treatment for Cutaneous Leishmaniasis

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Biochemical
Adverse Effects
on Meglumine
Antimoniate
Treatment for
Cutaneous
Leishmaniasis

ABSTRACT

Objective: To determine frequency of biochemical adverse effects in patients on meglumineantimoniate treatment for cutaneous leishmaniasis.

Study Design: Cross sectional study.

Place and Duration of Study: This study was conducted at the Department of Dermatology, Bolan Medical College/ Sandeman Provincial Hospital, Quetta from January, 2017 to December, 2018.

Materials and Methods: A total of 241 patients with the diagnosis of CL were included in this study. The patients were treated with intra-gluteal injections of MA (Glucantime; Aventis, France) at a dose of 20mg/kg/day for 21 days. Patients were interviewed regarding their basic demographics. Blood samples were taken at 2nd week after starting treatment. Blood was sent for complete blood count, liver functions tests, serum creatinine and serum amylase level. Data was analyzed using SPSS version 23.

Results: A total of 241 patients were included in the study. The mean age of the patients was found to be 26.04 ± 9.23 years. The gender distribution of patients showed that most of the participants were male in this study. Mean BMI was 29.25 ± 5.34 kg/m². Most of the patients were having their symptoms from 4-8 weeks. Regarding the abnormality in biochemical variables after start of treatment, it was observed that the most commonly deranged variable was serum amylase in 66 patients (27.3%), followed by alkaline phosphatase in 56 patients (23.23%), ALT levels in 47 patients (19.5%) and serum AST levels in 41 patients (17.01%). Stratification of all these variables was done for age, gender, BMI levels and duration since start of symptoms and was significant for very few of them.

Conclusion: It is concluded that biochemical changes in patients of cutaneous leishmaniasis taking meglumineantimoniate do occur. Therefore, we need to educate our patients and need to tell them about the expected changes before the start of treatment with meglumineantimoniate.

Key Words: Meglumine antimoniate; Leishmaniasis; Serum; Biochemical; Sandfly

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INTRODUCTION

Leishmaniasis is caused by a protozoan parasite of the genus *Leishmania*. The main vector for it is the Sand fly that infects vertebrates, which act as reservoirs of the disease⁽¹⁾.

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The disease is transmitted through sand flies which must have fed any person previously having the disease. However, the outcomes depends upon many factors including species of sand fly, immune system of the recipient as well as on type of *Leishmania*⁽²⁾. The cutaneous type of Leishmaniasis involves skin only and leaves a scar. However, it may evolve into diffuse cutaneous leishmaniasis, leishmaniasis recidivans, or mucocutaneous leishmaniasis (MCL)⁽³⁾. Cutaneous leishmaniasis (CL) is the commonest variety of leishmaniasis, while visceral leishmaniasis (VL) is the most severe one.

Several agents had been being used since ages for its treatment including antimony.^{(3)(4,5)}. Pentavalent antimonials are being used for treatment of leishmaniasis for more than six decades. However, their mechanisms of action are not yet well understood. It is not even clear whether the final active form is Sb(V) or Sb(III). It acts as a prodrug and undergoes biological reduction to its active ingredient, which acts against the

Leishmaniasis. It is now most commonly used agent against this particular disease⁽⁶⁾.

One recent study has found serious hepatic biochemical changes in patients taking meglumineantimoniate. Serum AST, ALT and alkaline phosphatase were elevated in 20%, 20% and 7%. In the same study serum total bilirubin was elevated in 6% of patients⁽⁷⁾. Another study has reported serious biochemical changes in pancreatic and renal metabolism. Hyperamylasemia was noted in 40% and increases serum creatinine was reported in 8%. Leukocyte was elevated in 8%⁽⁸⁾.

The aim of my study was to find the biochemical changes in patients on meglumineantimoniate treatment for cutaneous leishmaniasis. At the international level, a significant body of research has been done on this issue but the situation is very different in Pakistan, where not such any research of significance has been conducted on this subject. The present study is an endeavor in this direction, generating data, which could be utilized in early identification of adverse biochemical changes and developing treatment services for patients on meglumineantimoniate treatment for cutaneous leishmaniasis in our population.

MATERIALS AND METHODS

This Cross sectional was conducted at Department of Dermatology, Bolan Medical College/ Sandeman Provincial Hospital, Quetta. The Study duration was 2 years from January, 2017 to December, 2018. The sampling technique used was Non-probability consecutive sampling. Sample size was calculated using WHO calculator taking the prevalence of raised bilirubin (least proportion) in patients on antimoniate therapy i.e. 6%, margin of error $d=3\%$ and 95% level of confidence. Sample size came out to be $n=241$. We included all patients between the ages 18-60, diagnosed as leishmaniasis as per operational definition and on treatment for > 2 weeks. We Excluded all patients having CRF documented as serum Cr > 2.5 at presentation; Hepatitis A, B and C positive patients (determined by positive Elisa test for hepatitis A, B and C); and patients of chronic pancreatitis. The data collection was started after an approval from the CPSP. After taking ethical committee approval and explaining the procedure informed constant was taken. A total of 241 patients were recruited from Out Patient Department and wards of Department of Dermatology, Bolan Medical College/ Sandeman Provincial Hospital, Quetta on the basis of inclusion criteria. The patients were treated with intra-gluteal injections of MA (Glucantime; Aventis, France) at a dose of 20 mg/kg/day for 21 days. Patients were interviewed regarding their basic demographics. Blood samples were taken at 2nd week after starting treatment. Blood was sent for complete blood count, liver functions tests, serum creatinine and serum amylase level. The diagnosis of biochemical adverse effects were made as

per operational definitions and were noted in proforma by researcher. The patients having CRF documented as serum Cr > 2.5 at presentation or Hepatitis A, B and C positive patients determined by positive Elisa test for hepatitis A, B and C or patients of chronic pancreatitis documented on U/S abdomen were excluded from the sample to control effect modifiers so that bias in the study results can be overcome. The patients were assured for recovery and socioeconomic cultural values were considered while examining the female patients. Data was analyzed using software of Statistical Package of Social Sciences (SPSS version 23). Mean + SD were calculated for continuous variable of age, height, weight, BMI, daily dose and duration of treatment. Results on categorical variables of gender and patient outcome variable biochemical adverse effects i.e. Raised AST, raised ALT, raised Alkaline Phosphatase, raised total bilirubin, hyperamylasemia, raised creatinine and raised leukocyte count were expressed in frequencies and proportions. Stratification of age, gender, BMI and duration of treatment was done to see their effect on outcome variable. Assuming the P value of <0.05 as significant, Chi-Square was used to detect the difference between the categories.

RESULTS

A total of 241 patients were included in the study. The mean age of the patients was found to be 26.04 ± 9.23 years. Patients were further categorized according to age groups into 4 groups. The gender distribution of patients showed that most of the participants were male in this study. The mean BMI was calculated as 29.25 ± 5.34 kg/m².

Table No. 1: Demographic and clinical details of patients

	No. of patients
Age of patients	
18-30 Years	135 (56.01%)
30-40 Years	56 (23.23%)
40-50 Years	21 (8.7%)
51-60 Years	29 (12.03%)
Mean \pm SD (years)	26.04 ± 9.23
Gender: Male	
Female	64 (26.55%)
BMI: <25kg/m²	
25-30kg/m ²	176 (73.0%)
>30 kg/m ²	29 (12.0%)
Mean \pm SD (kg/m ²)	29.25 ± 5.34
Duration Since Start Of Symptoms	
<4 weeks	35 (14.5%)
4-8 weeks	115 (47.7%)
>8 weeks	91 (37.7%)
Mean \pm SD	8.32 ± 4.88 weeks
Duration Since Start Of Treatment	
≤ 10 days	138 (57.26%)
>10 days	103 (42.73%)
Mean \pm SD (Days)	10.8 ± 2.81

Table No. 2: Distribution of patients according to deranged Biochemical Variable

Biochemical Variables		No. of patients	%
Raised AST	Yes	41	17.0%
	No	200	83.0%
Raised ALT	Yes	47	19.5%
	No	194	80.5%
Raised Alkaline Phosphatase	Yes	56	23.2%
	No	185	76.8%
Raised Bilirubin	Yes	35	14.5%
	No	206	58.5%
Raised Amylase	Yes	66	27.3%
	No	175	72.7%
Raised Creatinine	Yes	19	7.9%
	No	222	92.1%
Raised Leukocyte Count	Yes	21	8.71%
	No	220	91.29%

Table No.3: Stratification of Biochemical variables with respect to age

Biochemical Variables	Age groups	Yes	No	P-Value
Raised AST	18-30 Years	23	112	0.754
	30-40 Years	8	48	
	40-50 Years	5	16	
	51-60 Years	5	24	
Raised ALT	18-30 Years	26	109	0.604
	30-40 Years	9	47	
	40-50 Years	6	15	
	51-60 Years	6	23	
Raised Alkaline Phosphatase	18-30 Years	31	104	<0.001
	30-40 Years	11	45	
	40-50 Years	6	15	
	51-60 Years	8	21	
Raised Bilirubin	18-30 Years	18	117	0.860
	30-40 Years	9	47	
	40-50 Years	4	17	
	51-60 Years	4	25	
Raised Amylase	18-30 Years	41	94	0.209
	30-40 Years	11	45	
	40-50 Years	8	13	
	51-60 Years	6	23	
Raised Creatinine	18-30 Years	7	128	0.297
	30-40 Years	5	51	
	40-50 Years	3	18	
	51-60 Years	4	25	
Raised Leukocyte Count	18-30 Years	8	127	0.028
	30-40 Years	4	52	
	40-50 Years	5	16	
	51-60 Years	4	25	

The mean duration since start of symptoms of patients in this study was found as 8.32 ± 4.88 weeks. Most of the patients were having their symptoms from 4-8 weeks. The mean duration since start of treatment of

patients in this study was found as 10.8 ± 2.81 days. Most of the patients were having their treatment from ≤10 days.

Table No.4: Stratification of Biochemical variables with respect to gender

Biochemical Variables	Age groups	Yes	No	P-Value
Raised AST	Male	27	150	0.234
	Female	14	50	
Raised ALT	Male	29	148	0.044
	Female	18	46	
Raised Alkaline Phosphatase	Male	38	139	0.289
	Female	18	46	
Raised Bilirubin	Male	18	159	0.001
	Female	17	47	
Raised Amylase	Male	51	126	0.395
	Female	15	49	
Raised Creatinine	Male	12	165	0.295
	Female	7	57	
Raised Leukocyte Count	Male	15	162	0.836
	Female	6	58	

Table No.5: Stratification of Biochemical variables with respect to BMI

Biochemical Variables	BMI (kg/m ²)	Yes	No	P-Value
Raised AST	<25	5	31	0.754
	25-30	32	144	
	>30	4	25	
Raised ALT	<25	6	30	0.696
	25-30	34	142	
	>30	7	22	
Raised Alkaline Phosphatase	<25	8	28	0.966
	25-30	41	135	
	>30	7	22	
Raised Bilirubin	<25	5	31	0.249
	25-30	23	153	
	>30	7	22	
Raised Amylase	<25	11	25	0.041
	25-30	42	134	
	>30	13	16	
Raised Creatinine	<25	4	32	0.578
	25-30	12	164	
	>30	3	26	
Raised Leukocyte Count	<25	4	32	0.026
	25-30	11	165	
	>30	6	23	

All these details are summarized in table 1 Regarding the abnormality in biochemical variables after start of treatment, it was observed that the most commonly deranged variable was serum amylase in 66 patients (27.3%), followed by alkaline phosphatase in 56 patients (23.23%), ALT levels in 47 patients (19.5%) and serum AST levels in 41 patients (17.01%). All details are given in table 2. Stratification of all these variables was done for age, gender, BMI levels and

duration since start of symptoms. All details are summarized in tables 3,4,5 and 6.

