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**Editorial****To Run Like Hell or Eat Like an Anorexic****Mohsin Masud Jan**

Editor

Many New Year's resolutions are about losing weight and that revolve around two ideas — eating less and exercise. Another year began in this January and some more new year's resolutions were made to keep up with. By now most of these will have been left behind in the dust. But even so, not all resolutions are and more importantly should be too difficult to keep up with. Here my intention is to focus entirely on health concerns in our everyday lives and not about matters eschatological.

Besides the ones dealing with personal relationships or plans about professional activities, most frequently resolutions are about health matters. Some decisions like giving up smoking are pretty obvious and do not even require a discussion.

Many New Year's resolutions are about losing weight and that revolve basically around 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. No, you do not have to run a few miles every day or do some strenuous gym stuff for exercise to be 'useful'. Even a twenty or thirty 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 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 even during inactivity. Some investigations suggest that exercising or even a brisk walk is more beneficial if done on a relatively empty stomach.

But, the big question remains, which diet is the best to lose weight, and for that a general rule of thumb, if there are dozens of commercially available or published diets then clearly none of them is good enough to wipe off all the others from the market place. 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 healthcare 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 upon 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 the 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.

My purpose today is to talk of general principles. 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. First, eat whatever you want but mostly plants. Second, avoid things 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 and stored but unlike those today they did not contain preservatives besides salt, vinegar or sugar, and there were no flavour enhancers or 'trans-fats' for taste improvement. In essence, all processed foods or precooked 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 in 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 people tend to eat more starch if they eat less fat.

Latest 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 bought 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 food 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. No, there are no miracles diets. All that is needed, is Discipline and Perseverance.

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# Mean Platelet Volume as an Indicator of Glycemic Control in Type 2 Diabetes Mellitus

Ghulam Murtaza Kaka<sup>1</sup>, Mumtaz Ali Memon<sup>2</sup> and Khalda Shaikh<sup>3</sup>

## ABSTRACT

**Objective:** To study platelet counts (PC), mean platelet volume (MPV) and glycated HbA1 in type 2 Diabetes mellitus (T2DM).

**Study Design:** Case control study

**Place and Duration of Study:** This study was conducted at the Department of Medicine, Indus Medical College Hospital, Tando Muhammad Khan, Sindh from March to November 2015

**Materials and Methods:** A sample of 150 subjects; comprising of Group A- controls (n=50), Group B- controlled diabetics (n=50) and Group C- (n=50) uncontrolled diabetics. DM was diagnosed according to American Diabetes Association. Permission was taken from ethics review committee of institute. Only willing subjects were included after they signed consent proforma voluntarily. Blood pressure, BMI, Blood glucose, Platelet counts, MPV and HbA1c were determined. Data was typed on Microsoft excel, and then pasted SPSS 22.0 sheet for statistical analysis. Chi square test, one way ANOV, post-Hoc Tukey Cramer and Pearson's association was used for analysis of data variables. All data was analyzed at Confidence interval of 95% ( $\leq 0.05$ )

**Results:** MPV was raised in Diabetics in particular with uncontrolled glycemic index as shown in table II. MPV showed negative correlation with platelets was found with MPV ( $r = -0.27, p = 0.03$ ). MPV was positively correlated with glycated HbA1 ( $r = 0.78, p = 0.0001$ ). HbA1c as high as 14.3% was noted in uncontrolled diabetics.

**Conclusion:** The present study reports raised Mean platelet volume in Diabetics in particular uncontrolled diabetics. MPV showed positive correlation with HbA1c and negative correlation with platelet count.

**Key Words:** Mean Platelet Volume, Platelets, Glycated HbA1 Diabetes mellitus

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## INTRODUCTION

Diabetes mellitus (DM) is one of the most common endocrinopathy characterized by chronic hyperglycemia as a result of relative or absolute insulin deficiency.<sup>1</sup> International Diabetes Federation (IDF) has reported a rise of diabetics from 285 million in 2010 to 439 million in 2030.<sup>2</sup> The epidemic of diabetes is quite particular to Pakistan and it now ranks sixth regarding diabetes burden.<sup>3</sup>

Pakistan National Diabetes Survey (PNDS) disclosed in their report that for each recognized patient of DM, there remain 2 undiagnosed cases of DM and 3 cases of impaired glucose tolerance (prediabetes) approximately.<sup>4</sup> Target organs of hyperglycemia induced damage in diabetics include nerves, eyes, heart, blood vessels and renal tissue.<sup>5</sup>

Diabetics show a deviation away from normal which has been reported. Mean platelet volume (MPV) is a clinical measure of platelet function and size,<sup>6</sup> which is related to megakaryocytic ploidy. Degree of megakaryocytic dispersion and fragmentation determines the size of platelet known as MPV. Increased MPV is attributed to cytokine stimulation such as thrombopoietin, IL-6 and IL-11.<sup>7</sup>

Increased MPV is reported in diabetic patients and is considered as a risk factor for micro vascular complications.<sup>8,9</sup> Hence diabetics are prone to thrombogenic tendency and vascular events. Increased thrombogenicity is produced by the granules with fresh mediators inside newly released platelets.

Many studies had reported MPV as an independent factor for risk of atherogenesis, thrombosis and embolism.<sup>10-14</sup>

Glycated hemoglobin A (HbA1c) is an established indicator of glycemic control<sup>10</sup> and MPV may be compared with it to set a new clinical indicator which is cheap and easily generated by using automated hematology analyzers.<sup>11</sup>

Therefore present case control study investigated the platelet counts, mean platelet volume and glycated HbA1 at our tertiary care hospital to probe into its validity as a test of glycemic control and a risk factor in diabetic patients.

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## MATERIALS AND METHODS

The present case control study was planned at eh Diabetic clinic, Department of Medicine, Indus Medical College Hospital, Tando Muhammad Khan, Sindh from March to November 2015. A sample of 150 subjects was selected as per criteria. Subjects were divided into 3 groups; Group A- controls (n=50), Group B- controlled diabetics (n=50) and Group C- (n=50) uncontrolled diabetics. Only those patients were included who were diagnosed according to American Diabetes Association criteria.<sup>5</sup> Duration  $\geq 5$  years and age  $>25$  and  $<60$  years were predetermined criteria of inclusion. Subjects with diabetic nephropathy, bleeding tendency, unknown duration of DM and taking anti platelet drug were strictly excluded. Permission was taken from ethics review committee of institute. Only willing subjects were included after they signed consent proforma voluntarily. Glycemic index was determined by HbA1C. Formula "Weight (kg)/Height (m<sup>2</sup>)" was used for calculating BMI. Systemic blood pressure was determined by mercury sphygmomanometer. Systolic BP  $\geq 140$  mmHg or diastolic BP  $\geq 90$  mmHg was criteria for diagnosing systemic hypertension.<sup>12</sup>

Preferably ante cubital vein was used for blood sampling. Glucose oxidase method and Hitachi 902, Roche (USA) analyzer were used for glucose and HbA1c detection.<sup>6</sup>

Data was typed on Microsoft excel, then pasted SPSS 22.0 sheet for statistical analysis. Chi square test, one way ANOV, post-Hoc Tukey Cramer and Pearson association was used for analysis of data variables. All data was analyzed at Confidence interval of 95% ( $\leq 0.05$ )

## RESULTS

Demographic characteristics of study subjects are shown in table I. The mean  $\pm$  SD age was noted as  $49 \pm 11.7$ ,  $47.36 \pm 5.98$  and  $47.64 \pm 9.01$  years among 3 groups ( $p \geq 0.09$ ). Of 150 study subjects, male and female in groups A, B and C were found as 23, 21, 25 and 27, 29, 25 respectively. Systolic blood pressure (SBP) was noted as mean  $\pm$ SD in three groups as  $120.8 \pm 6.2$ ,  $151.4 \pm 19.3$  and  $156.1 \pm 16.1$  mmHg respectively and diastolic blood pressure (DBP) as  $79.8 \pm 6.29$ ,  $130.60 \pm 21.4$  and  $131.1 \pm 19.1$  mmHg in groups A, B and C respectively. Blood glucose was noted as  $112.3 \pm 19.6$ ,  $230.5 \pm 70.89$  and  $265.0 \pm 92.5$  mg/dl in groups A, B and C respectively ( $p < 0.001$ ). The BMI calculated was found as  $27.3 \pm 5.35$ ,  $27.81 \pm 5.37$  and  $28.38 \pm 3.9$  kg/m<sup>2</sup> in groups A, B and C respectively. Mean duration of DM was found as  $10.56 \pm 4.13$  and  $11.3 \pm 2.69$  years in groups A and B respectively. Platelet count; MPV and HbA1c are shown in table II. Graph 1 shows the MPV among 3 groups. MPV was raised in Diabetics in particular with uncontrolled glycemic index as shown in table II. MPV showed negative

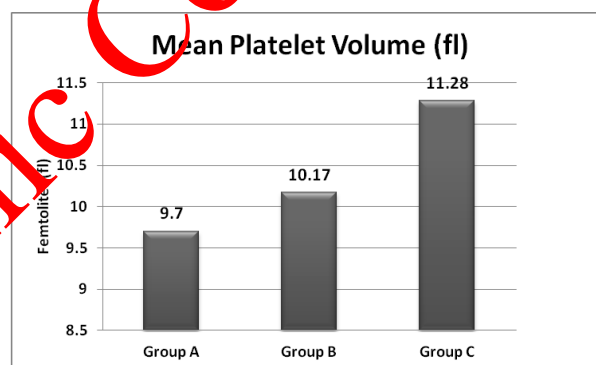
correlation with platelets was found with MPV ( $r = -0.27$ ,  $p=0.03$ ). MPV was positively correlated with glycated HbA1 ( $r = 0.78$ ,  $p= 0.0001$ ) (table II). Uncontrolled diabetics showed HbA1c as high as 14.3%, this indicates bad glycemic control.

**Table No. I. Platelet count, Mean Platelet volume (MPV) and Glycated HbA1 among controls and Diabetic subjects (n=150)**

	Group A	Group B	Group C	p-value
Platelet counts (x103/ $\mu$ l)	304 $\pm$ 67.4	384 $\pm$ 91.5	395 $\pm$ 89.9	0.001
MPV (fl)	9.7 $\pm$ 0.6	10.17 $\pm$ 0.8	11.28 $\pm$ 1.1	0.0001
HbA1c	5.15 $\pm$ 0.6	6.0 $\pm$ 0.5	9.93 $\pm$ 1.6	0.0001

**Table No.2. Pearson's correlation of MPV with platelet counts and HbA1c (n=150)**

	Platelet counts	HbA1c
r-value	0.27	0.78
P-value	0.03	0.0001



**Graph No.1. Mean Platelet volume among 3 groups**

## DISCUSSION

The present study is the first research being reported from our tertiary care hospital. The present study reported raised MPV in Diabetics particularly in those having HbA1c  $>7\%$  (uncontrolled glycemic index). Platelets counts were raised in Diabetic patients compared to controls as shown in table I. MPV showed negative correlation with platelets was found with MPV ( $r = -0.27$ ,  $p=0.03$ ). MPV was positively correlated with glycated HbA1 ( $r = 0.78$ ,  $p= 0.0001$ ) (table II). Uncontrolled diabetics showed HbA1c as high as 14.3%, this indicates bad glycemic control. The findings of present study in supported by previous studies which had reported raised MPV in diabetics.<sup>9-11</sup> MPV is reported as new risk factor for atherogenesis in diabetics. Various atheroma associated diseases such as brain stroke, transient ischemic stroke, acute myocardial infarction (AMI) and micro vascular complication of DM.<sup>13,14</sup>



The present study reports raised MPV and HbA1c in uncontrolled diabetics compared to controls (table I). Our findings are in agreement to previously cited studies.<sup>9-11</sup>

Bavbek et al<sup>15</sup> and Dolasik et al<sup>16</sup> reported increased platelet stickiness and raised MPV in diabetics with micro vascular complications and findings support present study. Positive association of MPV with glycated HbA1c of present study is supported by previous study of Dalamaga et al<sup>17</sup> Another previous study also has reported positive correlation of MPV with glycated HbA1<sup>18</sup> this is also in agreement to present findings. Papanas et al<sup>19</sup> has reported a positive correlation between MPV, HbA1c and diabetic micro vascular complications, this is consistent to our present study.

However, Papanas et al.<sup>19</sup> did not find any correlation of MPV with glycated HbA1 which is in contradistinction to present study. Raised MPV is a consistent finding to previous studies.<sup>20</sup>

Positive correlation of MPV of present study is supported by previous studies also.<sup>21,22</sup> A recent study has reported positive association of raising MPV with progressive diabetic nephropathy. Another previous study reported positive correlation of MPV with HbA1c.<sup>23</sup>

In view of above discussion, it is postulated that the MPV might be used as a clinical indicator and predictor of glycemic control and diabetic micro vascular complications, but this needs further authentication with large scale prospective studies. Another grave finding is very bad glycemic control as indicated by very high HbA1c of 14.3%, this indicates bad glycemic control. Another bad finding was none of psychiatric patients was aware of their blood glucose and blood cholesterol. MPV may be used as indicator glycemic control in addition to HbA1c but this needs further large scale, prospective studies to be conducted.

## CONCLUSION

The present study reports raised Mean platelet volume in Diabetics in particular uncontrolled diabetics. MPV showed positive correlation with HbA1c and negative correlation with platelet count.