Table No.6: Stratification of Biochemical variables with respect to duration since start of treatment

Biochemical Variables	Durations since start of symptoms	Yes	No	P-Value
Raised AST	≤10 days	21	117	0.371
	>10 days	20	83	
Raised ALT	≤10 days	26	112	0.735
	>10 days	21	82	
Raised Alkaline Phosphatase	≤10 days	25	113	0.026
	>10 days	31	72	
Raised Bilirubin	≤10 days	18	120	0.431
	>10 days	17	86	
Raised Amylase	≤10 days	37	101	0.781
	>10 days	29	74	
Raised Creatinine	≤10 days	11	127	0.971
	>10 days	8	95	
Raised Leukocyte Count	≤10 days	14	124	0.373
	>10 days	7	96	

DISCUSSION

The main objective of the study was to determine the frequency of the biochemical changes in patients on meglumineantimoniate (MA) for CL. The dosing regimen of MA which is being used for VL in the Mediterranean area has been found having a raised frequency of side effects, particularly in patients having Human Immunodeficiency Virus (HIV). The most frequent side effects was acute pancreatitis in these patients. Also, these adverse events led to stoppage and poor compliance for its usage and Leishmaniasis remained endemic worldwide, spreading across almost 88 countries^{(9),(10)}. In many of previously conducted trials, adverse events of MA had been studied mostly in adults and only small number of children had been part of these trials⁽¹¹⁾. In a study by Masmoudi et al, joint and muscle pains were found as the most common complications among 87 patients who received MA. They reported an adverse event rate of 21%⁽¹²⁾. In our study, the concentrations of direct and total bilirubin, creatinine, and hematologic parameters demonstrated rise after starting the treatment. The most common derangement was found in Serum Amylase level in this study. In a study by Shahian et al, who used MA among children with VL, no rise in serum Amylase levels was observed and they negated the routine monitoring of biochemical markers⁽¹³⁾. This is contradictory to our data, however, we included only adult patients in our study. In another study, hyperlipasemia was found in 54.8% and raised amylase levels in 19.4% of patients receiving MA⁽¹⁴⁾, which is similar to our results. Although mixed results are

available in the literature, however, continued monitoring of renal, hepatic, and pancreatic function during and immediately after antimonial treatment is prudent and has never been negated⁽¹⁵⁾.

My study also had some limitations. It was a single center study, so I recommend a multicenter study on the topic. Also it was a single group study, therefore more trials having more study limbs and with proper randomization is needed to reveal all the aspects. It is concluded that biochemical changes in patients of Leishmaniasis taking meglumineantimoniate do occur. Therefore, these patients need to be educated pre-handedly about the expected complications and these biochemical changes.

CONCLUSION

It is concluded that biochemical changes in patients of cutaneous leishmaniasis taking meglumineantimoniate do occur. Therefore, we need to educate our patients and need to tell them about the expected changes before the start of treatment with meglumineantimoniate.

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 Revisiting Critically: Syed Bilal Ahmed
 Final Approval of version: Syed Bilal Ahmed

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

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Comparative Study of Anterior Decompression for Caries Spine using Strut Graft with and without Instrumentation

Anterior Decompression for Caries Spine using Strut Graft

Muhammad Asif Saeed¹, Imran Idrees Butt², Maqsood Ahmed Khan³, Kamran Hamid⁴, Salman Imran Butt⁴ and Muhammad Haris Muazz⁴

ABSTRACT

Objective: To compare the anterior decompression for caries spine using strut graft with and without instrumentation.

Study Design: Comparative Study

Place and Duration of Study: This study was conducted at the Idris Teaching Hospital of Sialkot Medical College, Sialkot from January 2018 to July 2019.

Materials and Methods: A total of 60 patients were included into group A and Group B, 30 patients in each. Group A patients were managed with strut graft and instrumentation using Moss Miami system. Group B patients were treated by strut graft only. The sample size is based on the past 1 year record of the hospital and about this number of patient is expected to be available. Written Informed consent was taken from every patient included in this study. The permission of ethical committee was also taken Information was then collected using Performa. Participants were selected through non probability consecutive sampling technique.

Results: The outcome of and follow up of the patients immediate after operation, there was no patient of complete slippage and 50% slippage i.e. 100% patients were stable. On 3rd day, 100% patients were stable, on 1st month of discharge the patients were 100% stable, on 2nd month, there were 06(10%) patients of 50% slippage were found and there were 30/24(100/80%) patients were stable, on 3rd month there was 6(10%) patients of 50% slippage were found and 30/24(100/80%) patients were stable. On 4th month, 2 patients(3.33%) of complete slippage and 4 patients (6.66%) of 50% slippage were found and the rest of the patient were stable, on the fifth month the results were same as at the 4th month, at six month of discharge there were 2 patients (3.33%) of complete slippage and 04 patients(6.66%) of 50% slippage were found and the rest of the patient were stable.

Conclusion: We believe that graft with instrumentation is more effective than only graft from reducing the deformity and stabilizing the vertical column in patient who have tuberculosis of the spine.

Key Words: Caries spine, anterior decompression, strut graft with moss Miami and strut graft

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INTRODUCTION

Tuberculosis is the world's leading causes of the death, from a single infectious disease with 2 million death in 1990. It is the most endemic, chronic infection which paralyzes the society when it effects the spine due to its resultant neurological deficit. Despite the adequate control of pulmonary tuberculosis, the incidence of musculoskeletal tuberculosis is increasing¹.

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Progressive kyphotic deformity is a common end result of neglected TB spine. Anterior decompression along with anti-tuberculous chemo therapy will hasten formation of bone with prevention of kyphosis and its complication.² Spine instrumentation is needed to support the anterior strut graft in patients who have kyphosis that effect more than 2 levels. The anterior instrumentation is more effective than posterior instrumentation.³

Posterior decompression in the form of transpedicular fixation is necessary in short segment fixation only as it preserves the functional unit of spine.⁴

MATERIALS AND METHODS

A total of 60 patients were included into group A and Group B, 30 patients in each. Group A patients were managed with strut graft and instrumentation using Moss Miami system. Group B patients were treated by strut graft only. The sample size is based on the past 1 year record of the hospital and about this number of

patient is expected to be available. Written Informed consent was taken from every patient included in this study. The permission of ethical committee was also taken. Information was then collected using Performa. Participants were selected through non probability consecutive sampling technique. The permission of ethical committee of the research is also taken.

Sample selection:

Inclusion criteria:

1. All the patients were between 15-60 years of age of both sex with no previous spinal surgery having spinal tuberculosis from D7-L5 vertebrae were included
2. Having neurological status of any grade were included in this study
3. Tuberculous spine which involves less than 3 vertebrae included in this study
4. Patients not responding to conservative treatment were included in this study

Exclusion criteria:

1. Patients with caries of cervical and upper six segments of thoracic spine
2. Patients having congenital spinal deformity
3. Patients having myopathic and paralytical disorder

Data collection: Patients demographic information, history, clinical examination, investigations type of surgical procedure, the recovery and follow up were recorded in a special design performa. The data was analyzed by SPSS 10.0 version. As the outcome of this study was "quantitative" t-test were applied for significance.

Data Analysis: Data was entered and analyzed in SPSS v23.0. Quantitative variables include age, duration of dialysis and duration of PPI use and were expressed as mean \pm standard deviation. Qualitative variables include gender and presence of hypomagnesemia and were expressed as frequencies and percentages. Data was stratified for age, gender, duration of dialysis, duration of PPI use and type of PPI used to deal with effect modifiers. Post-stratification, Chi-square test was used. $P \leq 0.05$ will be considered significant.

RESULTS

At the age of 20-30 years there were 8 patients(13.33%) in group A and 12(20%) in group B. At the age of 31-40 years there were 8 patients (13.33%) in group A and no patient in group B. At the age of 41-50 years, there were 12 patients (20%) in group A and 6 patients (10%) in group B. At the age of 51-60 years there were 2 patients (3.33%) in group A and 12 patients (20%) in group B. At the age >60 years there were 4 patients in group A and no patient in group B as Shown in Table 1. There were 26 married patients (43.33%) in group A and 24 patients (40%) in group B. There were 4 unmarried patients (6.66%) and 6 patients (10%) in group B as shown in table 2.

There were 25 male patients (41.66%) in group A and 20 male patients (33.33%) in group B. There were 05 female patients (8.33%) in group A and 10 female patients (16.66%) in group B as shown in table 3

At the site of D7-D8, there were 6 patients(10%) in group A and no patient in group B. The site of lesion at D8-D9 there were 4 patients (6.66%) in group A and 6 patients (10%) in group B. At D9-D10, there were no patient in group A and 06 patients (10%) in group B. At D10-D11 there was no patient in group A but 06 patients(10%) in group B. At the D12 there were patients(6.66%) in group A but there were no patient in group B. At Lumbar region (L1-L2) there were 12 patients (10%) in group A and 6 patients (10%) in group B. At L2-L3 there were 4 patients (6.66%) in group A but there was no patient in group B. At L4-L5 there was no patient in group A but 6 patients (10%) in group B as shown in table 4.

In neurological status, there were 24 patients(40%) having normal tone in group A and also 24 patients (40%) having normal tone in group B but the tone was increased in 06 patients(10%) in group A and also 6 patients (10%) in group B. The reflexes were normal in 24 patients (40%) in group A and 12 patients(20%) in group B but the reflexes were exaggerated in 6 patients(10%) in group A and 18 patients (30%) in group B. The muscle power was normal(5/5) in 14 patients (23.33 %) and 12 patients (20%) in group B, muscle power was 2/5 in 4 patients (6.66%) in group A and 6 patients (10%) in group B, the muscle power was 2+ in 4 patients (6.66 %) in group A and 06(10%) in group B, the muscle power was 4/4 in 8 patients(13.33%) in group A and 6 patients(10%) in group B. Sensory system was normal in 20 patients(33.33%) in group A and 12 patients (20%) in group B, Below D7, there were 4 patients (6.66%) in group A and 6 patients(10%) in group B, below d 10 there were 6 patients (10%) in group A and also 6 patients (10%) in group B, the sensory system was normal, below umbilicus in 6 patients (10%) in group B and there was no patient in group A as shown in table 5. According to frankel's classification, the neurological status in class A and class B there was no patient in pre operative and post operative cases, in class C there was 4 pre operative patients(6.66 %) in group A and 6 patients (10%) in group B and there was no post operative case in A group and 2 patients (3.33%) in group B, in class D there were 12 pre operative patients (20%) in group A and 12 patients(20%) in group B, there were 2 post operative patients(3.33%) in group A and B in each group, in class E there were 14 pre operative patients (23.33%) in group A and 12 patients (20%) in group B and there were 28 post operative patients (46.66%) in group A and 26 post operative patients(43.33%) in group B as shown in table no 6

The outcome of and follow up of the patients immediate after operation, there was no patient of

complete slippage and 50% slippage i.e. 100% patients were stable.

Table No 1:Age Distribution

Age(Years)	Group A	Group B
20-30	4(6.66%)	12(20%)
31-40	8(13.33%)	-
41-50	12(20%)	6(10%)
51-60	2(3.33%)	12(20%)
>60	4(6.66%)	-

Table No. 2: Distribution of marital status

Married/Unmarried	Group A	Group B
Married	26(43.33%)	24(40%)
Unmarried	4(6.66%)	6(10%)

Table No.3:Gender Distribution

Gender	Group A	Group B
Male	25(41.66%)	20(33.33%)
Female	05(8.33%)	10(16.66%)

Table No.4: Distribution of Site of Lesion

Site of Lesion	Group A	Group B
Thoracic (D7-D8)	06(10%)	-
D8-D9	04(6.66%)	6(10%)
D9-D10	-	06(10%)
D10-D11	-	06(10%)
D12	04(6.66%)	-
Lumbar (L1-L2)	12(20%)	06(10%)
L2-L3	4(6.66%)	-
L4-L5	-	6(10%)

Table No.5: Distribution of Neurological Status

System	Group A	Group B
Tone(normal)	24(40%)	24(40%)
Increased	06(10%)	06(10%)
Reflexes(normal)	24(40%)	12(20%)
Exaggerated	06(10%)	18(30%)
Power(normal)5/5	14(23.33%)	12(20%)
2/5 both	4(6.66%)	6(10%)
2+both	4(6.66%)	3/5 both (6)(10%)
4/5	8(13.33%)	4/5 Lt,5/5 Rt (6)(10%)
Sensory System (Normal)	20(33.33%)	12(20%)
Below D7	4(6.66%)	6(10%)
Below D10	6(10%)	6(10%)
Below Umbilicus	-	06(10%)

Table No.6: Neurological Status according to Frankel's Grade classification Pre operative Post operative(6 months)

	Group A	Group B	Group A	Group B
A	-	-	-	-
B	-	-	-	-
C	4(6.66%)	6(10%)	-	2(3.33%)
D	12(20%)	12(20%)	2(3.33%)	2(3.33%)
E	14(23.33%)	12(20%)	28(46.66%)	26(43.33%)

Table No.7 : Outcome and follow ups

	Complete Slippage	50% Slippage	Stable
Immediate after operation	-	-	30/30(100/100%)
On 3 rd day	-	-	30/30(100/100%)
On discharge (1 st month)	-	-	30/30(100/100%)
2 nd month	-	0/6	30/24(100/80%)
3 rd month	-	0/6	30/24(100/80%)
4 th month	0/2	0/4	30/24(100/80%)
5 th month	0/2	0/4	30/24(100/80%)
6 th month	0/2	0/4	30/24(100/80%)

On 3rd day, 100% patients were stable, on 1st month of discharge the patients were 100% stable, on 2nd month, there were 06(10%) patients of 50% slippage were found and there were 30/24(100/80%) patients were stable, on 3rd month there was 6(10%) patients of 50% slippage were found and 30/24(100/80%) patients were stable. On 4th month, 2 patients(3.33%) of complete slippage and 4 patients (6.66%) of 50% slippage were found and the rest of the patient were stable, on the fifth month the results were same as at the 4th month, at six month of discharge there were 2 patients (3.33%) of complete slippage and 04 patients(6.66%) of 50% slippage were found and the rest of the patient were stable as shown table 7.

Comparison between group A and group B at the level of 1st month after operation and at 6 months after follow up, the $p < 0.05$ i.e. statistically not significant

DISCUSSION

Tuberculosis is most endemic, chronic infection, which paralyzes the majority when it effects the spine due to its resultant neurological deficit. Despite adequate control of pulmonary tuberculosis, the incidence of musculoskeletal tb increasing.⁵

There is continuous rise in the patients of TB spine not only in the under developed country but also in developed countries has led to a challenging problem and created an increasing demand on the orthopedic department.⁶

Moreover, this disease poses a very grave effect on financial & economical balance of the society. There disabilities demand a more quick, rewarding and practicable mode of treatment of the patients in the form of full physical recovery and quiescence of the disease. But the picture had been quite opposite and confusing regarding treatment option. Especially in the

anterior column disease which is the most frequent and most often lead to paraplegia. In the pre chemotherapy era, the balance was more in the favour of surgery. In this regard, Hodgson and Stock contributed the most and made the situation quite clear by establishing and popularizing anterior decompression and fusion as a definite mode of treatment of anterior column TB. But with the advent of chemotherapy, situation become more debatable regarding conservative vs surgical procedure. It was the trial of MRC & WP which made the situation quite clear but there last reports favour conservative approach .As this grave disease is quite endemic in Pakistan so need for local study was always felt.⁷⁻¹²

In our study, there were 70-80% patients were stable on Anterior Decompression For Caries Spine using Strut Graft With And Without Instrumentation, which correlates with study of Hodgson and Stock.

Lonestein reported lower rates of penetration , breakage ,collapse and psuedoarthrosis of the rib grafts. With use of anterior instrumentation than the use of posterior instrumentation.¹⁰⁻¹⁷

In our study, there were 70-80% patients were stable on Anterior Decompression for Caries Spine using Strut Graft With and Without Instrumentation, which correlates with study of Lonestein. Other authors have reported ,when more than 2 levels are involved there is anterior instability and the kyphosis progresses rapidly^{11,12,18-20}. However, we find that sufficient stability and correction can be obtained with anterior instrumentation and bone grafting after decompression of tuberculosis spine without increasing the rates of persistent and recurrent tuberculous infection.

The use of anterior instrumentation alone is possible only if the posterior column is intact. Anterior instrumentation should not be used to correct kyphotic deformity when posterior column is affected^{13,21,22,23,24}.

In our study ambulant chemotherapy was continued for 1 year .Complete neurological recovery was seen in 88% with an average duration of 8 months. Regarding the final outcome of grafting, group A was stable throughout the follow up. At the end of 4 month in group B 2 patients (3.33%) were found to have partial slippage of graft 50% slippage out of 6 patients (10%) and at the end of 5 month 2 patients (3.33%) were having partial slippage of graft. In group B at the end of six months 2 patients (3.33%) were having complete slippage of graft i.e. the graft was not confined and 4 patients showed partially graft slippage (50% slippage) And 24 patients (40%) were stable .We concluded that graft with instrumentation is more effective than only graft of reducing deformity and stabilizing the vertical column in patients who have TB of spine.

CONCLUSION

We concluded that graft with instrumentation is more effective than only graft of reducing deformity and

stabilizing the vertical column in patients who have TB of spine.

Author's Contribution:

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Hepcidin as a Marker of Anemia in Chronic Hepatitis C Infections

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ABSTRACT

Objective: To determine the level of serum hepcidin and iron studies in patients of chronic hepatitis C with anemia and to calculate sensitivity, specificity, negative predictive value, positive predictive value, diagnostic accuracy of serum hepcidin and to differentiate between patients of iron deficiency anemia and anemia of chronic disease.

Study Design: Diagnostic Study.

Place and Duration of Study: This study was conducted at the Department of Pathology, Post Graduate Medical Institute (PGMI) Lahore. Subjects were taken from Medical Outdoor / Liver Clinic, Lahore General Hospital from 01.06.2015 to 30.06.2016.

Materials and Methods: The study included 70 diagnosed patients of chronic hepatitis C which were divided into IDA group and ACD group. The IDA group comprised of 17(73.91%) males and 6(26.09%) females, while in ACD group there were 39(82.98%) males and 8(17.02%) females. The parameters studied were blood hemoglobin, total iron binding capacity, serum iron, percent transferrin saturation, serum ferritin and serum hepcidin and subsequent data was recorded. Mean \pm standard deviation, frequency distribution and percentages were calculated. Using serum ferritin as a standard 2x2 table was made to determine diagnostic accuracy of serum hepcidin.

Results: In the present study mean hemoglobin, MCV, serum iron, TIBC, ferritin and hepcidin in IDA and ACD groups were 7.21 ± 1.29 g/dL, 8.69 ± 0.86 g/dL, p-value < 0.001 , 63.30 ± 8.04 fL and 86.51 ± 6.61 , p-value < 0.001 , 30.98 ± 13.50 , 34.36 ± 17.53 μ g/dl, p-value > 0.05 , 431.91 ± 145.05 μ g/dl and 230.51 ± 89.74 μ g/dl, p-value < 0.001 , 20.37 ± 4.08 and 154.07 ± 144.01 , p-value < 0.001 , 2.39 ± 1.39 and 15.17 ± 7.21 ng/ml, p-value < 0.001 respectively. The Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of serum hepcidin levels was 91.3%, 87.23%, 77.78% and 95.35% respectively. Diagnostic accuracy of serum hepcidin levels was 88.57% with positive regression coefficient (beta) and hepcidin Odds ratio for Hepcidin was 71.750.

Conclusion: Low levels of serum hepcidin levels are significantly associated with decreased iron parameters in iron deficient patients of chronic hepatitis C and hepcidin could be a useful indicator of iron deficiency anemia and to differentiate iron deficiency anemia from anemia of chronic disease. Patients with decreased hepcidin level might get benefit by the use of iron therapy.

Key Words: ACD anemia of chronic disease, IDA Iron deficiency anemia, serum hepcidin, serum ferritin

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INTRODUCTION

Hepatitis C virus is a single-stranded enveloped RNA virus having positive polarity. This virus is a member of the hepaciviruses genus which belongs to Flaviviridae family.

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This is one of the most essential infectious agents for the human which is able to cause varying degree of liver disease. This virus is seen in almost all the regions of the world and almost 170 million are infected this comprises for greater than 3% of the world's population. The Hepatitis C virus can reside in the host for a long period.¹

HCV spreads mainly by blood contact accompanying intravenous drug use, transfusions and ill sterilized instruments. According to one estimate about 130-200 million people of the world are diseased by Hepatitis C virus.²

The iron is kept in its soluble state by the attachment of transferrin and which also acts as a main transporter for the release of iron to the cells through transferrin receptor, TfR1 and synthesis of toxic radicals is prevented by it. Almost 30% Transferrin in human is iron saturated. A level of saturation less than 16% entitles iron deficiency, and saturation more than 45% is a mark for overload of the iron. And when saturation level is more than 60%, the iron which is not attached

to the transferrin initiates accumulation and may cause damage of the parenchyma cells.³

Iron homeostasis in mammals is mainly controlled by hepcidin. Hepcidin is a 25-amino acid peptide hormone with a multifaceted linkage of 4 disulfide bonds.⁴ Ferroportin enables the outward movement of iron from intestinal cells, liver cells and macrophages after hepcidin binding, leads to reduced release of iron.⁵ A large diversity of factors, like hemojuvelin, transferrin receptor-2, bone morphogenetic protein 6, transferrin, the HFE gene, hypoxia and inflammation are involved in the regulation of hepcidin level.⁶

Hepcidin transcription is also regulated by inflammation. Cytokines such as IL-6 facilitate this reaction by prompting of hepcidin mRNA transcription by a signal transducer and activator of transcription 3 (STAT3), which then attaches to a STAT-responsive element inside the promoter of hepcidin. It has been reported that in patients with anemia of chronic inflammation or due to any severe inflammatory disorder, a 100-fold increase in urinary excretion of hepcidin observed. An infusion of IL-6 in human may prompts excretion of urinary hepcidin within two hours resulting in hypoferremia. This indicates that up-regulation of hepcidin which is mediated by IL-6 as a result of inflammation, have a key role in imbalance of iron homeostasis which is detected in acute as well as in chronic inflammatory diseases.⁷ A noteworthy relationship between hepcidin and serum ferritin has been observed as hepcidin transcription is mainly controlled according to concentration of iron in these patients. In this way conflicting the effects of HCV made despotic factors of hepcidin and hepcidin inspiration factors due to raised iron which are possibly included in the direction of hepcidin transcription in these patients of hepatitis C.⁸

Decreased or undetectable level of hepcidin is seen in iron deficiency, increased level in conditions like transfusion-induced iron overload and inflammatory diseases, and also showed high association with serum ferritin levels. It has been observed by Girelli, Nemeth and Swinkels that the patients of anemia of chronic disease are also threatened for having deficiency of iron.¹⁰ According to Tomas Ganz hepcidin is controlled in response to both by the erythropoietic requirements for iron and by iron concentrations. In mouse models, hepcidin-1 mRNA was shown to be suppressed by anemia and hypoxia and induced by iron loading.⁹ The patients with chronic disorders like chronic renal failure, inflammatory bowel disease, or using drugs like nonsteroidal anti-inflammatory drugs or antithrombotic drugs often present with chronic blood loss. In such situation hepcidin can distinguish iron deficiency anemia and anemia of chronic disease better than traditional marker such as iron studies. Patients having both iron deficiency combined with inflammatory disorders characteristically present with reduced serum

hepcidin as compared to those patients presenting with only anemia of chronic disease.¹⁰

AIM OF THE STUDY

The aim of this study is to demonstrate the role of serum Hepcidin in progress of anemia and in the control of iron homeostasis in chronic hepatitis C patients pointing the differentiation of the types of anemia in these patients.

Therefore this project is envisaged to study anemia in these patients and their evaluation by using serum Hepcidin as a new diagnostic tool to differentiate anemia in chronic hepatitis C patients, which will lead to better evaluation and management of these patients.

MATERIALS AND METHODS

The study was conducted at the Department of Pathology, Post Graduate Medical Institute (PGMI) Lahore. Subjects were taken from Medical Outdoor / Liver Clinic, Lahore General Hospital from 01.06.2015 to 30.05.2016 for 12 months. Non probability convenience sampling technique was used. The study was performed on 70 subjects. The patients were divided into two groups according to the results. Group 1 or Iron deficiency anemia (IDA) group: Inclusion criteria for this group was: low Hb (male <13 g/dl and female <12 g/dl), TSAT <20% and Ferritin concentrations <30 ng/ml. Group 2 or Anemia of chronic disease (ACD) group: Inclusion criteria for this group was: Hb concentration <13 g/dl for male and <12 g/dl for female and low TSAT <20% and normal 30-100 ng/dl or increased Serum Ferritin concentration >100ng/ml.

Ten ml of venous sample was collected under aseptic measures. About 3 ml blood sample was placed into EDTA vacutainer for hemoglobin determination. The remaining quantity of blood was collected in yellow vials and left for a while without anticoagulant to allow to clot. Then serum sample was obtained by centrifugation at room temperature at 3000 rpm/10 minutes to assay serum iron, serum ferritin, TIBC serum transferrin saturation and serum hepcidin. The serum was stored at -20 °C until analysis.