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

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# Association of Sensory Polyneuropathy with Restless Legs Syndrome

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## ABSTRACT

**Objective:** To determine the prevalence of restless legs syndrome (RLS) in elderly patients with pure sensory polyneuropathy and correlate the findings with other clinical features.

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

**Place and Duration of Study:** This study was conducted at the Dow University Hospital and Civil Hospital Karachi from 2013 to 2015.

**Materials and Methods:** 48 patients with Restless leg syndrome were evaluated in our multicenter, prospective study in 2 years for evidence of pure sensory neuropathy either they have demyelinating or axonal type.

Patients were evaluated according age at which symptoms started, the severity of symptoms, typical clinical findings and laboratory investigations.

**Results:** In 21 of the 48 (43.7%) patients, peripheral neuropathy was detected. Ten patients had pure sensory polyneuropathy and remaining have mixed sensory motor polyneuropathy. The pure sensory neuropathy group had comparatively intense and frequent symptoms of Restless leg syndrome. Some of them have family history of Restless leg syndrome. Patients with Mixed sensory motor polyneuropathy did not have similar strong symptoms of Restless leg syndrome and pain in legs.

**Conclusion:** The result suggests that Restless leg syndrome is triggered by painful paresthesias is primarily related with pure sensory neuropathy. Patients with mixed sensory motor neuropathy have less intense feature of restless leg syndrome. So the treatment options should be focused on medicines used for neuropathic pain.

**Key Words:** Neuropathy, Restless Leg Syndrome, elderly patients.

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## INTRODUCTION

Restless legs syndrome (RLS), also known as Willis Ekbom's disease, is a clinical syndrome described as a constant craving to move the lower limbs, often associated with paresthesias or muscle ache like sensations, restlessness<sup>1</sup>. The relationship between RLS and peripheral polyneuropathy is a universal fact. The thought that patients with predominant sensory symptoms complain intense symptoms of RLS, impelled this study.

Majority of cases are idiopathic, though the disorder is sometimes hereditary and may be related to some of the medical disorders, like chronic kidney disease, hypothyroidism and iron deficiency anemia<sup>2,3</sup>.

The pathophysiology of RLS is due to dysfunction of the dopaminergic system, perhaps on the level of striatal or spinal cord dopamine receptors, and the A-11

neuron group located in the hypothalamus<sup>4</sup>. These neurons control spinal excitability, variations of which in turn alter the sensory processing primarily of lower limbs afferents in brain stem<sup>5,6</sup>.

RLS is a clinical diagnosis depends on the history of the patient. The six important features are: unpleasant lower limb sensations, sensations triggered by rest and comforted by activity, compelling motor restlessness, and the symptoms are more during the evening or at night, ensuing insomnia, and association with periodic limb movements of sleep (PLMS).<sup>7</sup>

Restless legs syndrome is responsive to various medicines, including levodopa, dopamine agonists, benzodiazepines, opioids, pregabalin and sometimes to carbamazepine<sup>8</sup>.

## MATERIALS AND METHODS

This study was conducted at DUHS Karachi from January 2013 to March 2015. It was a cross sectional study. Forty eight patients were included in this study and sample size is calculated scientifically with confidence interval of 95%. The patients included in our study, were diagnosed cases of Restless leg syndrome.

**Assessment and Data Collection:** Data was collected on a pretested self-administered Performa after taking permission from ethical committee of the hospital. The

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purpose, risks and benefits of the study were explained to the patients and informed consent was taken.

The diagnosis of RLLS was established using the criteria defined by the International Restless Legs Syndrome Study Group: 1) A desire to move the legs, related to unpleasant sensations in the legs; 2) the urge to move or beginning or the worsening of unpleasant sensations during periods of inactivity, such as lying or sitting; 3) the urge to move or unpleasant sensations that are partially or completely relieved by motor activity, such as walking or stretching the limbs; and 4) the urge to move or unpleasant sensations that are worse in the evening or night than during the day or occur only in the evening or at night 5) The above symptoms are noted associated with other medical conditions like myalgias, venous stasis, arthritis, leg cramps or habitual foot tapping.<sup>9</sup>

Polyneuropathy was diagnosed clinically according to published criteria<sup>10</sup>, along with the Electrophysiological test.

**Data Analysis:** The data was entered by two persons to control the bias and analyzed with the help of SPSS Program version 18.0.

Frequency and percentage was calculated for categorical variables like Age group, sex, and presence of metabolic syndrome. Confounding effect was controlled through stratification of age and gender.

## RESULTS

Out of 48 patients 30 (62.5%) were male and 18 (37.5%) were female (Table No: 1). Mean age was  $42.23 \pm 8.7$ .

Out of 48 patients 21 have proven peripheral neuropathy clinically and electrophysiologically (Table No. 2). Other possible medical conditions related to restless leg syndrome were excluded through the investigations.

Ten patients (47.6%) had pure sensory neuropathy and remaining (52.4%) have mixed sensory motor neuropathy (Table no. 3). The pure sensory neuropathy group had comparatively intense symptoms of RLLS, and they reported pain in their feet with RLLS more frequently. Some of them also have family history of RLLS. Patients with Mixed sensory motor polyneuropathy did not have similar strong symptoms of Restless leg syndrome and pain in lower limbs.

**Table No.1: Frequency of Gender: Total No: 48**

Gender	Frequency
Male	30 (62.5%)
Female	18 (37.5%)

**Table No.2: Causes of Restless leg syndrome:**

Causes	Frequency
Peripheral Neuropathy	21 (43.7%)
Other causes eg, Iron Deficiency, Hypothyroid etc	12 (25.0%)
Idiopathic	15 (32.1%)

**Table No.3: Type of Neuropathy:**

Neuropathy	Frequency
Mixed Sensory Motor	11 (52.4%)
Pure Sensory	10 (47.6%)

## DISCUSSION

Restless leg syndrome is a common neurologic disorder, was first estimated to occur in 5 to 7 % in general population<sup>12,13</sup>. The diagnosis is mostly based upon patient's history and some investigations that exclude the other causes of leg cramps. The first criterion is continuous craving to move the lower limbs because of abnormal sensations.

Some studies have revealed that RLLS is more common in females. Berger et al. reported that RLLS affected females ten times as compare to males; while in our study it is more prevalent in males<sup>11</sup>. In addition, the role of estrogen in women, or iron deficiency should be noted. Some other risk factors such as old age, senile neuropathy and drugs consumption including dopamine antagonists, tricyclic antidepressants, serotonin reuptake inhibitors, excessive caffeine or alcohol intake, and nicotine may aggravate the symptoms in males too.

The causes of restless leg syndrome are Iron deficiency, hypothyroidism, lumbosacral polyradiculopathy dopamine antagonist drugs or peripheral neuropathy<sup>13,14, 15</sup>, similarly one fourth of total patients in our study have causes other than polyneuropathy.

Restless leg syndrome is frequently associated with peripheral polyneuropathy<sup>16</sup>. In our study 21 patients found to have mixed sensory motor polyneuropathy. In studies done in past restless syndrome can be associated with pure sensory polyneuropathy (Devigili, et al, 2008) and some time with sub clinical sensory polyneuropathy<sup>17,18</sup>. While in our study about 47% of total patients with polyneuropathy have pure sensory neuropathy and it was observed that they have more intense paresthesias as compare to the others.

## CONCLUSION

The result suggests that RLLS is triggered by agonizing paresthesias is mainly related to pure sensory neuropathy is not an uncommon cause. Patients with mixed sensory motor neuropathy have less intense feature of restless leg syndrome. The authors assume that the patients with the pure sensory neuropathy will respond well to neuropathic pain medications, for example pregabalin, rather than conventional therapy.

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

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# Incidence of Hyperamylasemia Leading to Respiratory Failure

Hyperamylasemia with Organophosphate Poisoning

## in Patients of Organophosphate Poisoning

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### ABSTRACT

**Objective:** To determine the frequency of Hyperamylasemia leading to respiratory failure in patients of organophosphate poisoning.

**Study Design:** Observational / descriptive study.

**Place and Duration of Study:** This study was conducted at the Department of Medicine Dow University of Health Sciences, Karachi from June 2014 to June 2015.

**Materials and Methods:** A total of 168 patients of Organophosphate poisoning fulfilling the inclusion criteria were included in the study. Blood was drawn after aseptic measures by a trained phlebotomist for Serum Amylase level and Arterial blood gases. Value more than 101U/L was taken as hyperamylasemia. PaO<sub>2</sub> less than 60mmHg or PCO<sub>2</sub> greater than 55mg was labeled as respiratory failure. All information was noted on proforma.

**Results:** There were 59% were male and 41% were female. Frequency of hyperamylasemia in patients of organophosphate poisoning was 44%. Frequency of respiratory failure in hyperamylasemia in patients was observed in 68%. Respiratory failure was significantly high in male than female (70% vs. 59%, p=0.019).

**Conclusion:** Hyperamylasemia is more frequently seen in organophosphate poisoning. In patients with respiratory failure the mortality is very high; therefore we recommended early diagnosis, careful monitoring and appropriate management of complications in reducing the mortality rate.

**Key Words:** Organophosphate, Respiratory failure, Hyperamylasemia

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### INTRODUCTION

Organophosphate compounds are diverse group of chemicals widely used in domestic and industrial settings, as insecticides, herbicides & fungicide<sup>1-4</sup>. However these compounds pose major health risks and hazards in the form of organophosphate poisoning. The problems associated with these compounds are not only affecting the developing world but are also common in the developed world<sup>1</sup>.

The following facts and figures about organophosphate poisoning stand out<sup>1</sup> it accounts for approximately 3 million poisoning cases around the globe<sup>2</sup> it is the cause of around 200,000 deaths every year<sup>3</sup> majority of such cases are largely populated in the Asian-Pacific region<sup>4</sup>

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It is projected that nearly 90 percent of such poisoning cases are suicidal with fatality rate of greater than 10 percent<sup>5</sup> 8 to 10 percent are accidental while less than 1 percent are estimated as homicide cases<sup>6,7</sup>.

The widespread use of organophosphates as a household and agricultural pesticide without regulation, is probably the most important reason for organophosphate poisoning. This reflects the necessity of early diagnosis, treatment and the implementation of advanced supportive care in ICU<sup>8,9,10</sup>.

Elevated amylase levels or Hyperamylasemia is frequently seen in organophosphate poisoning due to cholinergic stimulation of pancreas<sup>4</sup>. Studies conducted by Singh et al and Lee et al reported 37 patients out of 79 and 44 patients out of 121 with hyperamylasemia in patients with organophosphate poisoning respectively<sup>11,12</sup>.

Furthermore, respiratory failure is one of the serious complications associated with such poisoning.<sup>13</sup>

### MATERIALS AND METHODS

This study was carried out at the Department of Medicine Dow University of Health Sciences, Karachi from June 2014 to June 2015.

#### Sample Selection:

#### Inclusion criteria:

- Age  $\geq$  15yrs to  $\leq$  45yrs of both genders



• Diagnosed case of organophosphate poisoning presenting in 24hours of ingestion

#### Exclusion criteria:

- History of ingestion of any other material along with organophosphate poisoning
- Subjects with H/O of alcohol addiction
- Patients with acute abdomen
- Who had gone thru ERCP in previous 24hrs
- Concomitant respiratory illness

**Data Collection Procedure:** Data was collected on a pretest self administered Performa after taking permission from ethical committee of the hospital. Blood was drawn after aseptic measures by a trained phlebotomist for Serum Amylase level and Arterial blood gases.

**Data Analysis Procedure:** Data was analyzed with the help of SPSS program version 18. Frequency and percentages were calculated for gender, hyperamylasemia and respiratory failure. Stratification was done with regards to age, gender, duration of ingestion.

## RESULTS

One sixty eight diagnosed case of organophosphate poisoning presenting in 24hours of ingestion were included in this study. Age distribution of the patients is presented in figure 1. The average age of the patients was  $36.87 \pm 7.54$  years (table 1).

Out of 168 cases, 99(59%) were male and 69(41%) were female. Duration of ingestion of the most of the cases were 6 to 12 hours as presented in figure 2. Frequency of hyperamylasemia in patients of organophosphate poisoning was 44%. Frequency of hyperamylasemia was not significant among the groups (table 2). Similarly rate of hyperamylasemia was not significant between gender and in patients with <6 hours and 6 to 12 hours duration of ingestion as presented in table 3 and 4.

Frequency of respiratory failure in hyperamylasemia in patients of organophosphate poisoning was observed in 68% (50/74). Frequency of respiratory failure was not significant in age groups while respiratory failure was significantly high in male than female (70% vs. 30%;  $p=0.019$ ) as shown in table 8. Frequency of respiratory failure in hyperamylasemia was also not significant with <6 hours and 6 to 12 hours duration of ingestion patients as presented in Table 5.