Inclusion criteria:

1. Patients with age range of 20-60 years and of both sexes.
2. All patients with chronic Hepatitis C positive determined by PCR-HCV RNA for 6 months.
3. Hemoglobin level <12g/dl females and <13g/dl males determined by hematology analyzer.

Exclusion criteria:

1. Patients with a history of repeated and / or recent blood transfusions, hematinic/parenteral iron therapy.
2. Significant gastrointestinal bleeding, alcoholism.
3. Coexisting HBV or human immunodeficiency virus infection.

4. De-compensated cirrhosis, liver disorders other than HCV infection.
5. Current or previous antiviral therapy.
6. Connective tissue disorders such as Rheumatoid Arthritis, Systemic Lupus Erythematosus.
7. Evidence of renal disease.
8. Evidence of malignancy.

RESULTS

Distribution of Age in the Study Groups: The minimum age in the IDA study group was 28 years and maximum age was 57 years the Mean \pm SD 42.91 \pm 7.01. The minimum age in the ACD study group was 25 years and maximum age was 60 years the Mean \pm SD 41.701 \pm 9.12 (Table 3.1). The mean age of patients was 42.10 \pm 8.45 where as in IDA and ACD group mean age was 42.91 \pm 7.01 years and 41.70 \pm 9.12 years, the mean age in both groups was the same.

Table-No.1: Comparison of Age in both groups

IDA	ACD	Total
17(73.91%)	39(82.98)	56
6(26.09)%	8(17.02)	14
23	47	70

Key: IDA = Iron deficiency anemia, ACD = Anemia of chronic disease, n = frequency and %= Percentage

Table No.2: Comparison of Hb (g/dL) in both groups

		Mean	S.D
Hb g/dL	IDA (n=23)	7.21	1.29
	ACD (n=47)	8.69	0.86
	Total (n=70)	8.20	1.23

Key: IDA = Iron deficiency anemia, ACD = Anemia of chronic disease, Hb = Hemoglobin, n = frequency and % = Percentage, Hb, a. Independent sample test was applied

Table No.3: Comparison of MCV in both groups

		Mean	S.D
MCV	IDA (n=23)	63.30	8.04
	ACD (n=47)	86.51	6.61
	Total (n=70)	78.89	13.05

Key: IDA = Iron deficiency anemia, ACD = Anemia of chronic disease, Hb = Hemoglobin, n = frequency and % = Percentage, MCV = Mean cell volume, b. Mann Whitney U test was applied

Table No.4: Comparison of TIBC (µg/dl) in both groups

		Mean	S.D
TIBC µg/dl	IDA (n=23)	431.91	145.05
	ACD (n=47)	230.51	89.74
	Total (n=70)	296.69	145.45

Key: IDA = Iron deficiency anemia, ACD = Anemia of chronic disease, TIBC= Total Iron Binding Capacity, n = frequency and % = Percentage, b. Mann Whitney U test was applied.

Table-5: Comparison of S/Ferritin ng/ml in both groups

		Mean	S.D	Minimum	Maximum	p-value
S/Ferritin ng/ml	IDA (n=23)	20.37	4.08	14.30	28.00	<0.001 ^b
	ACD (n=47)	154.07	144.01	34.00	690.00	
	Total (n=70)	110.14	133.54	14.30	690.00	

Key: IDA = Iron deficiency anemia, ACD = Anemia of chronic disease, n = frequency, b. Mann Whitney U test was applied.

Table No.6 Comparison of S/Hepcidin ng/ml in both groups

		Mean	S.D	Minimum	Maximum	p-value
S/Hepcidin ng/ml	IDA (n=23)	2.39	1.39	1.50	7.10	<0.001 ^b
	ACD (n=47)	15.17	7.21	2.30	29.10	
	Total (n=70)	10.97	8.48	1.50	29.10	

Key: IDA = Iron deficiency anemia, ACD = Anemia of chronic disease, n = frequency, b. Mann Whitney U test was applied.

Table No.7: Diagnostic comparison of S/Hepcidin ng/ml in both groups

	Study Group		Total	
	IDA	ACD		
S/Hepcidin ng/ml	≤ 2.7	21	6	27
	> 2.7	2	41	43
Total		23	47	70

The Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of serum hepcidin levels was 91.3%, 87.23%, 77.78% and 95.35% respectively. Diagnostic accuracy of serum hepcidin levels was 88.57% with positive regression coefficient (beta) and hepcidin Odds ratio for was 71.750 that shows there 71.750 time more chances of IDA in cases having Hepcidin ≤ 2.7 .

DISCUSSION

In both anemia and state of hypsideremia, the raised level of serum hepcidin helps to differentiate anemia of chronic disease from iron deficiency anemia. A condition of mixed anemia can arise in conditions with chronic inflammatory diseases due to bleeding with or

without malnutrition. Under such conditions, the hypsideremia could neutralize the inflammation mediated hepcidin increase. A true iron deficiency may develop from non-intestinal absorption by hepcidin, when inflammation is present for a long time¹¹. In such settings, it is difficult to detect iron deficiency using traditional iron biomarkers, but hepcidin may be helpful. Patients with inflammatory disorders and concomitant iron deficiency typically have reduced serum hepcidin levels as compared with those with pure anemia of chronic disease.¹⁰

In the present study the mean MCV in IDA group was 63.30 ± 8.04 fL and in mean MCV in ACD group was 86.51 ± 6.61 fL with significantly lower MCV in IDA groups, p -value < 0.001 . According to Naqvi et al., 2014 MCV in his iron deficiency anemia patients was 78.15 ± 2.71 fL.¹² The results of the present study were similar to Duru et al., 2014 who showed MCV levels in iron deficient anemia patients and anemia of chronic disease patients to be 63.30 ± 5.9 and 75.32 ± 8.50 fL with a p -value < 0.001 .¹³ In one study by van Santen et al., 2011 mean MCV value in iron deficient anemia patients and anemia of chronic disease patients were 82.9 (80.8–87.3) and 91.4 (89.9–96.6) with a p -value < 0.03 .¹⁴

In the present study the mean total iron binding capacity (TIBC) $\mu\text{g/dl}$ was significantly higher in IDA group 431.91 ± 145.05 $\mu\text{g/dl}$ as compared to ACD group 230.51 ± 89.74 $\mu\text{g/dl}$, p -value < 0.001 . This was similar to Naqvi et al., 2014 where he reported mean TIBC in his iron deficiency anemia patients to be 470 ± 4.3 mg/dl.¹² Our results were in accordance with Duru et al., 2014 who showed mean serum TIBC levels in iron deficiency anemia patients and anemia of chronic disease patients to be 443.46 ± 43.96 and 310.30 ± 94.7 mg/dl with a p -value < 0.001 .¹³

In the present study mean Ferritin in IDA and ACD group was 20.37 ± 4.08 and 154.07 ± 144.01 ng/ml with significant difference, p -value < 0.001 . According to Naqvi et al., 2014 mean ferritin level in his iron deficiency anemia patients was 9.09 ± 1.35 ng/mL.¹² Duru et al., 2014 showed that mean serum ferritin levels in iron deficiency anemia patients and anemia of chronic disease patients were 4.10 ± 3.29 and 111.8 ± 158.2 ng/ml, p -value < 0.001 .¹³ According to Van Santen et al., 2011 mean Ferritin levels in iron deficient anemia patients and anemia of chronic disease patients were 11.5 (8.3–22.8) and 191 (102–262), p -value < 0.001 which was similar to our results.¹⁴ In the study conducted by Eun et al., 2015, he found the serum ferritin levels in iron deficient anemia patients and anemia of chronic disease patients to be 11.38 ± 10.13 and 111 ± 54.95 $\mu\text{g/ml}$ which are again similar to our results.¹⁵

In the present study the mean S/Hepcidin ng/ml in IDA group was 2.39 ± 1.39 and 15.17 ± 7.21 ng/ml with lower Hepcidin values in IDA when compared to ACD

group, p -value < 0.001 . This was in accordance with van Santen et al., 2011 and Choi et al., 2012.^{14,16} Results of Van Santen et al., 2011 study showed mean hepcidin levels in his iron deficient anemia patients and anemia of chronic disease patients to be 0.4 (0.4–0.8) and 7.4 (2.6–11.0) nmol/liter, p -value < 0.001 .¹⁴ Choi et al., 2012 has stated a serum hepcidin level of 2.07 ± 2.30 ng/ml, p -value < 0.0001 for his iron deficient anemia patient.¹⁶ Eun et al., 2015 found the serum hepcidin levels in iron deficient anemia patients and anemia of chronic disease patients to be 2.31 ± 3.24 and 10.52 ± 11.6 $\mu\text{g/ml}$ which were similar to our results.¹⁵

According to van Santen et al., 2011 serum hepcidin at < 2.4 nmoles/liter had a sensitivity of 89% and a specificity of 88% to distinguish iron deficiency anemia from anemia of chronic disease (combined state) from anemia of chronic disease similar to our present study results.¹⁴ Choi et al., 2012 showed serum hepcidin level of 2.07 ± 2.30 ng/ml, p -value < 0.0001 for his iron deficient anemia patient and according to his study hepcidin at 6.895 ng/mL had a sensitivity of 79.2% and specificity of 82.8% to make the diagnosis of iron deficiency.¹⁶ Pasricha et al., 2011 has reported that serum hepcidin less than 8 ng/mL showed a sensitivity of 41.5% and a specificity of 97.6% while hepcidin less than 18 ng/ml showed a sensitivity of 79.2% and a specificity of 85.6% for the diagnosis of iron deficiency anemia.¹⁷

There remains substantial uncertainty for the precise cutoffs of these indices to define iron deficiency and state of chronic inflammation. According to Pasricha et al., 2011 anemic patients without inflammation with hepcidin less than 0.5 nmol/l were considered to have iron deficiency anemia. And the patients with inflammation and hepcidin below 2.4 nmol/l or in case with hepcidin between 2.4 and 7.6 nmol/l combined with reduced reticulocyte hemoglobin, were considered to have combined iron deficiency anemia and anemia of chronic disease. Patients with inflammation and hepcidin above 7.6 nmol/l were considered to have anemia of chronic disease.¹⁷

Van Santen et al., 2011 has confirmed the use of hepcidin for the identification of iron deficiency anemia either alone or with concomitant inflammation in his patients with rheumatoid arthritis.¹⁴

CONCLUSION

In conclusion, the discovery of hepcidin has increased the possibility of understanding the disturbances of iron homeostasis especially in iron deficiency anemia and anemia of chronic disease. Our study demonstrated that

1. Low levels of serum hepcidin were significantly associated with decreased iron parameters including serum ferritin in iron deficient patients of chronic hepatitis C which could be a useful indicator of iron deficiency anemia.

2. Serum hepcidin and serum ferritin were normal in anemia of chronic disease group which was useful to label the anemia of chronic disease in patients of chronic hepatitis C.
3. The diagnostic comparison of serum hepcidin and serum ferritin showed a high sensitivity, specificity and diagnostic accuracy of serum hepcidin for the diagnosis of iron deficient patient and to differentiate these patients from anemia of chronic disease in chronic hepatitis C.

Author's Contribution:

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

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What Makes Hypertensive Patients Non-Compliant to Treatment? A Cross-Sectional Study from Peshawar

Causes Of Non-Compliance To Anti-Hypertensive Medications

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ABSTRACT

Objective: To determine the frequency of causes of non-compliance to anti-hypertensive medications.

Study Design: Cross-sectional / descriptive study.

Place and Duration of Study: This study was conducted at the Department of Medicine; Khyber Teaching Hospital Peshawar from January 2019 to June 2019.

Materials and Methods: This study was conducted on 178 non-compliant hypertensive patients recruited in the study through consecutive sampling and subjected to a detailed questionnaire-based interview to determine the causes of non-compliance to treatment.

Results: The mean age of the patients was 55.8 + 7.22 years. We had 53.37% males & 46.6% females in. The most common causes of treatment non-compliance identified were unaffordability (60.1%) followed by multiple drugs (39.9%), lack of information by caregiver & missed appointments (33.1% each) and occurrence of side effects (27%).

Conclusion: The most common causes associated with non-compliance to hypertension treatment include unaffordability, using multiple medications at one time, lack of information given to the patients by health care providers, missed follow-up visits on part of the patients and troublesome side effects of drugs causing discontinuation of treatment.

Key Words: Hypertension, Non-compliance, Drug treatment.

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INTRODUCTION

Hypertension is defined as persistent elevation of systolic blood pressure (SBP) of 140 mm Hg or more, or a diastolic blood pressure (DBP) of 90 mm Hg or more, or taking antihypertensive medication¹. As per WHO statistics, an estimated 1.13 billion people worldwide have hypertension, most (two-thirds) living in low- and middle-income countries². In 2015, 1 in 4 men and 1 in 5 women had hypertension².

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In view of the magnitude of the problem, it is considered as a pandemic of the 21st century.

Hypertension is a well-established major risk factor for stroke, myocardial infarction, vascular disease, and chronic kidney disease³. Being a chronic disorder, it requires life-long treatment and compliance to lifestyle modifications and treatment is a major determinant of adequate control. However; non-compliance is a major obstacle to the effective delivery of health care worldwide⁴. This also reflects in WHO official report which found that fewer than 1 in 5 people with hypertension have the problem under control².

Major barriers to compliance are thought to include the complexity of modern medication regimens, poor "health literacy" and lack of comprehension of treatment benefits, the occurrence of intolerable side effects, the cost of prescription medicine, and poor communication or lack of trust between the patient and his or her health-care provider⁵. Besides, compliance rates may be overestimated in the medical literature as compliance is often high in the setting of a formal clinical trial but drops off in a "real-world" setting⁶.

The World Health Organization has set a global target to reduce the prevalence of hypertension by 25% by 2025 (baseline 2010)². Effective achievement of this target besides other measures requires addressal of the potential challenges including the issue of non-

compliance. This study aims at identification of the major causes of non-compliance to anti-hypertensive treatment in the population of Khyber Pakhtunkhwa.

MATERIALS AND METHODS

This descriptive, cross sectional study was carried out in the department of Medicine, Khyber Teaching hospital Peshawar from January 2019 to June 2019. A total of 178 hypertensive patients were selected through non probability sampling after explaining the purpose and benefits of the study and a written informed consent was obtained.

For sample selection all patients who were non-compliant as per operational definition to anti-hypertensive drugs in the last 6 months and both gender were included in the study.

Patients aged below 18 years, patients with psychiatric illnesses as co-morbidity and patients who are known to be allergic to various anti-hypertensive drugs were excluded.

After approval from Head of the department of concerned medical unit, all non-compliant hypertensive patients having BP greater than 160/100 mmHg and meeting the inclusion criteria were enrolled in the study through OPD. All patients were subjected to detailed history and clinical examinations and careful scrutiny of past medical records and detailed history to detect the factors which led to non-compliance like unaffordability, lack of counseling by the caregiver, > 3 Antihypertensive drugs, missed appointments and side effects. All the demographic details and above mentioned information was recorded in a pre-designed proforma.

Data Analysis Procedure: Data was entered and analyzed by statistical package for social sciences (SPSS) version 17. Mean + SD was calculated for numerical variables like age. Frequencies and percentages were calculated for categorical variables like gender and factors (unaffordability, lack of counseling by the caregiver, missed appointments, side effects and > 3 Antihypertensive drugs). Factors were stratified among age, gender and educational status to see the effect modifications.

RESULTS

Tables.1 and 2 show the age, gender and education status-wise distribution of the study sample. Of the total 178 patients, the mean age of the patients was 55.8 + 7.22 years (range: 42-69 years). 53.37% (n=95) of the participants were males and 46.6% (n=83) were females. The mean duration of hypertension was 6.87 + 4.30 years.

Non-compliant patients were more likely to be male, uneducated and in the 51-60 years age- group. Non-affordability (60.1%) was found to be the most common reported cause of non-compliance followed in descending order by use of multiple (≥ 3)

antihypertensive drugs (39.9%), lack of counseling by the caregiver & missed appointments (33.1% each) and intolerable side effects of medications (27.0%). The commonly reported side effects of medications warranting discontinuation of treatment are listed in Table.4.

Chi-square test was applied for all the factors of non-compliance to determine association. The association between lack of counseling and educational status was found statistically significant with p value of 0.03 (Table.5).

Table No. 1: Age, Gender And Education Status Wise Distribution Of Sample (n=178)

		Gender		Total	%tage
		Male	Female		
Age groups	Less than or equal to 50 years	32	20	52	29.2%
	51 to 60 years	35	44	79	44.3%
	More than 60 years	28	19	47	26.4%
Total		95 (53.37%)	83 (46.62%)	178	100%

Table No. 2: Educational Status Wise Distribution Of Sample (n=178)

		Gender		Total	%tage
		Male	Female		
Education	Uneducated	17	57	74	41.57%
	Primary	22	9	31	17.4%
	Secondary and intermediate	28	11	39	21.9%
	University and above	28	6	34	19.1%
Total		95	83	178	100%

Table No. 3: Frequencies of Common Factors Leading to Non-Compliance (n=178)

Factors	Frequency	Percent
Unaffordability	107	60.1
3 or more drugs regimen	71	39.9
Lack of counseling	59	33.1
Missed appointments	59	33.1
Side Effects	48	27

Table No. 4: Frequency Of Drug-Related Side Effects (N=48)

Side effects	Frequency	Percent
Cough	19	39.6
Dizziness	13	27.1
Fatigue	10	20.8
Excessive urination	6	12.5
Total	48	100

Table No. 5: Education Status Wise Stratification Of Lack of Counselling (n=178)

		Counselling		Total
		No	Yes	
Education	Uneducated	32	42	74
	Primary	9	22	31
	Secondary and intermediate	13	26	39
	University and above	5	29	34
Total		59	119	178

P=0.03

DISCUSSION

Hypertension is currently one of the biggest single contributors to global mortality and extensive randomized trial data are consistent in showing that blood pressure reduction substantially reduces cardiovascular morbidity and mortality⁷.

This study aimed to probe into the common causes of non-compliance to anti-hypertensive treatment as a tool for guiding corrective measures logically. It revealed non-affordability (60.1%) to be the most common reported cause of non-compliance followed in descending order by use of multiple (≥ 3) antihypertensive drugs (39.9%), lack of counseling by the caregiver & missed appointments (33.1% each) and intolerable side effects of medications (27.0%).

Unaffordability was reported as the leading cause of non-compliance in this study. This finding is consistent with the results of a study conducted in Zambia in which unaffordability was reported by 61% participants⁸. Similarly, 58.9% of the non-compliant patients belonged to low socioeconomic class in a study conducted in Iraq⁹. While high cost of treatment is a universal issue in under developed and developing countries, financial hardship is a significant barrier to complying with treatment in developed countries as well. A survey conducted in United States in 2002 reported association between poor compliance and lack of funds for the purchase of drugs¹⁰. In contrast to our findings, a study conducted by Kabir, M. et al. in Nigerian hypertensive population, only 32.7% of the study population reported lack of funds to purchase drugs¹¹. This variation may be because of better awareness, higher income or provision of health insurance in that study population.

Our study showed that use of 3 or more antihypertensive drugs is another major contributor to non-compliance. This corroborates well with the results of a Malaysian study¹² where non-compliance depended on number of medications taken, being 40.7% for one drug, 49.2% for two drugs, 48.6% for three and 75% for more than three drugs (27). So as the number of medication increases the patient becomes more non-compliant. Similarly, Bramley et al. found that 75% of patients on mono-therapy for hypertension were highly compliant to treatment defined as medication possession ratio of 80-100%¹³.

In this study, 33.1% of the participants reported lack of counseling by their health care providers about their disease and its medications. This finding is consistent with the results of a study from Zambia which reported lack of counseling by health care providers in 38% of non-compliant patients⁸. Likewise, a study carried out in India showed that the compliance score of patients during their follow up period was better for the counseled group as compared to usual care group¹⁴. Similarly, Makaryus et al also found that educational process at hospital discharge can impact compliance after discharge¹⁵. Supporting this observation in a prior study that discharge counseling was associated with improved compliance after hospital discharge¹⁶.

Our study found missed appointments as a factor leading to non-compliance in 33.1% of the study population. This finding is supported by a study conducted in Zambia which observed 29% of the non-compliance was due to missed appointments⁸. Another study conducted in Bangladesh on medication non-adherence revealed that one third of patients missed their visit when called for follow up¹⁷. It is common for patients to improve their medication adherence shortly after and before an appointment with a health care provider, which has been termed "white coat compliance"¹⁸. In contrast, a study conducted in Nigeria¹⁹ reported a lower toll of missed appointments (15.8%). This variation may be partly explained by higher educational and high socioeconomic status of the study participants.

In our study, 27% of the patients attributed their non-compliance to treatment to intolerable side effects of anti-hypertensive drugs. This finding is comparable with results of a study conducted by Al-Mehza, Amal M., et al.²⁰ which attributed poor compliance to side effects of drugs in 33.3% of patients. Likewise, in a study by Buabeng KO, 33% of the patients cited side effects as a reason for non-compliance²¹. Tendency towards non-compliance due to intolerable drug-related side effects has been endorsed by Bramley et al from Malaysia¹³ and Hyman and Pavlik from the United States²².

CONCLUSION

The most common causes of non-compliance to treatment of hypertension were unaffordability, use of multiple (≥ 3) antihypertensive drugs at one time, lack of information to patients by health care providers and irregular clinic attendance and intolerable drug-related side effects.

Recommendations: The authors therefore, recommend a broader recognition of the problem of non-compliance and implementation of effective strategies in daily practice to improve compliance.

1. Provision of free or if not possible, cheaper anti-hypertensive drugs in government hospitals and pharmacies.
2. Minimum and effective medications should be prescribed by doctors to improve compliance.

3. Patients should be thoroughly counseled by health care providers about duration of therapy, possible side effects of medications and also complications of non-compliance.
4. Appointments/Follow-up dates should be given in written form rather than verbal.

Furthermore, studies are needed in other parts of Pakistan on factors effecting compliance in hypertension and how such findings can be used for guiding local hypertension-control efforts.

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Metformin in Polycystic Ovary Syndrome Patients

Zubia Bugti

ABSTRACT

Objective: To determine the effect of metformin on the clinical presentation and metabolic disturbances of polycystic ovary syndrome.

Study Design: Observational study.

Place and Duration of Study: This study was conducted at the Department of Obstetrics and Gynecology Unit-I, Sandeman Provincial Hospital, Bolan Medical College, Quetta from 09-09-2018 to 06-06-2019

Materials and Methods: Fifty patients with clinical signs and symptoms of polycystic ovaries syndrome attending the OPD of department of obstetrics and gynecology Unit-I, Sandeman provincial hospital, Bolan medical college Quetta.

Results: A total of fifty women with Polycystic Ovary Syndrome were included in the study. The average age of the patients was found 26.46 ± 1.40 (95% CI: 23.64 to 29.28) years.

The signs and symptoms, of Acne was present in 33 patients (66 %), Hirsutism was present in 43 patients (86 %), Menstrual Irregularity was present in all patients (100 %), Obesity was present in 28 patients (56 %) and Infertility was present in 37 patients (74 %), were present in the patients before treatment.

Improvement in the signs and symptoms, of Acne was seen in 2 patients (6.06 %), Hirsutism was seen in 2 patients (4.65 %), Menstrual Irregularity was seen in 13 patients (26 %), Obesity was seen in 4 patients (5.40 %) and Infertility was seen in 2 patients (5.40 %), after 3 months' treatment.

Improvement in the signs and symptoms, of Acne was seen in 5 patients (15.15 %), Hirsutism was seen in 6 patients (13.95 %), Menstrual Irregularity was seen in 34 patients (68 %), Obesity was seen in 12 patients (42.85 %) and Infertility was seen in 5 patients (13.51 %), after 6 months' treatment.

Conclusion: Metformin administration to women who have signs and symptoms of polycystic ovarian syndrome is associated with marked improvement in menstrual irregularity resulting in regular menstrual cycles and achievement of pregnancy. Improvement in other signs and symptoms of PCOS was also seen with administration of Metformin for six months.

Key Words: Polycystic Ovary Syndrome, An ovulation, Menstrual Irregularities, Hirsutism and Infertility, Metformin.