**Table No.1: Descriptive Statistics of Patients**

Variables	Mean $\pm$ SD	95%CI	Max-Min	Range
Age (Years)	$36.87 \pm 7.54$	35.52 to 38.21	45-15	30
Duration of Ingestion (hours)	$7.68 \pm 2.46$	6.12 to 8.74	12-1	11

**Table No.2: Hyperamylasemia in Patients of Organophosphate Poisoning with Respect to Age Groups**

Age Groups	Hyperamylasemia		P-Values
	Yes n=74	No n=94	
15-20 yrs	10(13.5%)	25(26.6%)	0.144
21-30 yrs	22(29.7%)	23(24.5%)	
31-40 yrs	30(40.5%)	28(29.8%)	
40-45 yrs	12(16.2%)	18(19.1%)	

Chi-Square= 5.146

**Table No.3: Hyperamylasemia in patients with respect to gender (n=168)**

Gender	Hyperamylasemia		P-Values
	Yes n=74	No n=94	
Male	45(60.8%)	54(57.4%)	0.66
Female	29(39.2%)	40(42.6%)	

Chi-Square= 0.194

**Table No.4: Hyperamylasemia in patients with respect to duration of ingestion (n=168)**

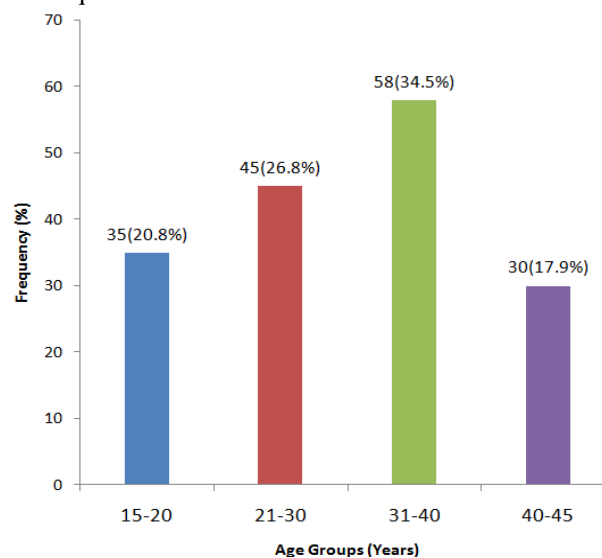
Duration of Ingestion	Hyperamylasemia		P-Values
	Yes n=74	No n=94	
< 6 hours	23(31.1%)	40(42.6%)	0.127
6 to 12 hours	51(69.9%)	54(57.4%)	

Chi-Square= 2.325

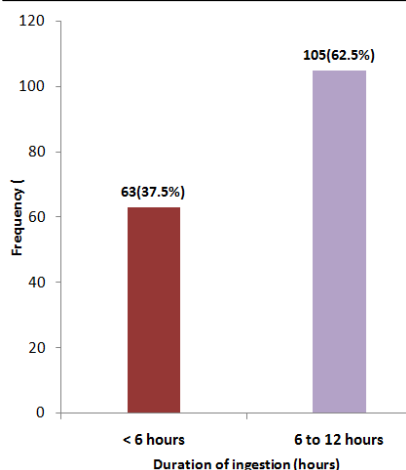
**Table No.5: Respiratory failure in hyperamylasemia in patients of organophosphate poisoning with respect to duration of ingestion (n= 74)**

Duration of Ingestion	Hyperamylasemia		P-Values
	Yes - n=50	No - n=24	
< 6 hours	15(30%)	8(33.3%)	0.77
6 to 12 hrs	35(70%)	16(66.7%)	

Chi-Square= 0.084



**Figure No.1: Bar graphing showing age distribution of the patients n=168**



**Figure No.2: Duration of ingestion of the patients n=168**

## DISCUSSION

In Pakistan, the prevalence of depression is high and suicidal tendencies are increasing<sup>14</sup>. Insecticide intake as a suicidal attempt has been seen very often in our society and in other developing countries as it is readily available in every home<sup>8,15,16</sup>.

Ingestion of Organophosphates for suicidal purposes is a major problem, especially in developing countries. Ops (organophosphates) not only affect Acetylcholinesterase but also may alter the liver, kidney, pancreas and the other organ functions<sup>17</sup>.

In our study Frequency of hyperamylasemia in patients of organophosphate poisoning was 44% (74/168). Martin Rubi et al<sup>18</sup> have reported only three patients with pancreatitis in a total number of 506 cases of organophosphate intoxication. The finding of hyperamylasemia was closely related to clinical severity and presence of shock. This makes a percentage of 5.66%. Sahina and others<sup>19,20</sup> have reported acute pancreatitis in 6 patients among 47 making a percentage of 12.7%.

Dagli and Shaikh<sup>21</sup> reported transient elevated amylase in 47 of 75 patients with malathion poisoning and three of their patients had hyperglycemia. Different scoring systems have been used to grade severity of poisoning<sup>22,23</sup>.

In present study frequency of respiratory failure in hyperamylasemia in patients of organophosphate poisoning was observed in 68%. Frequency of respiratory failure was not significant in age groups while respiratory failure was significantly high in male than female (70% vs. 30%; p0.019). In Eddleston et al study<sup>24</sup> ninety of 376 patients (24%) required intubation, 52 (58%) within 2 hrs of admission while unconscious with cholinergic features. Twenty-nine (32%) were well on admission but then required intubation after 24 hrs while conscious and without cholinergic features.

Harputluoglu and Eddleston have reported to acute pancreatitis on admission after an attempted suicide by the ingestion of excessive organophosphate in human. In these reports, leukocyte count and serum amylase levels were very high measured when compared to reference range<sup>24,25</sup>.

## CONCLUSION

Organophosphate compounds poisoning is a serious and lethal condition and needs early diagnosis and appropriate treatment. Hyper amylasemia is more frequently seen in organophosphate poisoning. In patients with respiratory failure the mortality is very high; therefore we recommended early diagnosis, careful monitoring and appropriate management of complications in reducing the mortality rate.

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

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# Rifled Fire-Arm: The Predominant Weapon in All Medico-Legal Deaths in Lahore

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## ABSTRACT

**Objective:** The main objective of Medico-legal autopsy is to find out the cause of death but it also helps in finding the manner of death. From this we also find out the criminal behavior of the society and usage of different kinds of weapons related with the cause of death and particularly the types of fire-arm weapons which is more in concern with the present study. This study was especially conducted to find out the predominance of rifled fire-arms weapons amongst all fire-arm deaths.

**Study Design:** Observational / descriptive study.

**Place and Duration of Study:** This study was conducted at the Department of Forensic medicine & Toxicology K.E.M.U. Lahore during the period of 2006-2008.

**Materials and Methods:** This study includes 2979 medico-legal autopsies. The information was gathered from post-mortem reports, police documents and hospital records. Not only the kind of weapon was studied but all other parameters were taken into consideration like, cause & manner of death, sex, age, season and areas of injuries on the body.

**Results:** The analysis quite distinctly highlighted that amongst 2979 deaths, 1255 were because of fire-arms weapons (43.13%). Out of these 1192 (92%) deaths were by rifled weapons, whereas 103 (8%) were by smooth bored fire-arm weapons. Total number of male deaths by fire-arms was 1066 (82.95%), whereas females were 219 (17.05%). All homicidal cases were 788, 46 suicidal, 97 accidental and in 354 the manner remained un-determined. The manner amongst males was, 652 homicidal, 42 suicidal, 82 accidental and in 290 it was un-determined. And in females 136 were homicidal, 4 were suicidal, 15 accidental and in 64 the manner remained un-determined. The ratio of homicidal to suicidal was 17.1:1 and homicidal to accidental ratio was 8.1:1. In 92% cases the rifled fore-arms weapons was used and in 8% it was smooth bored. The rifled fire-arms injuries had multiple entry wounds in 52.9% of deaths and there was single entry wound in 47% death. While there was single entry wound in 66% deaths in smooth bored weapons and in 34% of cases multiple wounds were observed. The range of fire in (56.8%) homicidal deaths was distant, whereas in 30.4% it was close range. Close contact fire was seen in 1.4% of suicidal deaths. 16% cases showed blackening, 10.58% cases had tattooing and in 2.25% cases there was burning.

**Conclusion:** The fire-arms weapon is the most predominant mean of un-natural deaths. Amongst them the usage of rifled weapons is more than the smooth bored. So this needs formulation of effective law for control of these weapons.

**Key Words:** Kind of Weapon, Rifle, Smooth Bored, Manner of Death, Homicide, Suicide

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## INTRODUCTION

The objectives of medico-legal autopsy are to find out the kind of weapon, whether blunt, sharp or fire-arm etc. and the nature of injury which may be ante-mortem or post-mortem. It also helps to find out not only the cause of death but also the medical cause of death.

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Which means it finds out the organic or systemic damage and the chain of events which is the mode of death. It also gives important information about the manner of death i.e., homicidal, suicidal or accidental.<sup>1</sup> The un-Natural deaths, either caused by physical damage or poisoning, must be thoroughly investigated<sup>2</sup>. Any mark of injury raises a suspicion of foul play, so it must be thoroughly investigated. At times it becomes difficult to declare the injury as homicidal, suicidal or accidental, however the opinion can be framed by thorough investigation. This includes the autopsy findings and other relevant facts of the case under investigation. These facts include circumstantial evidence, crime scene investigation, all the details about injuries and kind of weapon also<sup>3</sup>.

Most of the medico-legal autopsies are homicidal, which reflects the criminal tendency of the society<sup>4,5</sup>. Religion of Islam takes very strict notice of homicide,

and it is declared a heinous crime against humanity. In Holy Quran it is said as, "Whoever kills another person is as if he killed the whole humanity (human race)"<sup>6</sup>.

In 1993 in USA the homicidal deaths were at its maximum but in 1998 it was reduced tremendously which was almost equal to that of 1968. In USA this number of homicidal deaths is higher than any other developed nation. The Colombia having 146.5 homicidal deaths per 100,000 males is at highest level. The South Africa & Nigeria have similar tendency. The highest toll of homicidal killings in USA is by raising the number of fire-arm deaths. When this was compared with other countries where fire-arms are common, even then this number in USA was more. Small fire-arms are most common cause of homicidal killings in USA as compared to other countries where rifled and smooth bored guns are common.<sup>8</sup>

## MATERIALS AND METHODS

This study was carried out at the Department of Forensic medicine & Toxicology K.E.M.U. Lahore, during the period of 2006-2008.

This study includes 2979 medico-legal autopsies. The information was gathered from post-mortem reports, police documents and hospital records. Not only the kind of weapon was studied but all other parameters were taken into consideration like, cause & manner of death, sex, age, season and areas of injuries on the body.

## RESULTS

**Kind of Weapon:** Various means were used to cause un-natural death. Out of these 2979 un-natural deaths the deaths caused by fire-arms weapons were 1285 which was 43.13% of total deaths. This was highest amongst other cause of deaths (Table No. 1)

**Table No. 1 Kinds of Weapon in all 2979 Deaths**

Kind of Weapon	Total No. of Cases	%age of Weapon
Blunt Weapons	403.0	13.52%
Sharp Edged Weapons	235.0	8.5%
Fire-arm Weapons	1285.0	43.13%
Poisoning of All Kinds	74.0	2.48%
All types of Burns	50.0	1.68%
Asphyxial Deaths	220.0	7.38%
Electrocution Cases	19.0	0.64%
Drowning Cases	17.0	0.57%
Bomb Blast Deaths	65.0	2.18%
Natural Deaths	347.0	11.65%
Un-Determined Cases	213.0	7.15%
Total No. of Cases	2979.0	100.00%

**Manner of Death:** In these 2979 cases, the incidence of homicide was 70.36%, suicidal 3.42%, accidental 7.42%, un-determined 7.15% and 11.65% deaths were because of natural causes. (Table No. 2)

**Table No. 2: Percentage of 2979 cases in reference to manner of death**

Manner of Death	Total Cases	%age
Homicidal	2096	70.36
Suicidal	102	3.42
Accidental	221	7.42
Un-Determined	213	7.15
Natural	347	11.65
Total	2979	100.00

**Table No. 3: Age and Sex Distribution of Total 2979 Cases**

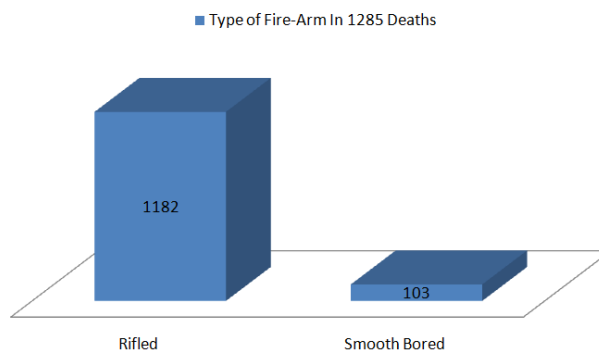
Age	Male	%age	Female	%age	Total	%age
0 - 11 months	30	1.25	15	2.60	45	1.51
1 - 10 yrs	35	1.46	28	4.86	63	2.12
11 - 20 yrs	200	8.32	124	21.53	324	10.88
21 - 30 yrs	738	30.71	173	30.03	911	30.58
31 - 40 yrs	620	25.80	110	19.10	730	24.51
41 - 50 yrs	382	15.90	50	10.42	442	14.84
51 - 60 yrs	213	8.80	22	3.82	235	7.89
61 - Onward yrs	185	7.70	44	7.64	229	7.67
Total	2403	80.66	576	19.34	2979	100.00

**Age and Sex Distribution:** When all 2979 cases of un-natural deaths were scrutinized, it was highlighted that males were more in number 2403 as compared to 576 females. The age group which was predominant was between 21-30 years of age. (Table No. 3).