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INTRODUCTION

Polycystic Ovary Syndrome (PCOS) can be found in 5–10% women in reproductive age. Women with PCOS are characterized by hyperandrogenaemia, hyperinsulinemia, hypothalamic-pituitary-ovarian axis dysfunction, and deranged adipokines secretion from the adipose tissue. These specific alterations interact in different tissues, such as fat, liver, muscle and ovaries, resulting in a variety of phenotypes of the syndrome.

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MATERIALS AND METHODS

A recent survey showed that metabolic disorders, obesity, and type 2 diabetes (T2D) were recognized as the most important long-term concerns related to PCOS¹. Moreover, longitudinal studies showed that worsening of insulin resistance (IR) over time in obese PCOS women is a risk factor for the early development of T2D².

Prenatal androgen overexposure has a direct and permanent effect on the developing female offspring, with a consequent increase in beta-cell number. This provokes altered pancreatic islet function with consequent primary hyperinsulinemia response to glucose, which implies future metabolic derangements³. It was shown recently that impaired cortisol activity in granulosa cells and follicular fluid in ovaries of women with PCOS and IR could cause further aggravation of tissue specific IR⁴.

A better understanding of the pathogenesis of insulin resistance that is associated with the complications of

polycystic ovary syndrome had led to novel therapies- chiefly insulin lowering medication⁵.

Based on current guidelines, metformin is indicated in PCOS in some scenarios to improve fertility for management of menstrual irregularity if women are unable to take OCPs, and in co-existent prediabetes or DM2, where lifestyle modification fails. However key knowledge gaps remain on the efficacy of metformin and its specific role in PCOS, including in weight management⁶.

Women of reproductive age group (15-45) attending the outpatient department of Gynea/Obs BMCH/SPH Quetta with presence of hirsutism, acne, episodes of irregular menstrual bleeding, infertility will be advised ultra sound pelvis, serum androgen level (free testosterone), serum insulin level, LH/FSH ratio. Patients meeting the inclusion criteria were included in the study. Other causes of androgen excess e.g. adrenal gland tumor, late onset congenital adrenal hyperplasia, Cushing syndrome and increased level of insulin as in diabetes mellitus were ruled out. Use of any medication for acne and menstrual irregularity were stopped in the beginning of the study so as to control the confounding factors.

History of present condition and its duration were obtained and examination was done. After explaining the treatment modalities for polycystic ovary syndrome and their advantages and disadvantages, informed consent will be taken for study participation. Laboratory investigation (LH/FSH levels, serum free testosterone & insulin level) were performed the pelvic ultra sound for all patient's same ultra machine to control bias in the study.

These patients were prescribed, Tab. Metformin 500mg, 1 tablet for the first week. Patients were asked to return after 1 week. If there are no gastrointestinal symptoms, then 2 tablets of 500mg were given daily in the 2nd week and the patients were followed up for another 1 week. If still no symptoms this was maintained for 3 months and she was followed up after 3 months. Metformin will be continued for 3 months more. The effect of metformin will be observed by improvement in sign and symptoms such as hirsutism, menstrual cyclicity, acne, & levels of LH, serum androgen & insulin. Record was maintained on an especially designed Performa. Data was analyzed on computer by using the software SPSS V.10 Frequency and percentage was computed for categorical variables like presenting complaints, sign and symptoms (acne, hirsutism, and menstrual, cycle). Mean and standard deviation was estimated for quantitative variables like age, weight, blood pressure. Paired 't' test was used to compare effect of metformin in women with polycystic ovary syndrome before and after treatment for six months/ $P \leq 0.05$ was considered as significant.

RESULTS

A total of fifty women with Polycystic Ovary Syndrome were included in the study. The average age of the patients was found 26.46 ± 1.40 (95% CI: 23.64 to 29.28) years.

The signs and symptoms, of Acne was present in 33 patients (66 %), Hirsutism was present in 43 patients (86 %), Menstrual Irregularity was present in all patients (100 %), Obesity was present in 28 patients (56 %) and Infertility was present in 37 patients (74 %), were present in the patients before treatment.

Improvement in the signs and symptoms, of Acne was seen in 2 patients (6.06 %), Hirsutism was seen in 2 patients (4.65 %), Menstrual Irregularity was seen in 13 patients (26 %), Obesity was seen in 4 patients (5.40 %) and Infertility was seen in 2 patients (5.40 %), after 3 months' treatment.

Improvement in the signs and symptoms, of Acne was seen in 5 patients (15.15 %), Hirsutism was seen in 6 patients (13.95 %), Menstrual Irregularity was seen in 34 patients (68 %), Obesity was seen in 12 patients (42.85 %) and Infertility was seen in 5 patients (13.51 %), after 6 months' treatment.

DISCUSSION

Polycystic ovarian syndrome (PCOS) is a heterogeneous collection of sign and symptoms that gathered together from a spectrum of disorders with a mild presentation in some, while in others severe disturbance of reproductive, endocrine and metabolic function. The pathophysiology of the PCOS appears to be multifactorial and polygenic.

The definition of the syndrome has been much debated. More recently, in an attempt to resolve this conflict, a joint consensus meeting of American society for the Reproductive Medicine & and European society of Human Reproduction and Embryology (ASRM / ESHRE) refined the definition of PCOS⁷.

A large retrospective study that compared 2566 women with PCOS with 2566 age matched controls in Australia and used several linked health datasets showed that having PCOS was associated with an increased risk of obesity (16 versus 3.7%), adult-onset diabetes (12.5 versus 3.8%), hypertensive disorder (3.8 versus 0.7%), ischemic heart disease (0.8 versus 0.2%), asthma (10.6 versus 4.5%), endometrial cancer (0.4 versus 0.02%), stress/anxiety (14 versus 5.9%), depression (9.8 versus 4.3%) and mortality (0.7 versus 0.4%). Women with PCOS had twice as many hospital admissions as women without the condition over the 15-year follow-up (Hart and Doherty, 2015)⁸.

Insulin resistance is further exacerbated by overweight and obesity, common finding in PCOS [risk ratio (95% confidence interval (CI)): 1.95(1.52, 2.50) and 2.77 (1.88, 4.10), respectively, for women with PCOS compared with controls from a systematic review⁹.

Consistently, weight loss through lifestyle modification comprising dietary modification, physical activity and/or behavioral change), medications (metformin, orlistat, incretin mimetics) or bariatric surgery improves insulin resistance, reduces hyperandrogenism and alleviates PCOS clinical severity¹⁰.

A Cochrane review²⁴ including 816 women across nine studies compared metformin with placebo or no treatment, before or during assisted reproductive technology cycles. Clinical pregnancy rates were improved in the metformin group (OR 1.52, 95% CI 1.07–2.15; five studies; n = 551). However, the number of events dropped from 775 for the pregnancy rates to 551 for the live birth rates (live birth rates are not reported in some studies), which may have weakened the power of the meta-analysis with regards to live birth rates. There was no effect on the miscarriage rate. Women given metformin were, however, at significantly reduced risk of ovarian hyperstimulation syndrome (OHSS) when a long gonadotrophin-releasing hormone (GnRH) agonist protocol was used. Metformin decreased the risk of OHSS in these patients, probably by modulating the ovarian response to the stimulation. However, currently, the short GnRH antagonist protocol is recommended for women at risk of OHSS, for which the role of metformin is unclear¹¹.

More recently, a subgroup analysis in a systematic review also indicated that metformin therapy combined with lifestyle modification achieved limited impact in obese women with PCOS¹².

Furthermore, metformin alone does not improve weight loss compared to placebo or no treatment¹³.

Hyperinsulinemia generally suggests a lack of receptor sensitivity to insulin effects for unknown reasons.¹⁴ Treatment with insulin-sensitizing agents is a relatively recent therapeutic strategy in women with polycystic ovary syndrome (PCOS) and insulin resistance¹⁵.

Several insulin-sensitizing agents have been tested in the management of PCOS. Metformin is the only drug currently in widespread clinical use for PCOS¹⁶.

Recent studies report that insulin-sensitizing agents, such as metformin, reduce hyperinsulinemia, reverse the endocrinopathy of PCOS and normalize endocrine, metabolic and reproductive functions, leading to the resumption of menstrual cyclicity and ovulation¹⁷.

Importantly, the action of metformin is not associated with an increase in insulin secretion, and hence, with hypoglycemia. It is possible that the weight loss which often accompanies protracted metformin therapy may account for some of the beneficial effects observed in many studies¹⁸.

Kolodziechczyk et al. treated 39 women with PCOS and fasting hyperinsulinemia with metformin (500mg X3 per day) for 12 weeks, and found a significant decrease in fasting insulin and total testosterone and an increase in SHBG, leading to a decrease in the free testosterone index. In addition, there was a significant decline in

mean BMI, waist-to-hip ratio, hirsutism, and acne, as well as an improvement in the menstrual cyclicity. No changes in LH level or in LH-to-FSH ratio were observed. The greatest decline in testosterone and its free index occurred in the patients with the most pronounced hyperandrogenemia. Women with high levels of DHEAS exhibited less improvement in menstrual cycle regularity, no change in hirsutism, and an increase in the levels of IGF-I¹⁹.

CONCLUSION

Metformin administration to women who have signs and symptoms of polycystic ovarian syndrome is associated with marked improvement in menstrual irregularity resulting in regular menstrual cycles and achievement of pregnancy. Improvement in other signs and symptoms of PCOS was also seen with administration of Metformin for six months.

Author's Contribution:

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

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Role of Diffusion Weighted MRI in Assessment of Deep Myometrial Invasion by Endometrial Tumor-Comparing with Histopathology

Diagnosing of
Endometrial
Tumor by MRI

Sadia Anjum¹, Abdul Sattar¹, Saeeda Rana² and Nasreen Hamid³

ABSTRACT

Objective: To evaluate the diagnostic accuracy of Diffusion Weighted Magnetic Resonance Imaging in Assessment of deep myometrial invasion by endometrial tumor, taking histopathology as a gold standard.

Study Design: cross sectional study.

Place and Duration of Study: This study was conducted at the Department of Diagnostic Imaging in Nishtar Hospital, Multan, Pakistan from October 2016 to October 2018.

Materials and Methods: Total 75 patients having endometrial carcinoma, ages between 20-60 years were included. Patients with previous uterine surgery, receiving radiotherapy and chemotherapy, claustrophobia and cardiac pacemakers were excluded. Diffusion weighted MRI of the abdomen and pelvis was done in all. DW-MRI finding were interpreted by consultant radiologist for presence or absence of deep myometrial invasion. After surgery specimens were sent to the institutional pathology laboratory for histopathology. MRI findings were compared with histopathology. Data was analyzed using SPSS-18. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy were calculated.

Results: Total 75 patients fulfilling inclusion criteria were included. 38 (True Positive) had deep myometrial invasion on histopathology. Among 35 DW-MRI negative patients, 01 (false negative) had deep myometrial invasion on histopathology ($p=0-0001$). Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of diffusion weighted imaging in assessment of deep myometrial invasion by endometrial tumor, taking histopathology as gold standard was 97.43%, 94.44%, 95.00%, 97.14% and 96.00% respectively.

Conclusion: Study concluded that DW-MRI is a highly sensitive and accurate noninvasive modality for diagnosing deep myometrial invasion by endometrial tumor.

Key Words: Endometrial cancer, myometrial invasion, diffusion weighted imaging.

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INTRODUCTION

Endometrial cancer is currently the most common gynecological malignancy of the female pelvis in the united states and European countries and its incidence is increasing in other parts of the world.¹ The histological tumor grade and depth of myometrial invasion correlates strongly with the prevalence of lymph node metastasis and with patient survival. The myometrial invasion ratio determines the FIGO stage and thus has a direct impact on management.²

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To date, magnetic resonance imaging (MRI) is an accurate imaging technique for preoperative assessment of endometrial cancer and for evaluating the depth of myometrial invasion. A recent meta-analysis demonstrated that contrast enhanced MRI was substantially better than ultrasonography, CT scan, or non-contrast MRI.