**Type of Fire-Arm Weapon:** Out of 1285 deaths caused by fire-arms weapons, 1182 (92%) were caused by rifled arms and only 103 (8%) were by smooth bored weapons. (Table No. 4) (Fig No. 1)

**Table No. 4: Percentage of Type of Weapons in all 1285 fire-arm Deaths**

Type of Fire-Arm	Number of Cases	Percentage
Rifled Weapon	1182.0	92.0%
Smooth Bored Weapon	103.0	8.0%
Total No. Of Cases	1285.0	100.0%



**Figure No.1: Type of Fire Arm in 1285 Deaths**

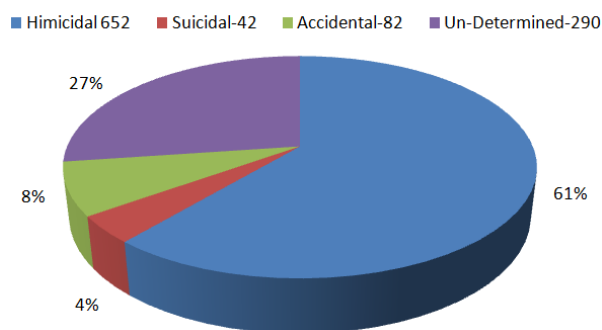


Figure No. 2: Manner of Death in Males = 1060

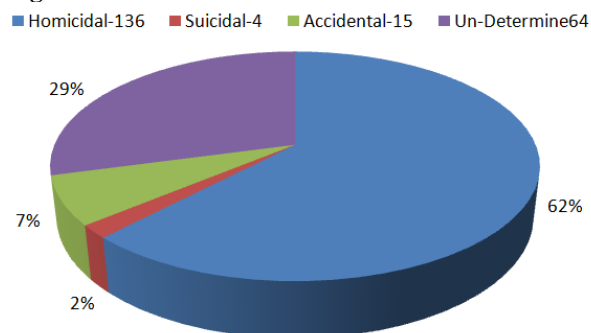


Figure No.3: Manner of Deaths in Females=219

**Manner of death in both genders:** In 1060 fire-arms deaths in males 652 (61%) were homicidal, in 290 (27%) manner remained un-determined. 82 (8%) were accidental and in 42 (4%) the manner of death was suicidal. Figure 2

Whereas in 219 females with fire-arms deaths 136 (62%) were homicidal, in 64 (29%) manner remained un-determined. 15 (7%) deaths were accidental and in 4 females (2%) it was suicidal. Figure 3

## DISCUSSION

In our study of 2979 cases, it was distinctly observed that, 2096 deaths were homicidal showing an incidence of 70.36%. In these 2979 deaths, those caused by fire-arms weapons were 1285 showing an incidence of 43.13%. This was a quite higher in number as compared to deaths caused by other means. It is lower as compared to the study carried out at Peshawar by Marri et al in 2002<sup>24</sup>. Similarly it is again lower than the studies carried out by Sahito 61.80% in the Province of Sindh<sup>13</sup>, by Molina and Di Maio 52.0% in Bexar<sup>14</sup>, by Qadir & Aziz 46.0% in Larkana in 1998<sup>15</sup>. In our study incidence is higher than the study carried out Azmak 17.03% in Edirne<sup>16</sup>.

The incidence of fire-arm deaths was low in Newfoundland and Costa Rica because the fire-arms are not available freely as shown in the study of Avis<sup>37</sup> & Lester<sup>38</sup>. In contrast to that fire-arm deaths are rising in number in our USA. This was shown in the study of Chu<sup>7</sup> in California, also in Italy the number is more as shown Solarino<sup>19</sup> and Verzeletti<sup>20</sup>, and by

Demetriades<sup>6</sup> in Los Angeles. This higher incidence is because of free and easy access to fire-arms.

**Kind of Weapon:** Out of 2979 medico-legal autopsies 1285 deaths were due to fire-arms weapons as shown in our study. In 92% of cases the fire-arm weapon was rifled and smooth bored in 8%. This finding is quite similar to that Chaudhry<sup>23</sup> quoting rifled weapons as 87% and smooth bored 12.7%. The handguns were used in 100% of suicidal cases as shown in the studies carried out by Verzeletti in Bari, Italy<sup>20</sup> and Alfawal Saudi Arabia<sup>21</sup>. In our study the most common weapon used was rifled, which is quite in contrast to that quoted by Avis<sup>17</sup> which showed shot-gun as common weapon.

**Manner of Death:** The homicidal incidence in our study of 2979 cases subjected to autopsy at Lahore is 70.36%, which is almost the same as other previous studies (68%, 68.73%)<sup>27,28</sup>. It was higher than that of study in 91-95 (55.2%)<sup>29</sup>. Other cities showed higher incidence than our study as Faisalabad (79.66%)<sup>30</sup>, Peshawar (77.7%)<sup>31</sup>, and D.I. Khan (76%)<sup>34</sup>.

In our study the suicidal incidence is higher (3.5%), than the previous studies carried out in Lahore (0.62%)<sup>27</sup>, (0.58%) in D. I. Khan<sup>34</sup>, (1.26%) in Peshawar<sup>31</sup>, but lower than 19.50% in India and Western countries<sup>33</sup>. Accidental incidence is 7.42% is lower than 17.13%<sup>34</sup> in D. I. Khan and 17.7%<sup>31</sup> in Peshawar.

**Incidence of Sex:** There is higher incidence of homicidal deaths 80.60% in males as compared to females which were 19.30% in our study. In study of Qadir it was 85.50% males and 19.50% females<sup>15</sup>. The study carried out by Chaudhry<sup>43</sup> showed 91.0% males and 9.0% females, In Edirne<sup>16</sup> Azmak noted 82.0% males and 18.0% females and Kohli<sup>22</sup> in India found 90.70% males & 9.30% females in as homicide. The males showing the higher incidence because of the reason that it is a male dominated society. In big cities however females are exposed to outside house society for education, jobs and other house-hold works, for which they becomes exposed to physical violence. In Sind Sahito<sup>13</sup> had shown higher incidence of females because of KaroKari.

**Incidence of Age:** In this study it is highlighted that, there is higher incidence of 38.90% in 3<sup>rd</sup> decade of age and then in 4<sup>th</sup> decade 25.40%. This result is similar to those of Qadir<sup>15</sup>, Azmak 54%<sup>16</sup>, Kohli 46.7%<sup>22</sup>, and Chaudhry 38%<sup>23</sup> in 3<sup>rd</sup> decade of life. Molina<sup>14</sup> pointed out the mean age of 41.60 years for the suicide and 32.60 in cases of homicide. All the studies showed that, the victims were mostly young. So it that, the young people especially the males has easy access to fire-arms in comparison to females. The extreme age groups both in young & old ages were not vulnerable. The studies of Chao<sup>25</sup> and Dikshit<sup>24</sup> showed the same results but it differs from those of Chu<sup>7</sup> and Rachuba<sup>26</sup>, in which they have found out 15-19 years and 10-25 years the most vulnerable respectively.



**Type of Weapon:** Our study revealed that out of 2979 medico-legal autopsies, 1285 death were because of fire-arm injuries. The rifled weapons were used in 92% of cases and non-rifled in 8%. It is similar as Chaudhry quoted rifled 87% and non-rifled 12.7%<sup>23</sup>. Verzeletti et al in Bari, Italy<sup>20</sup>, and Alfawal et al in Eastern Saudi Arabia had quoted as usage of handguns in 100% suicidal cases, 56% in homicidal and 71% accidental cases<sup>21</sup>. Commonest weapon used in our study was rifled in contrast to Avis who quoted short guns as the frequent<sup>17</sup>.

**Manner n Fire-Arms Death:** Our study showed that in 61.32% the manner is homicidal, in 3.58% it is suicidal and in 7.55% it is accidental. In 27.55% of cases the manner remained un-determined. The study of Verzeletti in Italy showed that 60.40% of the deaths were suicidal, 35.90% were homicidal and 3.70% cases were accidental in Bressica<sup>20</sup>. At Bari<sup>19</sup> Solarino reported that, the homicidal manner was the commonest (88.42%), the suicidal was 11.43% and the accidental manner was only 0.13%. Elfawal<sup>21</sup> had reported the homicidal manner in 48.0%, the suicidal were 28.0% and accidental manner was 24.0% in Saudi Arabia. In Delhi Kohli<sup>22</sup> showed that, the homicide was 92.60%, the suicide 6.50% and in 0.90% the manner was accidental. Azmak<sup>16</sup> in a study in Turkey reported that in 58.30% deaths the manner was homicidal. Molina<sup>14</sup> reported 52.20% deaths were homicidal, in 45.80% the manner was suicidal, in 01.60% accidental and in 0.40% the manner of death remained un-ascertained.

## CONCLUSION

Our study has shown that the usage of fire-arms weapon is most common kind of weapon used in all un-natural deaths. Homicidal manner showed a higher incidence in these deaths by fire-arms weapons. The most vulnerable age found in this study is young especially the 3<sup>rd</sup> decade. Male showed a higher incidence than those of females. The other important finding is that amongst all fire-arms weapons used for all un-natural deaths, the rifled weapon is the most common weapon. This clearly shows that there is increase in the usage of fire-arms and it is a great threat to the society. The need of the time is to analyze the factors which are responsible. The strong enforcement of legislation is required.

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

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# A Comparative Study to Evaluate the Chronotropic Action of Citalopram, Fluoxetine and Paroxetine on Intact Frog's Heart

Ayesha Shahnawaz, Naila Abrar and Munir Ahmad Khan

## ABSTRACT

**Objective:** To compare the chronotropic action of citalopram, fluoxetine and paroxetine on frog heart.

**Study Design:** Experimental animal study

**Place and Duration of Study:** This study was conducted at Yusra Medical and Dental College, Islamabad from October 2015 to February 2016.

**Materials and Methods:** Stunning and pithing of the frog was done following which the heart was exposed. The apex was attached to a force transducer. Heart rate readings were recorded on Power lab. Three groups were designed. In every set of experiments basal readings (without drug) were initially recorded that served as the control and then the tissue was treated with one antidepressant. In Group I we documented the effects of citalopram. In Group II we observed the effects of fluoxetine and in Group III we noted the effect of paroxetine. Statistical analysis was done using SPSS version 22. A p value of less than or equal to 0.05 was considered statistically significant.

**Results:** The isolated heart tissue sample was exposed to 0.5ml of drug. Citalopram at a concentration of 1.54mM reduced the heart rate from 30 to 19 beats/min. Fluoxetine at a concentration 1.6mM brought down the heart rate from 23 to 20 beats/min. Whereas, paroxetine at a concentration of 1.2mM increased the heart rate from 21 to 23 beats/min.

**Conclusion:** Citalopram out of the three chosen drugs caused the most marked reduction in heart rate. Fluoxetine caused a subtle reduction in heart rate. Paroxetine on the other hand caused a mild increase in heart rate.

**Key Words:** SSRI's, Citalopram, fluoxetine, paroxetine, chronotropic, frog heart

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## INTRODUCTION

Depression contributes to a major global health burden; with over 150 million people being affected by it worldwide<sup>1</sup>. The mainstay of the treatment revolves around cognitive behavioral therapy and pharmacological intervention. For many years physicians relied on tricyclic antidepressants (TCAs) and Monoamine Oxidase Inhibitors (MAOIs). The TCAs presented with a myriad of adverse effects such as anticholinergic, cardiotoxic and neurological effects<sup>2</sup>. Clinical data also revealed the large propensity with which the TCAs caused fatal outcomes in case of over dosage, owing to their low margin of safety<sup>3</sup>. The MAOIs have also become an obsolete choice due to their adverse effects and potentially life threatening food and drug interactions<sup>4</sup>.

The Selective Serotonin reuptake inhibitors (SSRIs) were introduced in the 1980's, and since their advent the pharmacological choices for the treatment of depression have been revolutionized.

The SSRIs increase the availability of monoamine neurotransmitters in the synaptic cleft by selective inhibition of the serotonin transporter (SERT) present on the presynaptic membrane<sup>5</sup>. The SSRIs were instantaneously preferred over TCAs and MAOIs due to their greater efficacy, tolerability, limited deleterious effects and a safer profile even with over dosage of the drug. The SSRIs were developed with the objective of having a class of drugs with minimal interactions with other receptors, as; the TCAs had considerable unwanted interactions with receptors like muscarinic, histamine,  $\alpha$  adrenergic etc. Therefore, the narrow spectrum of adverse effects with this new class of drugs was fundamentally attributed to the drugs lack of affinity for miscellaneous receptors and specificity for the SERT receptor<sup>2</sup>.

A lot of work has been done to undermine the toxic profile of the SSRIs. The SSRIs have been documented to cause adverse effects such as weight gain, sexual dysfunction and sleep disturbances<sup>6</sup>. They may also produce an assortment of other side effects such as gastrointestinal disturbances and CNS related

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symptoms<sup>7</sup>. The adverse effects associated with the SSRIs differed from those produced by conventionally used TCAs and MAOIs. Also the adverse effects were milder and resulted in less fatal outcomes as compared to older therapeutic choices. One of the salient features distinguishing the TCAs from the SSRIs was the latter group's relative safe cardiac profile<sup>2</sup>. The TCAs were known to cause cardiac effects like tachycardia, intraventricular conduction delay and prolongation of the QT interval at therapeutic dosage and life threatening arrhythmias at over dosages<sup>8</sup>.

Whereas the SSRI Citalopram, at therapeutic dosage has been shown to cause only a mild bradycardia with otherwise unappreciable effects on cardiac conductance<sup>9</sup>. With over dosage of greater than 400mg, the drug may result in a fatal outcome due to prolongation of the QTc interval<sup>10</sup>. Fluoxetine when studied for its cardiac profile, showed subtle changes in the cardiovascular profile, such as a decrease in heart rate and an increase in supine systolic pressure and ejection fraction in patients with compromised ejection fraction. However no significant changes on cardiac conductance were noted<sup>11</sup>. Paroxetine also causes a fall in heart rate and an increase in supine blood pressure<sup>12</sup>. Our study focuses on the comparison between the three SSRIs, Citalopram, Fluoxetine and Paroxetine with reference to their ability to cause bradycardia in the isolated frog heart. The aim of the present study was to compare the action of citalopram, fluoxetine and paroxetine on the heart rate of an intact frog heart preparation.

## MATERIALS AND METHODS

The experimental work was carried out in the Laboratory of the Department of Pharmacology and therapeutics, at Yusra medical and dental college, Islamabad for a period of 5 months (October 2015-February 2015). Healthy frogs of both sexes weighing approximately 500gm were included. Animals with a resting heart rate of < 10 beats/min or > 35 beats / min were excluded from the study. Animals were kept in the animal house of the institution at room temperature and humidity of 60%. All animal handling procedures were conducted in accordance with the Guide for the care and use of Laboratory animals of the National institute of health, as well as the guidelines of the Animal welfare Act. After stunning and pithing of the frog, the precordium was dissected to expose the heart. The tissue was kept aerated and was intermittently bathed with amphibian ringer's solution. The frog was laid on a cardboard sheet. The heart was mounted on the force transducer (ML856). All observations were recorded on power lab machine.

The animals were divided in to three groups:

Group I. (n=6) Treated with Citalopram

Group II. (n=6) Treated with Fluoxetine

Group III. (n=6) Treated with Paroxetine

Baseline heart rate readings were recorded for each tissue sample. Next, the effect of drug was observed on individual groups. Group I, II and III were incubated with a single application of 0.5ml of citalopram, fluoxetine and paroxetine respectively. After an incubation period of 5 minutes the heart rate was recorded. Each tissue sample was only used once.

Citalopram, fluoxetine and paroxetine were purchased from Medizan laboratories (pvt) ltd Pakistan. Stock solutions for citalopram, fluoxetine and paroxetine were prepared at 1.5mM, 1.6mM and 1.3mM respectively. A single application of 0.5ml of the drug was used for each group.

## RESULTS

The results were statistically analyzed by using SPSS version 22 and paired T test was used to evaluate the significance within a group. A p value of 0.05 or less was considered to be statistically significant.

**Group I:** The resting heart rate was documented. The tissue was next incubated with 0.5ml of 1.54mM of citalopram. The application of citalopram lead to an appreciable negative chronotropic effect. The heart rate decreased from a mean basal value of 29beats/min to 19beats/min as shown in Table 1 and figure 1.

**Table No 1: The effect of citalopram on heart rate.**

Sr. No	Basal heart rate	Citalopram treated heart rate
1	27.27	20.47
2	25.64	18.51
3	33.89	20.76
4	33.33	19.60
5	33.14	19.23
6	24.79	17.80

**Group II:** After recording the resting heart rate, the tissue samples were preincubated with 0.5ml of 1.6mM of fluoxetine. The presence of the drug decreased the pacemaker activity of the heart from a mean value of 23beats/min to 20beats/min as shown in Table 2 and figure 1.

**Table No 2: The effect of fluoxetine on heart rate.**

Sr. No	Basal heart rate	Fluoxetine incubated heart rate
1	19.16	16.94
2	20.33	16.94
3	24	22.9
4	23.52	22.64
5	26.31	22.9
6	27.14	23.16

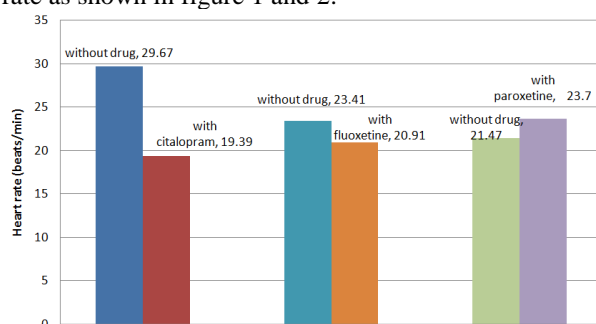
**Group III:** Intrinsic heart rate was noted. Subsequently the pretreatment of group III with 0.5 ml of 1.3mM of paroxetine was performed. The presence of paroxetine induced a positive chronotropic effect. The heart rate

increased from a basal value of 21 beats/min to 24beats/min as shown in Table 3 and figure 1.

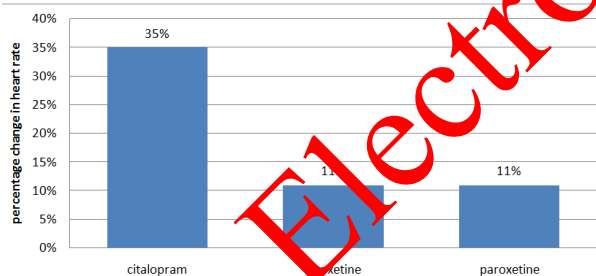
**Table No 3: The effect of paroxetine on heart rate.**

Sr. No	Basal heart rate	Paroxetine incubated heart rate
1	21.34	23.48
2	20.40	22.74
3	21.58	24.51
4	22.13	23.38
5	19.54	22.50
6	23.87	25.63

Henceforth it was observed that citalopram brought the greatest change in the resting heart rate of the intact frog heart. It decreased the basal heart rate by 35%. The drug fluoxetine caused an 11% decrease in heart rate whereas paroxetine resulted in an 11% increase in heart rate as shown in figure 1 and 2.



**Figure No 1: A graphical representation of the effects produced on heart rate by citalopram, fluoxetine and paroxetine. Each drug is compared with its control values (without drug).**



**Figure No 2: a comparison of the percentage change in heart rate caused by citalopram, fluoxetine and paroxetine.**

## DISCUSSION

SSRIs have been documented to have a benign cardio toxic profile compared to the TCAs<sup>7</sup>. Nevertheless they still exert a mild effect on the chronotropic action as seen in our experimental design.

In our study we compared three commonly used SSRIs in terms of the changes in the cardiac pacemaker activity caused by them. It was seen that the resting heart rate of the frog was influenced by all the three antidepressants. Citalopram induced the greatest change by decreasing the resting heart rate (30±4 to 19±1 beats

per minute; p=0.001). Fluoxetine also resulted in a similar effect but produced less pronounced bradycardia (23±3 to 20±3 beats per minute; p=0.05). Paroxetine on the other hand, exhibited a mildly positive chronotropic effect and increased the basal heart rate (21±1 to 23±1 beats per minute; p<0.05) as shown in figure 1a.

The Sino atrial node maintains the auto rhythmicity of the heart. The establishment of an action potential depends on ion conductance through the voltage dependent sodium, calcium and potassium channels. Any changes in ion conductance would result in a change that may be appreciated on an electrocardiogram. Citalopram has already been documented to produce electrophysiological effects on isolated heart tissue samples obtained from rabbit, canine, rat and guinea pig. It has shown to alter ion conductance through sodium and Calcium channels<sup>13,14</sup>. In our study 1.54mM of citalopram produced a significant decline in heart rate. Pacher *etal* have similarly demonstrated that citalopram caused inhibition of the L-type calcium channels in guinea pig myocytes at a concentration of 100 µM<sup>15</sup>. The decrease in the heart rate observed in our study is also hypothesized to be attributable to the ability of the drug to inhibit the long lasting Calcium channels of the Sinoatrial node.

Citalopram is generally considered a safer choice for depressed patients. On the other hand clinical studies conducted by Geoffrey *etal* demonstrated that over dosage of citalopram not only causes bradycardia but also leads to pronounced prolongation of the QT interval<sup>16</sup>.

Amongst all the SSRIs, so far the most well studied is Fluoxetine. It has been observed to influence electrophysiological parameters on animal cardiac tissue samples. It has shown to have an inhibitory action on cardiac sodium and Calcium channels<sup>13,14</sup>. Our study validated the drugs negative chronotropic action on frog heart. The proposed mechanism of action of fluoxetine is suspected to be through inhibition of the cationic channels. Although in comparison with citalopram the amplitude of the depressor effect was relatively subtle.

In the study conducted by Pacher *etal* it was corroborated that fluoxetine has no significant influence on the amplitude of potassium currents. The cardiac effects observed with Fluoxetine were also due to the inhibition of sodium and Calcium channels, as with the case of citalopram<sup>17</sup>. Studies have shown the drug's enhanced ability at inhibiting the L-type of Calcium channels as compared to the other ion channels involved in the generation of an action potential<sup>15</sup>. When compared with citalopram, Fluoxetine proved to be a more potent inhibitor of these channels<sup>18</sup>.

Apart from the action on Calcium channels, fluoxetine was also shown to have an inhibitory action on hERG K<sup>+</sup> channels resulting in a prolongation of the QT interval in HEK cells<sup>19</sup>. Contrary to this, clinical studies

have proven that fluoxetine has a very feeble role in influencing heart rate or repolarization<sup>20</sup>.

Relatively sparse data is available on the cardiac profile of paroxetine. Paroxetine has so far been documented to exert a mild bradycardia<sup>21</sup>. Our study conversely showed that paroxetine caused a mild tachycardia. Pollock *et al* demonstrated that the subtle change in heart rate could be attributed to the weak antimuscarinic action of the drug<sup>22</sup>. In this respect paroxetine may have a similar profile to that of the tricyclic agents that also cause profound tachycardia due to their anticholinergic activity. As we used a single concentration of the drug in our experiment, the dose related adverse effects in the case of over dosage cannot be quantified from our study. The toxic profile of conventionally used TCAs corroborate that over dosage results in sinus tachycardia and marked ECG changes, such as prolongation of the QRS complexes<sup>23</sup>. Such evidences have postulated grounds for us to speculate similar effects with paroxetine.

## CONCLUSION

When comparing the three SSRIs we used in our experimental protocol it may be concluded that, citalopram results in profound bradycardia. This outcome may pose complications in patients with preexisting bradycardia occurring as a result of either metabolic disturbances like hypothyroidism or due to diseases directly affecting the heart's rhythm like sick sinus syndrome and other arrhythmias. Also, the concurrent administration of SSRIs with other drugs producing bradycardia, like the Beta blockers and calcium channel blockers, may precipitate the complication. Thus, the use of citalopram should be rationalized in such cases, and monitoring of cardiac indexes should be undertaken. Over dosage of the drug as mentioned earlier may also result in a deleterious outcome<sup>16</sup>.

Fluoxetine, also resulted in a slight decrease in heart rate. Although the change in this case was about one third to that observed with citalopram. Thus, it may be suitable to assume that fluoxetine would serve as a safer choice in depressed patients with concomitant bradycardia.

Paroxetine shared congruency with the TCAs with respect to the influence on heart rate. Paroxetine brought a negligible increase in heart rate. It may be contemplated that the anticholinergic activity of the drug may give rise to complications in case of drug toxicity. However, the translation of our experiment in to clinical subjects may be quite different from what we have observed.

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

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# Demographic and Clinical Characteristics of 100 Consecutive Patients with Diabetic Foot Presented in Nishtar Hospital Multan

Muhammad Ayub<sup>1</sup>, Muhammad Naveed Shahzad<sup>2</sup> and Muhammad Afzal Sajid<sup>1</sup>

## ABSTRACT

**Objective:** To study the incidence of infected diabetic foot among diabetic admissions on the surgical floor.

**Study Design:** Quasi-experimental study

**Place and Duration of Study:** This study was conducted at the Surgical Unit-IV, Nishtar Hospital Multan from June 2013 to March 2016.

**Materials and methods:** The study on diabetic foot management was carried out involving 100 patients with septic foot complications in diabetics.

**Results:** Out of 100 patients, 59 (59%) were male, 41 (41%), were female, 76 (76%) patients were admitted through emergency, 18 (18%) through outpatient department and only 6 (6%) patients were referred from physicians. Family history of diabetes was found in 45% of the patients in both parents. As regards age, most of the patients i.e. 50 (50%) patients were in age group 61-70 years. In 25 (25%) patients left foot was involved, right foot was involved in 55 (55%) patients while in 20 (20%) patients both feet were involved. As regards management of patients, 15 (15%) patients were taking insulin, 30 (30%) were on OHA, 30 (30%) were controlled by diet and remaining 20% had no treatment. Planter infection and infection on dorsal aspect was seen in 30% patients respectively.

**Conclusion:** No aspect of regimen of therapy for diabetics is more important than the proper care of his feet

**Key Words:** Demography, Clinical Characteristics, Diabetic Foot

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## INTRODUCTION

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia, hyperlipidaemia and hyperaminoacidaemia accompanied by relative or absolute deficiency i.e. it is caused by a decrease either in the secretion or activity of insulin and is associated frequently with specific lesions of microcirculation, neuropathic disorders and a predisposition to atherosclerosis<sup>1,2</sup>.

Management of many medical conditions is relatively easy if patient has only one affliction but in practice many medical illnesses have complications which require surgery and diabetes is one of them. Diabetes is a challenge for general surgery. It offers a serious bar to any kind of operation.