Moreover, dynamic contrast enhanced MRI (DCE-MRI) is considered more accurate than T2W imaging in tumor detection and in assessment of myometrial invasion due to greater contrast and clear demonstration of border between the tumor and myometrium in the early phase. However, recent concerns with respect to the development of nephrogenic systemic fibrosis in patients with renal insufficiency, who undergo contrast enhanced MRI, are increasing the need of non-enhanced imaging. A few studies reported that DWI might be useful for detecting the depth of myometrial invasion with high diagnostic accuracy as well as predicts tumor grade. DWI with apparent diffusion coefficient (ADC) measurement yields quantitative information, which reflects cellularity of the tissue, and may be helpful to differentiate relatively hypercellular

endometrial cancer from normal endometrial and benign endometrial lesions.³

The rationale of this study was to determine the diagnostic accuracy of diffusion weighted MRI in assessment of myometrial invasion by endometrial tumor in local population. This study will not only be a useful addition in the existing literature but our general population will also be provided a non-invasive imaging modality for pre-operative assessment of endometrial carcinoma.

MATERIALS AND METHODS

This cross-sectional study was carried out in department of radiology Nishtar Medical College & Hospital, Multan-Pakistan in two years from Oct, 2016 to Oct,2018 on 75patients. Socio-demographics such as age, gender and duration of symptomswere collected. Those patients who have age range between 20 to 60 years and havingendometrial carcinoma of more than three months’ duration were included in the study to determine the diagnostic accuracy of DWIin detection of depth of invasion of myometrium.

Informed consent was taken before performing MRI. All the sequences were done during a single breath hold at two b-values (0mm2/sec and 1000 mm2/sec) and scan time of 3-4 minutes. DW MR findings were interpreted by consultant radiologist for presence or absence of deep myometrial invasion. All patients underwent surgery in the concerned ward and histopathology was send to the institutional pathology laboratory. DW-MRI findings were compared with histopathology findings.

Data was entered and analyzed using computer program SPSS-18. Descriptive statistics were applied to calculate mean and standard deviationfor quantitative variables. Frequencies and percentages were calculated for the qualitative variables. Sensitivity, specificity, PPV, NPV and

diagnostic accuracy of DW-MRI were calculated. Effect modifier were controlled by stratification. Chi-square test was applied post stratification and p-value ≤0.05 was considered as significant

RESULTS

Total 75 patients fulfilling inclusion criteria were included. Mean age of patients was 37.25±6.57 years with range of (35-60) years. The overall mean duration of disease was 43.82±12.55 months, with range of 45(19-64) months. All patients were subjected to Diffusion Weighted Magnetic Resonance Imaging.DW-MRI supported the diagnosis of deep myometrial invasion by endometrial tumor in 40(53.33%) patients and no deep myometrial invasion in 35 (46.66%) patients. Histopathology findings confirmed deep myometrial invasion by endometrial tumor in 39(52.00) patients and no deep myometrial invasion in 36(48.00%) patients. In DW-MRI positive patients ,38

True Positive (50.66%) had deep myometrial invasion and 02 False positive (2.66%) had no deep myometrial invasion on histopathology. Among 35, DW-MRI negative patients, 01 (False Negative) had deep myometrial invasion on histopathology, whereas 34 (True Negative) had no deep myometrial invasion on histopathology (p=0.0001) as shown in table I

Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of DW-MRI in diagnosis of deep myometrial invasion taking histopathology as gold standard were 97.43%, 94.44%, %, 95.00%,97.14% and 96.00 % respectively. The stratification according to gender, age, and duration of disease was done and sensitivity, specificity and diagnostic accuracy were also calculated post stratification.

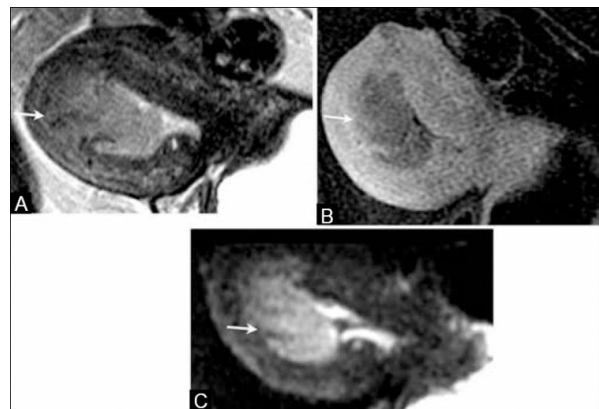


Figure No.1: I68 yr. female with endometrial cancer. DW-imaging showing >50%myometrial invasion by tumor.

Table No. 1: Diagnostic Accuracy of Dw-Mri in Assessment of Deep Myometrial Invasion by Endometrial Tumor (n=75)

Dw-Mri Findings	Histopathology Findings		Total
	Positive	Negative	
Positive	True positive(a) 38 (50.66%)	False positive (b) 02(2.66%)	a + b 40(53.33%)
Negative	False negative(c) 01 (1.33%)	True negative (d) 34(45.33%)	c + d 35(46.66%)
Total	a + c 39(52.00 %)	b + d 36(48.00%)	75 (100%)

Sensitivity= a / (a + c) x 100 = 97.43%

Specificity= d / (d + b) x 100 = 94.44%

PPV = a / (a + b) x 100 = 95.00%

NPV = d / (d + c) x 100 = 97.14%

Accuracy = a + d / (a + d + b + c) x 100 = 96.00%

Post stratification association of outcome with age and duration of disease were calculated using chi square test considered p≤0.05 as significant. The results showed

significant association with age, marital status, menopause status and duration of disease.

Significant association was observed with marital status, menopause status and duration of disease.

DISCUSSION

Magnetic resonance imaging (MRI) is more accurate approach for the assessment of endometrial carcinoma staging compared with ultrasonography and CT before surgery. The combination of T2W and DWI fuses morphological and functional observations, which can improve the anatomical localization of lesions, and the entire procedure takes <30 seconds.⁴ Reports have shown that the fused images are very good modality for displaying anatomical structure and functional information, and improve the accuracy of diagnosis.⁵

This study is conducted to determine the accuracy of diffusion DW-MRI in assessment of deep myometrial invasion by endometrial tumor, taking histopathology as gold standard. DW-MRI supported the diagnosis of deep myometrial invasion by endometrial tumor in 40 (53.33%) patients and no deep myometrial invasion in 35(46.66%) patients. Histopathology findings confirmed deep myometrial invasion by endometrial tumor in 39(52.00 %) patients and no deep myometrial invasion in 36(48.00 %) patients. In DW-MRI positive patients, 38 (True Positive) had deep myometrial invasion and 02(False positive) had no deep myometrial invasion on histopathology. Among 35, DW-MRI negative patients, 01 (False Negative) had deep myometrial invasion on histopathology, whereas 34 (True Negative) had no deep myometrial invasion on histopathology (p=0.0001).

Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of DW-MRI in diagnosis of deep myometrial invasion taking histopathology as gold standard were 97.43%, 94.44%, 95.00%, 97.14% and 96.00% respectively.

Noninvasive DWI depicts differential molecular diffusion movements of water with in various tissues. With DWI, increased cellularity and few mesenchymal structures between the glands in endometrial carcinomas may restrict water diffusion when compared with a normal endometrium.⁶ Several research groups have analyzed the usefulness of DWI in the detection and assessment of myometrial invasion in endometrial cancer. Researchers have reported that staging errors were excluded when incorporating DWI, and conventional MRI based on the fusion of DWI lesions for endometrial cancer is more sensitive for the effective assessment of lesions.⁷

In a recent prospective study published in European Radiology in 2010, Rechichi et al. found that DW-MRI was very accurate in assessing myometrial invasion with sensitivity, specificity, positive and negative

predictive value of 84.6%,70.6%,52.4%, and 92.3%.

⁸The crossponding values for dynamic MRI and T2W imaging were 69.2%,61.8%,40.9%,84.0% and 92.3%,76.5%,60.0%96.3% respectively. The inter-observer agreement in assessing the depth of myometrial invasion was substantial for both T2W and DW imaging (k=0.91 and 0.74 respectively) and moderate for dynamic imaging (k=0.45). They suggested that DWI could potentially replace dynamic imaging as an adjunct to routine T2W for preoperative evaluation of endometrial cancer.⁹

Shen et al. compared the use of DW-MRI and DCE-MRI in the evaluation of depth of myometrial invasion and found that the diagnostic accuracy was 62% for DW-MRI compared to 71% for DCE-MRI. However, both DW-MRI and DCE-MRI images were acquired in the sagittal plane only. This may have contributed to a relatively low accuracy in the evaluation of myometrial invasion as the presence of two orthogonal planes is mandatory for an accurate assessment.¹⁰ DW-MRI was also useful in detection of drop metastasis in the cervix or metastasis foci outside the uterus, such as adnexa or peritoneum. In et al demonstrated an accuracy of 88% in determining the depth of myometrial invasion using fused T2W and DW images at 3.0 T.¹¹

In a study, magnetic resonance imaging had a high negative predictive value for the presence of deep invasion (87% overall and 95% for grade I disease). However, although the positive predictive value for the presence of any myometrial invasion was high, negative predictive values were poor (35% for all grades and 46% for grade I). In another study, for the detection of outer half myometrial invasion, overall sensitivity of MRI was 0.73 (95% CI,0.59-0.83) and specificity was 0.83(95% CI,0.76-0.89).¹² Magnetic Resonance Imaging improved the sensitivity and negative predictive value of endometrial biopsy alone in predicting the women with endometrial cancer who require full surgical staging (0.73 vs 0.65 and 0.80 vs 0.78, respectively)¹²

Ryoo UN et al in his study found the sensitivity, specificity and accuracy for identifying any myometrial invasion (superficial or deep as 0.81, 0.61 and 0.74 respectively; these values for deep myometrial were 0.60,0.94 and 0.86 respectively. The sensitivity, specificity and accuracy of MR imaging for detecting lymph nodes metastasis were 50.0%,96.6% and 93.0% respectively.¹³ The patients who were older, had more deliveries and a larger tumor size more frequently had incorrect prediction of deep myometrial invasion (p=0.034,p=0.044,p=0.06, respectively).¹⁴ A higher tumor grade, a histology other than the endometrioid type, myometrial invasion on MR findings and a larger tumor size were associated with a more frequent false negative prediction of lymph node metastasis (p=0.018,p=0.017,p=0.002,p=0.047, respectively).A

large tumor size was also associated with more frequent false-positive results ($p=0.009$).¹⁵

CONCLUSION

This study concluded that DW-MRI is a highly sensitive and accurate non –invasive modality for diagnosing deep myometrial invasion by endometrial tumor, and has improved patient care by early screening timely and proper treatment and avoiding unnecessary diagnostic biopsies, which consequently reduces patient's morbidity and mortality. So we recommend that diffusion weighted MRI should be used routinely as a prime modality for pre-operative status of assessment of deep myometrial invasion by endometrial tumor for selecting proper treatment option and post-operative management plan for these particular patients which will result in reducing the morbidity and mortality of these patients.

Author's Contribution:

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

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Frequency of Diabetes Mellitus and Impaired Fasting Glucose in Patients with Lichen Planus Attending a Tertiary Care Hospital Quetta

Diabetes Mellitus
and Impaired
Fasting Glucose
with Lichen
Planus

Habib Ullah¹, Syed Bilal Ahmed¹, Sajida Jabeen² and Syed Shamsuddin¹

ABSTRACT

Objective: The objective of the study was to determine the frequency of diabetes mellitus and impaired fasting glucose in patients with lichen planus.

Study Design: Cross sectional study.

Place and Duration of Study: This study was conducted at the Department of Dermatology, Bolan Medical College/ Sandeman Provincial Hospital, Quetta for a period of six months.

Materials and Methods: After taking ethical committee approval this study was started. A total of 155 patients with the diagnosis of LP were included in this study. Male and female ratio, frequency and percentage was calculated for patient having LP with diabetes mellitus and impaired fasting glucose. Data was stratified in different age group, gender and duration of symptoms to control effect modifier. Data was analyzed using SPSS version 17.

Results: A total of 155 patients were included in the study. Out of total 155 patients, mean age of the patients was 42.69 ± 8.64 years. Males were predominantly higher 91 (58.7%) as compared to females 64 (41.3%). Frequency of impaired fasting glucose was observed in 1 (0.6%) whereas diabetes mellitus in 26 (16.8%) of the patients.

Conclusion: The frequency of diabetes mellitus was found higher in patients with lichen planus. Therefore, we need to educate our patients and also need to discuss with our colleagues to exclude diabetes mellitus in patients of LP.