Diabetes is universal with widely varying prevalence rates in different populations and within the same population. Foot problems are common reason for hospital admission among diabetes patients. The presentation of diabetic foot disease may lack the drama of acute surgical and medical conditions but the consequences are often more serious<sup>3</sup>.

One reason for common lack of interest is that foot tends to lie between specialties, not entirely the domain of physician or surgeon. In most of the cases there is late referral from the Physicians. One of the reasons for this large number of foot problems is low IQ and low standards of education of our patients. Diabetics don't take prophylactic care of their feet. Diabetics with or without foot lesions do not undertake regular chiropody, and tend to ignore demonstrations and discussions on foot care. They do not maintain a high standard of foot hygiene<sup>4</sup>.

There is more emphasis on infected diabetic foot lesions. Pathophysiological alterations incriminated in the causation of these infections are disturbed general and local immunity, defective function of leukocytes particularly polymorphs, tissue hypoglycemia, anesthesia making the area susceptible to unnoticed trauma, circulatory insufficiency and delayed wound healing<sup>5</sup>.

Foot salvage is most important as far as management of diabetic foot lesions is concerned. If regular foot care were carried out as routinely as urine monitoring, the morbidity from foot lesions would have been drastically reduced.

In the management there is side by side control of diabetic foot and the overall stress associated with surgical procedure. Total stress is the sum of factors such as length of operation, type of anesthesia used,

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amount of physical trauma and patient's psychological reaction.

The purpose of this study has been to study the incidence of infected diabetic foot among diabetic admissions on the surgical floor. This incidence will highlight that foot problems are one of the common reasons of hospital admissions among the diabetic patients.

## MATERIALS AND METHODS

This is a quasi-experimental study. The study on diabetic foot management was carried out in Nishtar Hospital Multan involving 100 patients with septic foot complications in diabetics over a period of 3 years from June 2008 – June 2011. 76 patients were admitted through emergency, 18 patients through outpatients department and 6 were referred by physicians.

All the cases were prepared for operation under general anesthesia with endotracheal intubation. All the previous treatment of diabetes was stopped and insulin therapy was started. Intravenous line was maintained with Normal Saline or 5% Dextrose Water with 16 units of plain insulin. Insulin therapy was monitored by serial blood sugar or urine sugar studies done one hourly. During this period patients were closely watched for hypoglycemia. Pre-operative antibiotics were started.

## RESULTS

Out of 100 patients, 59 (59%) were male, 41 (41%) were female, 73 (73%) were diabetic. Family history of diabetes was found in 45% of the patients in both parents. As regards age, most of the patients i.e. 50 (50%) patients were in age group 61-70 years. Age range was 34-70 years (Mean age =  $56.68 \pm S.d.8.106$ ). In 25 (25%) patients left foot was involved, right foot was involved in 55 (55%) patients while in 20 (20%) both feet were involved. As regards management of patients, 15 (15%) patients were taking insulin, 30 (30%) were on OHA, 35 (30%) were controlled by diet. Planter infection and infection on dorsal aspect was seen in 30% patients respectively. Penetrating trauma and insect bite were the major causing agents. Bacteriological agents i.e. staphylococcus were present in 66% of the patients. Operative treatment is shown in table 1.

## DISCUSSION

As seen in this study the patients who developed septic foot complications formed about 18.8% of the total diabetic patients admitted in the ward. The rest of the diabetics were admitted with enlarged thyroids, gallstones, enlarged prostates, hernias, lump breasts and road traffic accidents. This %age is comparable with those of Western countries.

In the Western World lesion of foot are responsible more than 1/5 of the hospital admissions of diabetic patients (Pratt 1965).

**Table No.1: Demographic & clinical characteristics of our patients**

Site of involvement		
Site	No. of patients	%age
Left foot	25	25.0
Right foot	55	55.0
Both feet	20	20.0
Management of diabetes		
Management	No. of patients	%age
Insulin	15	15.0
OHA	35	35.0
Diet	30	30.0
No treatment	20	20.0
Foot involvement and function		
Involvement/ function	cases	%age
Whole foot functionless	10	10.0
Planter infection	30	30.0
Infection on dorsal aspect	30	30.0
Both aspects involved	20	20.0
Forefoot infection	10	10.0
Causing agents		
Agents	cases	%age
In growing tonal	10	10.0
Penetrating trauma	30	30.0
Insect bite	30	30.0
Callosities/corns	20	20.0
Neuropathy	10	10.0
Bacteriological agents		
Agents	No. of patients	%age
Staphylococcus	66	66.0
Streptococcus	20	20.0
Clostridia	03	03.0
Pseudomona	01	01.0
E-Coli	02	02.0
Klebsiella	02	02.0
Bacteroides	01	01.0
Proteus	03	03.0
Actinomycosis	02	02.0
Operative treatment		
Treatment	cases	%age
Debridement Alone	10	10.0
Ray Amputation	30	30.0
Mid Tarsal Amputation	30	30.0
Syme's Amputation	20	20.0
Mid Crural Amputation	10	10.0
Klebsiella	02	02.0

According to another study at autopsy 29% of diabetics (543 of 1854) have gangrene or amputation of an extremity (Warren, et al, 1966). In Sweden foot problems account for 25% of all diabetics in patient care (Bolton, 1990). the %age of patients with septic foot in Diabetes may be much higher in our country but as there is no prophylactic measure for foot problems in our country because of low IQ. Of our patients and moreover there is no system to educate those at high

risk to prevent foot lesions, lesser number of people come to hospitals.

There is a sex predilection for the males in cases of foot sepsis due to diabetes mellitus in our study whereas in western countries there is no sex predilection. This is perhaps due to the fact that males in our society work in outdoors and are more prone to penetrating trauma and trauma to neuropathic feet as they work bare footed.

As in western countries the patients who developed septic foot complications tend to be elderly. About 60% of the patients were above the age of 50 years. The higher incidence in elderly is probably due to the fact that overall incidence of non-insulin dependent diabetes mellitus is more and this type of diabetes is seen more in the elderly.

Diabetic neuropathy although frequently accompanied by pain and parasthesias, causes its greatest problem by the opposite effect, the loss of pain sensation. The patient without pain sensation unwittingly allows his foot to endure repeated trauma until trophic changes and frequently secondary infection develops. In the study neuropathic feet were the commonest underlying cause of foot sepsis in diabetes. In US diabetes is estimated to affect 5% of general population and it is the most common cause of neuropathy. Although studies reveal an incidence of neuropathy of up to 60% (Asbury and Brown, 1982), the incidence of clinical neuropathy is generally estimated at between 10 to 20% of those with diabetes. In a recent study of 500 diabetics 39% of patients had significant atherosclerotic disease involving medium and large sized arteries of lower limb (Janka, Standle et al, 1980)

Diabetic foot infections are polymicrobial. In my study culture sensitivity reports show that in 72% cases Staphylococcus Aureus, in 64% of cases pseudomonas, and in 27% of cases streptococcus were the major infecting agents. Besides this E. coli, Klebsiella, Bacteroids, Proteus and Clostridia were isolated from the septic foot. These results can be compared to a study carried out on 42 patients with foot sepsis in diabetes (Fierer et al, 1972).

According to this study Staphylococcus aureus was isolated from 20 cases, streptococcus from 22 cases, Klebsiella from 19 cases, Bacteroides fragilis from 25 cases, anaerobic gram positive cocci in 32 cases and clostridia in 19 cases. This study underscores the importance of anaerobes in these infections. Compared to this in our study gram positive cocci and gram negative bacilli were the main infecting agents.

In the management of diabetic foot infections it is most important that before surgery patient must have a complete physical examination and laboratory evaluation. In this study besides routine investigations every patient had his serial blood and urine sugar studies done. It is vitally important that the patient's diabetes is well controlled pre-operatively. Patients were not allowed to go to the surgery with a very high

blood sugar. A few hours delay may free the patient from acidosis, ketosis and extreme hyperglycemia, thereby making the total surgical procedure including anesthesia management and immediate post-operative period, easier and safer for the patient. Besides any patient to be operated upon for foot sepsis in diabetes, is to discontinue all his previous treatments and to put him on insulin therapy. The goal of blood sugar control and insulin administration should be the avoidance of extreme degrees of hyperglycemia and ketosis, as well as avoidance of hypoglycemia.

In my study the diabetic patients undergoing foot surgery were all given general anesthesia. This allows adequate time for proper debridement. Under no condition the surgery on septic foot be performed under any kind of local blocks, as they may compromise further the blood supply to the tissues. All the operations should be performed by experienced Surgeon.

Another very important aspect of management of diabetic foot is that there should be a proper debridement of foot. All the necrotic tissue should be removed and incision should be made well through the healthy tissue. All the tissue spaces should be opened as they are potential source of infection. Failure to confine a web space infection may lead to disaster and may end up with below knee amputation. Most importantly planter fascia should be incised and the central planter space which lies deep to it should be opened up. Thorough wound toilet should be performed with saline and hydrogen peroxide. All these principles were followed and the end result in most of the cases was excellent. Once all the necrotic tissue and infective foci were removed, leaving behind the healthier tissue, the wound healed nicely. During post-operative management of all these cases the blood sugar levels were very closely monitored in our patients. This is very important because had the diabetes not been adequately controlled the foot wound would never have healed. Importance of this is shown by the fact that in two of our cases adequate control of diabetes could not be achieved early on so they had to be taken to the operating table thrice and one of the patients ultimately ended up with above knee amputation.

Out of 34 cases, in 13 cases amputations at different levels had to be performed i.e. in 38% of cases amputations were performed. A recent European study stated that 22,000 lower limb amputations are now being performed annually in US. Almost two thirds of these are being performed on diabetic patients. About 5/15 of all diabetics have an amputation in some part of life (Robson and Edstrom, 1977).

According to a study risk of loss of limb due to gangrene is increased approximately six to eight folds in diabetics. The average yearly rate of amputation for diabetics is 80 per 10,000 with somewhat higher value in diabetics older than 65 years of age (National

Diabetes Data Group, 1980). Although exact figures for the number of amputations performed for septic feet in diabetes for our country is not known but it bound to be high as health care facilities in our country are scarce. Where amputations had to be carried out, they were carried out through healthy tissue. This will save serial amputations which are the result of amputations carried out through unhealthy tissues.

## CONCLUSION

No aspect of regimen of therapy for diabetics is more important than the proper care of his feet. Prevention of foot lesions is of utmost importance in treating the diabetic patients. Proper prophylaxis is instrumental in preventing foot loss in diabetic patients.

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

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# Pattern of Ear Diseases in Surgical Pathology

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## ABSTRACT

**Objective:** The purpose of this study is, firstly, to find the pattern of ear diseases in the community, as no such pattern study is currently available. Secondly, to impart awareness regarding microscopic appearances of the common ear diseases encountered in this pattern study.

**Study Design:** Observational / descriptive study.

**Place and Duration of Study:** This study was conducted at the Surgical Pathology archives of the Laboratory of Charsada Teaching Hospital affiliated with Jinnah Medical College Peshawar from 2010 to 2015.

**Materials and Methods:** In this study, all the cases of ear diseases from surgical pathology archives of the laboratory of Charsada Teaching Hospital were retrieved. All the slides and the diagnoses for the retrieved cases were reviewed by the histopathologist and the final diagnoses were recorded; the disease pattern was determined, keeping in view the number of cases for each diagnostic category and the patient's age.

**Results:** The review of these cases between 2010 and 2015 showed that most of the biopsy specimens were from external ear while few were from the middle ear. The first five commonest conditions constituted almost two thirds of the total number of cases. The congenital anomalies and juvenile xanthogranulomas were most common in the first decade of life. Benign and malignant tumors were uncommon and seen mostly after the third decade of life.

**Conclusions:** Congenital anomalies and inflammation associated diseases are common in the first three decades of life, whereas benign and malignant neoplasms are more common after the third decade of life.

**Key Words:** Accessory tragus, cholesteatoma, keratosis obturans, angiolymphoid hyperplasia with eosinophilia, ear diseases.

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## INTRODUCTION

Ear diseases are quite common in clinical practice; however, ear biopsies are not frequently encountered in surgical pathology practice. External ear and to some extent middle ear are accessible to biopsy procedure. External and middle ear are composed of bone and cartilage covered over by muscles, soft tissue and skin with adnexa. Therefore, ear is prone to all the diseases that can affect these component structures individually. Usually, masses or non-resolving inflammatory lesions will be biopsied to ascertain their nature. The purpose of this study is, firstly, to find the pattern of ear diseases in the community, as no such pattern study is currently available. Secondly, to impart awareness regarding microscopic appearances of the ear diseases encountered in this pattern study.

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## MATERIALS AND METHODS

In this laboratory based retrospective study, all the cases of ear diseases between the year 2010 and 2015 from surgical pathology archives of Charsadda Teaching Hospital affiliated with Jinnah Medical College Peshawar were retrieved. All the ear biopsy cases were considered irrespective of patient age, gender, or ethnic origin. As a first step all the slides and the diagnoses for the retrieved cases were reviewed and the final diagnoses were noted down; the second step involved recording the number of cases for each diagnostic category; and as a final step, all the diagnoses were tabulated in order of most common to least common, and the disease prevalence tabulated according to the patient's age.