Key Words: Lichen Planus, Diabetes Mellitus, Impaired fasting glucose

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INTRODUCTION

Lichen planus (LP) is an immunologically mediated mucocutaneous disease that is triggered by varied etiological agents and present as various forms i.e. reticular, atrophic, papular, bullous, plaque, ulcerative and follicular with different prognosis.¹ Clinically, LP presents as flat-topped, violaceous papulosquamous eruptions on the skin affects the skin, scalp, oral cavity, nails and genitals and is classically described as pruritic, purple (violaceous), polygonal, and papules or plaques.^{1, 2} Papules may be isolated or may coalesce to form larger plaques.

Oral lichen planus presents as white stripes in reticular pattern. Diagnosis can be made based on clinical findings.² Onset of LP is common in middle age (30–60 years of age). However, the prevalence of lichen planus in people with type 1 or type 2 diabetes has been noted to be 2–4%.²

LP also arises in association with various other systemic conditions such as hypertension, diabetes mellitus and Hepatitis C and many research works are now producing evidence that abnormal glucose tolerance associated with lichen planus supported the possibility that, lichen planus and disorder of carbohydrate metabolism could be related.^{3, 4} Lauritano D et al. reported incidence of diabetes mellitus was 24.1% (24 out of 87) in Oral lichen planus patients.⁴ Ara S A et al. reported incidence of diabetes mellitus was 10% (5 out of 50).⁵

Diabetes mellitus (DM) is defined as a syndrome in which hyperglycemia occurs because of insulin defects and skin lesions can be seen in DM according to dysregulation of glucose, insulin, and lipids.⁶

Previous researchers have also found association of DM and abnormal glucose tolerance test among patients with LP.^{5, 6} Atefi N et al. reported 20% (16 out of 80 LP) had diabetes and 17.5% (14 out of 80 LP) had Impaired fasting glucose.⁶ Shah S M A et al. reported no

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association between oral lichen planus and diabetes mellitus.⁷

The rationale of this study was to find the frequency of DM and Impaired fasting glucose and if found a greater frequency we would screen patients of LP for diabetes mellitus and impaired fasting glucose (IFG) as these disorders are usually indolent and can cause serious complications if left undiagnosed.

MATERIALS AND METHODS

This Cross sectional was conducted at Department of Dermatology, Bolan Medical College/ Sandeman Provincial Hospital, Quetta. The Study duration was 6 months. The sampling technique used was Non-probability consecutive sampling. Sample size was calculated using WHO calculator taking the Prevalence of diabetes mellitus and impaired fasting glucose in Lichen Planus⁶ = confidence level = 95%, Absolute precision required = 6%, n= 155 patients.

We included all patients between the ages 30-60 years, diagnosed as lichen planus as per operational definition. We Excluded all Patient taking drugs like Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), Anti-hypertensive i.e. ACE Inhibitors, Beta Blockers and Thiazide diuretics and heavy metals like Mercury and Penicillamine (Because these are effect modifier and could produce bias in the study). The data collection was started after an approval from the concerned department. After taking ethical committee approval and explaining the procedure informed constant was taken. A total of 155 patients were recruited from Out Patient Department of Department of Dermatology, Bolan Medical College/ Sandeman Provincial Hospital, Quetta on the basis of inclusion criteria. Blood samples of the patients' were sent and the diagnosis of diabetes mellitus or impaired fasting glucose were made as per operational definitions and were noted in proforma by researcher. Data was analyzed using software of Statistical Package of Social Sciences (SPSS version 17). Mean + SD were calculated for continuous variable of age, sex, frequency of symptoms and presence or absence of diabetes mellitus or impaired fasting glucose. Assuming the P value of <0.05 as significant, Chi-Square was used to detect the difference between the categories.

RESULTS

A total of 155 patients were included in the study. Out of total 155 patients, mean age of the patients was 42.69±8.64 years. Males were predominantly higher 91 (58.7%) as compared to females 64 (41.3%). (Fig 2) Mean duration of symptoms was 7.45 ±1.07 months. Table No.1 & Table 2

There were 85 (54.8%) patients with ≤7 months of duration. (Fig 3).

Frequency of impaired fasting glucose was observed in 1 (0.6%) whereas diabetes mellitus in 26 (16.8%) of the patients. (Fig 4 & 5)

Majority 81 (52.3%) of the patients were presented with >40 years of age. (Fig 1).

Table No.1: Age of the Patients n=155

Age of the patients (in years)	Mean ±SD	Minimum	Maximum
	42.69 ±8.64	30	60

Table 2: Duration of Symptoms n=155

Duration of symptoms (in months)	Mean ±SD	Minimum	Maximum
	7.45 ±1.07	6	9

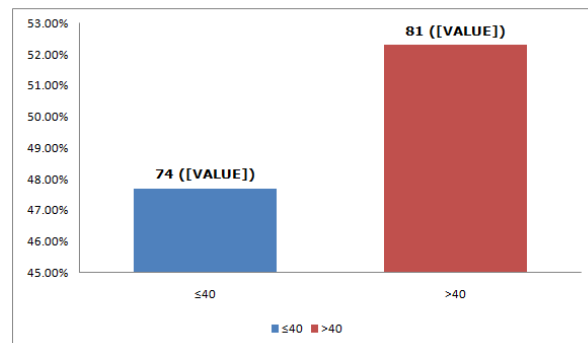


Figure No.1: Age Group of the Patients

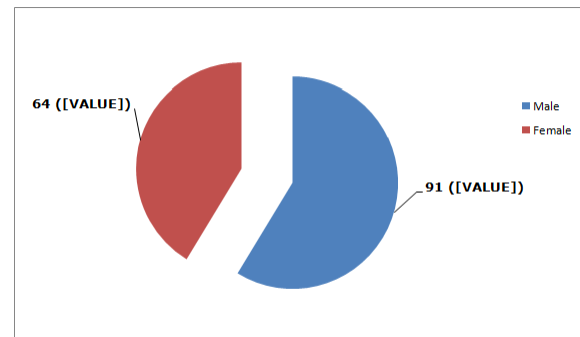


Figure 2: Gender Distribution of the Patients

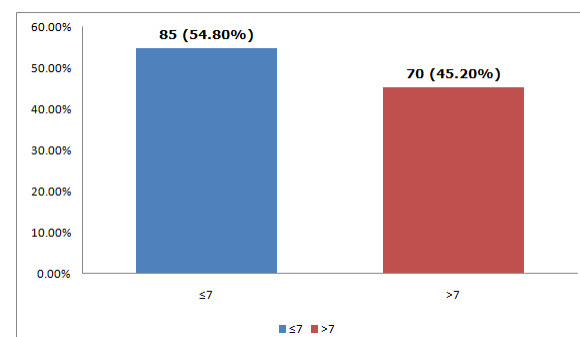


Figure No.3: Duration of Symptoms

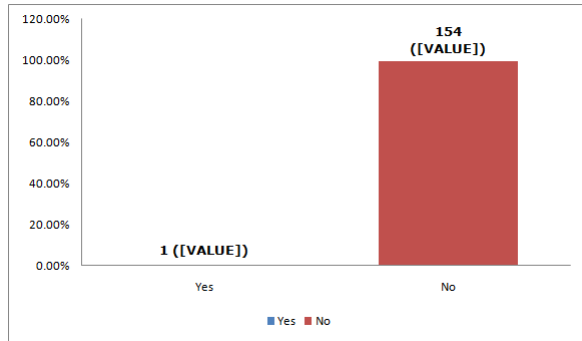


Figure No.4: Frequency of Impaired Fasting Glucose

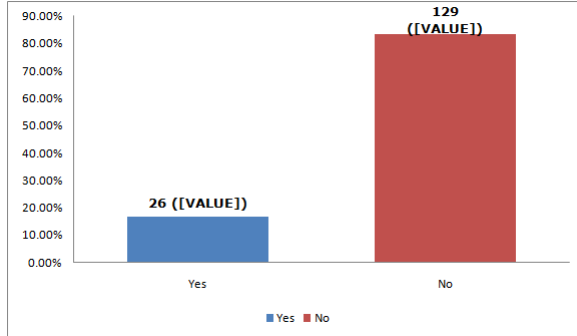


Figure No.5: Frequency of Diabetes Mellitus

Table No.3: Comparison of Age with Impaired Glucose Level n=155

Age (in years)	Impaired glucose level		Total	p-value
	Yes	No		
≤40	0 (0)	74 (48.1)	74 (47.7)	0.338
>40	1 (100)	80 (51.9)	81 (52.3)	
Total	1 (100)	154 (100)	155 (100)	

Table No.4: Comparison of Gender With Impaired Glucose Level n=155

Gender	Impaired glucose level		Total	p-value
	Yes	No		
Male	0 (0)	64 (41.6)	64 (41.3)	0.400
Female	1 (100)	90 (58.4)	91 (58.7)	
Total	1 (100)	154 (100)	155 (100)	

Table No.5: Comparison of Duration of Symptoms with Impaired Glucose Level n=155

Duration of symptoms (in months)	Impaired glucose level		Total	p-value
	Yes	No		
≤7	0 (0)	85 (55.2)	85 (54.8)	0.269
>7	1 (100)	69 (44.8)	70 (45.2)	
Total	1 (100)	154 (100)	155 (100)	

Table No.6: Comparison of Age with Diabetes Mellitus n=155

Age (in years)	Diabetes Mellitus		Total	p-value
	Yes	No		
≤40	10 (38.5)	64 (49.6)	74 (47.7)	0.299
>40	16 (61.5)	65 (50.4)	81 (52.3)	
Total	26 (100)	129 (100)	155 (100)	

Table No.7: Comparison of Gender with Diabetes Mellitus n=155

Gender	Diabetes Mellitus		Total	p-value
	Yes	No		
Male	9 (34.6)	55 (42.6)	64 (41.3)	0.449
Female	17 (65.4)	74 (57.4)	91 (58.7)	
Total	26 (100)	129 (100)	155 (100)	

Table No.8: Comparison of Duration of Symptoms with Diabetes Mellitus n=155

Duration of symptoms (in months)	Diabetes Mellitus		Total	p-value
	Yes	No		
≤7	20 (76.9)	65 (50.4)	85 (54.8)	0.013
>7	6 (23.1)	64 (49.6)	70 (45.2)	
Total	26 (100)	129 (100)	155 (100)	

Comparison was done to see the effect of age, gender and duration of symptoms on the outcome (impaired fasting glucose and diabetes mellitus). Results are shown in table 3-8.

DISCUSSION

LP also arises in association with various other systemic conditions such as hypertension, diabetes mellitus and Hepatitis C and many research works are now producing evidence that abnormal glucose tolerance associated with lichen planus supported the possibility that, lichen planus and disorder of carbohydrate metabolism could be related.^{3,4}

The findings of this study have showed considerable of cutaneous lichen planus patients with diabetes mellitus. Previous researchers have also found association of DM and abnormal glucose tolerance test among patients with LP.⁴ Atefi N et al. reported 20% (16 out of 80 LP) had diabetes and 17.5% (14 out of 80 LP) had Impaired fasting glucose.⁶ Shah S M A et al. reported no association between oral lichen planus and diabetes mellitus.¹⁰ In this study, frequency of impaired fasting glucose was observed in 1 (0.6%) patients.⁷

Literature review revealed that skin disorders presented in 79.2% of people with diabetes. A study of 750 patients with diabetes found that the most common skin

manifestations were cutaneous infections (47.5%), xerosis (26.4%), and inflammatory skin diseases (20.7%).⁸ Individuals with type 2 diabetes are more likely than those with type 1 diabetes to develop cutaneous manifestations. Cutaneous disease can appear as the first sign of diabetes or may develop at any time in the course of the disease.

In our study, it was observed that duration of the disease is significantly associated with the presence of diabetes in lichen planus patients.

Cutaneous lichen planus may resolve spontaneously within one to two years, although lichen planus affecting mucous membranes may be more persistent and resistant to treatment. Recurrences are common, even with treatment. High-potency topical corticosteroids are first-line therapy for cutaneous lichen planus.^{8,9} Oral antihistamines (e.g., hydroxyzine [Vistaril]) may be used to control pruritus. Hypertrophic lesions are treated with intralesional triamcinolone acetonide (Kenalog), 5 to 10 mg per mL injection (0.5 to 1 mL per 2-cm lesion).⁹

CONCLUSION

The frequency of diabetes mellitus was found higher in patients with lichen planus. Therefore, we need to educate our patients and also need to discuss with our colleagues to exclude diabetes mellitus in patients of LP.

Author's Contribution:

Concept & Design of Study:	Habib Ullah
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Revisiting Critically:	Habib Ullah
Final Approval of version:	Habib Ullah

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

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