## RESULTS

The review of cases of ear disease between 2010 and 2015 showed that most of the biopsy specimens were from external ear while few were from the middle ear, Table 1. Congenital anomalies and juvenile xanthogranulomas were most common in the first decade of life. Inflammatory aural polyp was common in the second decade. Cholesteatoma straddled the second and third decades; while keratosis obturans was straddling the third and fifth decades. Angiolymphoid hyperplasia with eosinophilia was common in the third decade.

Benign adnexal tumors were common in the fourth and fifth decades while malignant tumor (squamous cell carcinoma) was seen in the ninth decade.

**Table No.1: %age of ENT diseases.**

Sr. No.	Diseases	Number of cases (n)	%age
1.	Congenital anomalies	23	22.5
2.	Epidermoid cyst	20	19.6
3.	Cholesteatoma	15	14.7
4.	Keratosis obturans	10	9.8
5.	Inflammatory aural polyp	9	8.8
6.	Juvenile Xanthogranuloma	7	6.9
7.	Keloid	4	3.9
8.	Angilymphoid hyperplasia with eosinophilia	3	2.9
9.	Seborrheic keratosis	3	2.9
10.	Chondrodermatitis nodularis	2	1.9
11.	Nodular fasciitis	2	1.9
12.	Fungal infection	1	0.98
13.	Trichoepithelioma	1	0.98
14.	Syringoma	1	0.98
15.	Squamous cell carcinoma	1	0.98
	Total Cases	102	

## DISCUSSION

Surgical specimens from the external and middle ear are fairly uncommon in hospital based surgical pathology practice. Main indications for biopsy from this site being: mass lesion, an eroding lesion, or non-resolving inflammation.

In our study, most of the cases belonged to the congenital anomaly category, encompassing mainly accessory tragi and pre-auricular sinuses (n=23, 22.5%), Table 1. These were most common in the first decade of life Table 2, as the alarmed parents brought their children (with obvious abnormalities near the ear) for early consultation. Microscopically accessory tragi were composed of fibro-fat tissue with or without central cartilage and covered by skin with adnexal structures. The preauricular sinuses were composed of stratified squamous epithelium-lined sinus tract surrounded by lymphocytes and plasma cells. Both are anomalous derivatives of first and second branchial arches appearing as skin colored nodules (sessile or pedunculated) or pits (preauricular sinuses) in front of the ears. Though accessory tragi are benign, they may be associated with certain syndromes like Delleman's syndrome, Goldenhar's syndrome, Haberland's syndrome, and Townes-Brock's syndrome<sup>1</sup>. Therefore, it is advisable to assess the neonate/infant with branchial arch anomalies for any associated renal, ocular, vertebral, and brain anomalies.

The second most common ear biopsy diagnosis in the study was epidermoid cysts (n= 20, 19.6%), Table 1. The commonly affected sites were the pinna and outer

external auditory canal. It presented as a nodule at the site of trauma or ear piercing. They were common in third and fourth decades of life Table 2. They were characterized by a cyst wall lined by keratinized stratified squamous epithelium replete with granular cell layer, the cyst lumen contained keratin flakes. Epidermoid cysts though totally benign, may be part of Gardner's syndrome especially if multiple cysts are found all over the body<sup>2,3,4,5</sup>. Therefore when multiple epidermoid cysts are encountered all over the body, colonoscopy to detect the presence of colonic polyps is mandatory.

Cholesteatoma (n= 15, 14.7%), the third common biopsy diagnosis, mostly occurred in the middle ear (11 cases) with only two cases in the mastoid and two cases in the external auditory canal. Chronic ear discharge and conductive deafness were the main complaints. Microscopically it was characterized by multiple keratin flakes mostly admixed with acute inflammatory cells, with thin to normal thickness keratinizing stratified squamous epithelium with variable amount of acute and chronic inflammatory cells in the sub-epithelial stroma. It was common in the second and third decades of life Table 2, though literature states it to be common in the first and second decades. This depicts difference in the age groups affected by preceding otitis media in different communities. Its importance lies in the fact that in spite of being benign, it is erosive and an expansive lesion that may result in bone necrosis, cavitation and remodeling; therefore, it merits regular follow-up<sup>2,4,6</sup>.

Keratosis obturans (n= 10, 9.8%), the fourth common biopsy diagnosis was common in the third and fifth decades of life Table 2. It mostly presented with conductive deafness Table 1. It was composed of compact keratin flakes; the lining epithelium of affected external auditory canal was variably acanthotic showing hyperkeratosis and parakeratosis. Contrary to cholesteatoma, this is an innocuous, non-eroding and non-cavitating lesion. It is said to result from failure of the self-cleaning mechanism of the external auditory canal due to some unknown cause<sup>4</sup>. Evacuation of the keratinous ball is all that is required for the management.

Inflammatory aural polyp (n=9, 8.8%) was the fifth common biopsy diagnosis, mostly affecting the middle ear and presented as a soft, easy to bleed, polypoid granulation tissue associated with middle ear infections; therefore, seen commonly in the second decade Table 2. Microscopically, it was usually partially covered by ulcerated cuboidal to stratified squamous epithelium with underlying lobular capillary proliferation, the stroma being heavily infiltrated by acute and chronic inflammatory cells<sup>4</sup>; the ulcerated portion was covered by acute inflammatory exudate with few superficial bacterial colonies.

**Table No.2: ENT diseases – decade wise**

Diseases	Decades of Life									
	1 <sup>st</sup>	2 <sup>nd</sup>	3 <sup>rd</sup>	4 <sup>th</sup>	5 <sup>th</sup>	6 <sup>th</sup>	7 <sup>th</sup>	8 <sup>th</sup>	9 <sup>th</sup>	Total
Congenital anomalies	14	4	3	2	-	-	-	-	-	23
Epidermoid cyst	2	3	4	7	3	-	1	-	-	20
Cholesteatoma	1	6	4	2	1	1	-	-	-	15
Keratosis obturans	-	1	3	1	5	-	-	-	-	10
Inflammatory aural polyp	1	4	2	-	1	-	-	1	-	9
Juvenile Xanthogranuloma	5	2	-	-	-	-	-	-	-	7
Keloid	-	1	3	-	-	-	-	-	-	4
Angiolympoid hyperplasia with eosinophilia	-	-	2	-	1	-	-	-	-	3
Seborrheic keratosis	-	-	-	-	-	2	1	-	-	3
Chondrodermatitis nodularis	-	-	-	-	-	-	-	2	-	2
Nodular fasciitis	-	-	1	1	-	-	-	-	-	2
Fungal infection	-	-	-	-	-	1	-	-	-	1
Trichoepithelioma	-	-	-	-	1	-	-	-	-	1
Syringoma	-	-	-	1	-	-	-	-	-	1
Squamous cell carcinoma	-	-	-	-	-	-	-	-	1	1

Juvenile xanthogranuloma (n= 7, 6.9 %) was the sixth common biopsy diagnosis received. It was found to be common in the first two decades Table 2, presenting as a pink- to red- to tan nodules on the skin. Microscopically, it was composed of circumscribed infiltration by foamy macrophages, multinucleate Touton type of giant cells, lymphocytes, and scattered few eosinophils. Two thirds of these cases are reported to occur in the first year of life, mostly presenting as a solitary lesion<sup>7</sup>.

Keloid (n= 4, 3.9%) was the seventh common biopsy diagnosis in this study, more common in the third decade, occurring at the ear lobule and pinna, mostly secondary to trauma or ear piercing. The dermis showed many irregularly arranged thick hyalinized collagen bundles in hypocellular matrix without adnexal structures. The epidermis was mostly atrophic. Spontaneous occurrence of keloids has been reported in diseases like Ehlers-Danlos syndrome type IV, Rubenstein-Taybi and Gouin's syndrome, and scleroderma<sup>4</sup>.

The eighth common biopsy diagnosis was shared by angiolymphoid hyperplasia with eosinophilia and seborrheic keratosis, each represented by 3 cases, Table 1. Angiolymphoid hyperplasia with eosinophilia (n= 3, 2.9%) Table 1, also known as epithelioid hemangioma, was found to affect the skin of pinna, immediate periauricular area, and outer part of external auditory canal. It presented clinically as pruritic cutaneous nodules in third decade of life Table 2. Microscopically, it showed dermal lymphoid hyperplasia marked by lymphoid aggregates, lymphoid follicles, and interstitial lymphoplasmacytic infiltrate admixed with macrophages and eosinophils. There were many scattered thick-walled blood vessels lined by prominent epithelioid endothelial cells, containing enlarged hyperchromatic nuclei. The epidermis was mostly unremarkable. This disease needs to be differentiated from Kimura's disease which is characterized by subcutaneous location accompanied by regional

lymphadenopathy, blood eosinophilia, and increased IgE levels<sup>2,3,4,5</sup>. Seborrheic keratosis (n=3, 2.9%) was common in the sixth decade Table 2. It presented as greasy exophytic lesions located on the pinna. Microscopically, there was regular epidermal acanthosis due to proliferation of basaloid cells with many true and pseudohorn cysts. It should not be confused with basal cell carcinoma, which is characterized by irregular proliferation of basaloid cells extending into the dermis with surrounding clefts and degenerative dermal changes. Those lesion, which suddenly increases in size or number, may be associated with an internal malignancy (Leser-Trelat sign)<sup>7</sup>.

The ninth common biopsy diagnoses were chondrodermatitis nodularis helicis and nodular fasciitis, each represented by two cases, Table 1. Chondrodermatitis nodularis helicis (n= 2, 1.9%) was seen in the eighth decade Table 2, presenting as an ulcerated nodule over the helix of pinna. Microscopically, it showed central ulceration covered by inflamed granulation tissue extending down to involve the cartilage. The surrounding intact epidermis showed acanthosis, hyperkeratosis, and parakeratosis. There were focal upper dermal changes of solar elastosis. It is a disease of unknown etiology; the suggested etiologies include ischemia, pressure, trauma, actinic, cold, or immune mediated injury<sup>4,7</sup>. Nodular fasciitis (n= 2, 1.9%) was seen affecting the pinna and outer part of the auditory canal in the third and fourth decades Table 2, it presented as an enlarging mass of two to three weeks duration. Microscopically, it was occupying the dermis and subcutaneous tissue, composed of loosely arranged spindle shaped cells in variable myxoid stroma with undulating collagen bundles with some infiltration by mature lymphocytes.

The tenth position was shared by four biopsy diagnoses, namely fungal infections, trichoepithelioma, syringoma and squamous cell carcinoma; these diagnostic categories were represented by one case each. Fungal

infection (n=1, 0.98%) presented in sixth decade in an old diabetic patient Table 2, characterized by poor disease control accompanied by intractable headache and ear discharge. The middle ear biopsy showed necrotic bone fragments with scattered clusters of broad ribbon-like hyphae with parallel but undulating walls and irregular branching. Also, there was acute and chronic inflammatory infiltrate with scattered multinucleate giant cells with some ingested hyphae. In ambiguous situations staining the sections with PAS (Periodic Acid Schiff) and GMS (Grocott's Methenamine Silver) stains will highlight the presence of fungi<sup>8</sup>. Trichoepithelioma (n=1, 0.98%) presented as a solitary, skin colored, cutaneous nodule over the ear lobule in the fifth decade Table 2. Microscopically, there was a circumscribed dermal proliferation of basaloid cells with peripheral cellular palisading and small petal-like protrusions, surrounded by some fibromyxoidstroma, without formation of hair. Multiple trichoepitheliomas may occur as an autosomal dominant familial condition or be part of Brooke-Spiegler syndrome when together with multiple cylindromas<sup>7</sup>. Syringoma (n= 1, 0.98%) was seen as a small pale skin nodule at the tragus, in the fourth decade, Table 2. Microscopically, it showed upper dermal proliferation of tubular structures of different sizes, some with comma-like solid cellular extensions. The tubular structures were lined by double layer of cuboidal cells, with some luminal secretions. It should be remembered that multiple syringomas may be seen in Costello syndrome and Down's syndrome<sup>4</sup>. Squamous cell carcinoma (n=1, 0.98%) presented as an ulcerated 1 cm nodule over the upper part of right helix in the ninth decade Table 2. Microscopically, it showed pleomorphic malignant squamous cells invading the upper dermis with formation of keratin pearls, but without involvement of the perichondrium, cartilage or the regional lymph nodes. The adjacent dermis showed solar elastosis and mild lymphoplasmocytic infiltration. The chance of involvement of the regional lymph nodes has been found to be directly proportional to the primary tumor size; moreover the disease prognosis depends on the tumor stage<sup>4</sup>. There is no available prior national or international study for pattern of ear diseases in surgical pathology. However, some clinical studies for ear diseases are available. In a ten year hospital-based retrospective study for geriatric patients, conducted at the ENT Department of University College Hospital, Ibadan, Nigeria<sup>9</sup>, it was found that impacted cerumen, hearing loss, and chronic suppurative otitis media were the three most common diseases of the ear in elderly. In another prospective cross-sectional study among 2000 children (aged between 5 and 13 years), it was found that impacted wax followed by chronic suppurative otitis media and otitis media with effusion were the most common ear diseases in rural school children of Nepal<sup>10</sup>. A similar study, conducted in Kalyanpuri,

Delhi, a total of 1398 school children (aged between 5 and 14 years) were studied for ear diseases, impacted wax was the commonest problem (23.4%) followed by ear infections (10.0%) and hearing impairment (7.2%)<sup>11</sup>.

## CONCLUSION

The congenital anomalies along with inflammation associated diseases are most common in the first three decades of life; being responsible for two thirds of all the surgical pathology biopsies of the ear, whereas, neoplasms are more common after the third decade of life.

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

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# A Clinical Experience of Patients with Heat Stroke at Karachi During a Devastating Heat Wave in 2015

Muhammad Yahya, Krishan Lal, M. Khalid Hasan Khan and Urwah Inam

## ABSTRACT

**Objectives:** To review the clinical presentations, management and outcomes of heat stroke patients presented to Hamdard University Hospital, Karachi in summer 2015.

**Study Design:** Observational / descriptive study.

**Place and Duration of Study:** This study was conducted at the Hamdard University Hospital (Taj Medical Complex), Karachi from 15<sup>th</sup> to 30<sup>th</sup> June 2015.

**Methods:** A retrospective analysis of database of 51 patients presented with high grade fever ( $>104^{\circ}\text{F}$ ) and altered sensorium was performed. All data were transferred to proforma which included patient's demographic features (name, age and sex), clinical and laboratory parameters, treatment given, duration of hospital stay, outcomes (death or alive) and reasons of mortality. The SPSS version 19 was used for statistical analyses.

**Results:** Majority of the patients (63%) were between 61-80 years of age group with mean $\pm$ SD age was  $69.24\pm 11.28$  years. Males were affected more than females (60.7% vs. 39.3% respectively). Out of 51, 41 (80.4%) had co-morbidities and were on regular medications. The mean $\pm$ SD Glasgow Coma Scale at the time of presentation was  $10.29\pm 4.33$ . The major laboratory derangements were hyponatremia (68.6%), elevated blood urea (52.9%), serum creatinine (41.2%) and alanine transferase (15.6%). Standard treatment strategies were provided to all patients. Out of 51, 19 (37.3%) patients were expired as a result of multi-organ failure, shock, arrhythmias and rhabdomyolysis.

**Conclusion:** Heat stroke is common in older males especially those who had co-morbidities. It carries a significant mortality due to multiorgan failure and shock.

**Key Words:** Heat stroke, Heat wave, Mortality.

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## INTRODUCTION

Heat-related illnesses are group of disorder characterized by heat exhaustion and heat stroke, and if untreated, may lead to mortality as a consequence of multiorgan dysfunction syndrome. It has a substantial effect on million of peoples worldwide. According to World Health Organization (WHO) statistical report, extreme temperature events contributed 23.8% of all disasters in 2012.<sup>2</sup> Hence, it is one of the foremost environmental hazards that requires well-timed reporting of its occurrence, management and complications. The classical heat stroke is manifested as an elevated core body temperature ( $>40^{\circ}\text{C}$ ) associated with central nervous system (CNS)

abnormalities like delirium, coma, seizures due to exposure of heat waves.<sup>3</sup> Elderly population with pre-existing co-morbidities, children, outdoor labors, athletes and those who are on medications that impair temperature homeostasis have been identified as most vulnerable cohorts in literature.<sup>4-6</sup> In urban areas, both heat island effect and higher population density have been considered as contributing factors of heat events.<sup>7,8</sup> In addition, rising trends in global climate change has been noticed and are anticipated to progress in future.<sup>9</sup> According to technical report of Pakistan Meteorological Department, the frequency of heat waves has been continuously increasing in Pakistan for past five decades.<sup>10</sup>

In June 2015, Karachi, a metropolitan city of Pakistan, experienced a heat wave for period of 5-days from 19<sup>th</sup> to 23<sup>rd</sup> June with the reported highest temperature  $44.8^{\circ}\text{C}$  on 20<sup>th</sup> June.<sup>13</sup> Although, more than 1000 deaths have been noticed during this time period,<sup>14</sup> the exact mortality is seem to be under-reported by reason of lesser contribution of various centers publishing their statistics on heat stroke patient's management and outcomes. The purpose of this study was to review the clinical presentations, management and outcomes of heat stroke patients presented to Hamdard University Hospital, Karachi in summer 2015.

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## MATERIALS AND METHODS

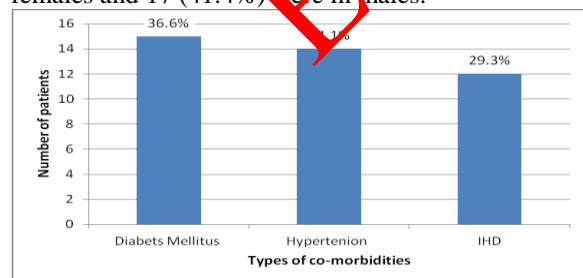
A retrospective review of database of all patients having body temperature  $>104^{\circ}\text{F}$  with altered sensorium presented at Hamdard University Hospital (Taj Medical Complex), Karachi from 15<sup>th</sup> to 30<sup>th</sup> June 2015 after heat wave exposure was accomplished. Clinical information was retrieved and those who had other causes of high grade fever like malaria, dengue, typhoid, meningitis, urinary tract infection and pneumonia were excluded from the study.

All clinical records were updated into proforma designed for the study. It included patient's demography (name, age, and sex), co-morbidities, drug history, Glasgow Coma Scale (GCS), pulse rate (in beat/min) and temperature (in  $^{\circ}\text{F}$ ), laboratory parameters [Complete blood count (CBC), blood urea and serum creatinine (in mg/dL), serum electrolytes (in mEq/L), and liver function test (LFTs) and creatinine phosphokinase (CPK)], electrocardiogram (ECG), chest X-ray and CT scan brain findings, outcomes (alive or death), reasons of death, management and duration of stay (in days).

Statistical analyses were conducted by SPP version 19. Qualitative data were represented by frequencies and percentages. Mean and standard deviation was employed for quantitative data.

## RESULTS

A total of 51 patients having high grade fever ( $>104^{\circ}\text{F}$ ) with altered level of consciousness were presented during study period. Mean $\pm$ SD fever was  $105.24\pm0.86^{\circ}\text{F}$ . The age of patients ranged from 40 to 87 years with mean $\pm$ SD age was  $69.24\pm11.23$  years. Among these, 22% patients were in 40-50 years, 63% in 61-80 years, and 15% were in age group above 80 years. Of these 51 patients, 31 (60.7%) were males and 20 (39.3%) were females. The co-morbidities were noticed in 41 (80.4%) patients, 24 (58.6%) were in females and 17 (41.4%) were in males.



(IHD=Ischemic heart disease)

**Figure No.1: Types of co-morbidities**

Figure 1 shows the types of co-morbidities encountered in this study. All of these patients were on regular medications. These included oral hypoglycemics (29.5%), insulin (7.3%), calcium channel blockers (17%), beta blockers (9.7%), diuretics (4.9%), anti-

platelets (7.3%), anti-hyperlipidemics (7.3%) and proton pump inhibitors (17%).

At the time of arrival, pulse was impalpable in 11 (21.6%) patients. 29 (56.8%) patients had a pulse rate between 120-130 beats/min and 11 (21.6%) had a rate between 131-140 beats/min. The mean $\pm$ SD pulse rate was  $128.80\pm7.55$  beats/min. The GCS at the time of presentation were ranged from 6 to 14 with mean $\pm$ SD GCS was  $10.29\pm4.33$ . Table 1 shows the laboratory parameters of all patients. The hyponatremia (serum sodium  $<135$  mEq/L), and elevated blood urea ( $>40$  mg/dL), serum creatinine ( $>1.4$  mg/dL) and alanine transferase ( $>36$  U/L) were observed in 35 (68.6%), 27 (52.9%), 21 (41.2%), and 8 (15.6%) patients respectively. ECG was performed in 28 (54.9%) patients. Out of these 28, ventricular tachycardia was demonstrated in 08 (28.6%) patients. Chest X-rays was done in 44 (86.2%) patients. Of these 44, bronchitic changes due to age or smoking was noticed in 16 (36.4%) and cardiomegaly was observed in 04 (9.1%) patients. CT scan was advised on the basis of clinical parameters. In this study, 12 (23.5%) patients were subjected to CT scan brain; amongst them, cerebral edema was encountered in 04 (33.3%) patients.

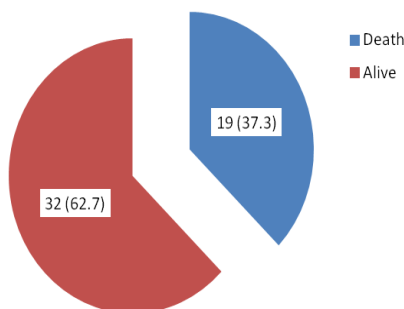
**Table No. 1: Laboratory parameters**

Laboratory parameters	Mean	SD
Hemoglobin (gm/dL)	11.84	1.59
WBC ( $\text{mm}^3$ )	9357.14	4062.22
Platelets (per HPF)	216448.98	86101.21
Urea (mg/dL)	57.69	33.22
Creatinine (mg/dL)	2.07	1.21
Sodium (mEq/L)	125.69	12.96
Potassium (mEq/L)	3.32	0.54
Chloride (mEq/L)	92.67	9.41
Bicarbonate (mEq/L)	21.98	2.66
Total bilirubin (mg/dL)	1.19	0.77
Alanine transferase (U/L)	78.98	142.82
Alkaline phosphatase (U/L)	93.90	37.71
Creatinine phosphokinase (U/L)	897.56	913.41

SD=Standard deviation

Standard treatment of heat stroke was employed in all patients. These included cooling of patient by applying ice, maintenance of adequate hydration by intravenous fluids, cardiovascular monitoring, and administration of sedatives and analgesics. In addition to these, treatment of complications due to heat stroke was also started. Cardioversion and anti-arrhythmic medications were instituted in patients who developed ventricular tachycardia. The intravenous mannitol was given to two (3.9%) male patients who developed rhabdomyolysis. Later these patients required hemodialysis. Ventilatory support was started in 03 (5.9%) patients who had GCS less than 08.

The duration of stay ranged from 1 to 13 days with mean+SD stay was 6.61+2.87 days. The mortality was noticed in 19 (37.3%) patients in this study (Figure 2). Of these 19, 09 (47.4%) were females and 10 (52.6%) were males. The reasons of death were multiorgan failure, shock, arrhythmias and rhabdomyolysis (Table 2).



Data are shown in numbers followed by percentages in figure  
**Figure No.2: Outcomes**

**Table No.2: Reasons of mortality**

Reasons of mortality	Male n=10	Female n=09
Multi-organ failure	03 (30)	02 (22.2)
Shock	03 (30)	03 (33.3)
Cardiac arrhythmias	01 (10)	00 (0)
Rhabdomyolysis	02 (20)	00 (0)
Shock and cardiac arrhythmias	01 (10)	04 (44.5)

Data are shown in numbers followed by percentages in parentheses

## DISCUSSION

Heat stroke is the devastating public health problem. It commonly involves extreme of ages and especially those who have previous co-morbidities.<sup>4-6</sup> In this study, heat stroke afflicted 63% of patients between 61 to 80 years of age group with average age of 69 years. The males were affected more than females. In a large retrospective study, Pivrot et al observed older male population >65 years of age as an independent predictor of heat stroke.<sup>15</sup> Similarly, Kalaiselvan et al also encountered older age males in their case series who were affected by heat-related illnesses.<sup>16</sup> Most of them had diabetes mellitus and hypertension as co-morbidities.<sup>16</sup> In this study, large proportion of patients also had diabetes mellitus and hypertension.

In literature, associations of certain drugs with heat stroke have been documented.<sup>5</sup> It has been suggested that certain drugs like vasoconstrictors, calcium channel blockers and beta blocker are responsible for alteration in thermoregulatory mechanism of the body resulting in increase susceptibility to heat stroke.<sup>17</sup> In this study, significant proportion of patients (26.7%) were already taking calcium channel blockers and beta blockers.

In heat stroke, abnormalities are frequently noticed in serum electrolytes, blood urea, serum creatinine, coagulation profiles, LFTs and creatinine

phosphokinase. In this study, hyponatremia, and elevated blood urea and creatinine were encountered in 68.6%, 52.9% and 41.2% patients respectively. Kalaiselvan et al in their case series found hyponatremia in 73% and raised serum creatinine in 57% patients, which is nearly comparable to this study.<sup>16</sup> The derangements in liver enzymes in heat stroke were first reported by Kew et al in 1970.<sup>18</sup> Arguad et al reported 40% elevation of alanine transferase levels in their case study.<sup>19</sup> In contrast to results of Arguad et al, 15.6% patients had elevated alanine transferase in this study.

The role of hyperthermia in causation of cerebral edema has been argued in literature. Sharma mentioned that the alteration in blood brain barrier resulting in vasogenic edema is the main etiologic factor of heat-related illness.<sup>20</sup> In addition, edema secondary to hyponatremia and direct effect of elevated temperature on neurons of basal ganglia, hypothalamus and cerebellum have been stated in literature as well.<sup>16</sup> Although, variations in neurological symptoms were noticed in this study, cerebral edema was noticed in four patients on CT scan brain.

Early recovery of hyperthermia, fluid and electrolyte management, cardiovascular monitoring, sedation and analgesia, and prompt recognition and treatment of complications are the standard care of heat stroke patients.<sup>17</sup> In this study, all patients were treated on the same line. Rhabdomyolysis was treated initially with intravenous mannitol administration and adequate hydration, and later by hemodialysis. Trujillo and Fragachan also adopted similar management strategies in their patient.<sup>21</sup>

There are wide ranges of mortality reported in literature. Misset et al reported 62.6% in-hospital mortality in France.<sup>22</sup> The 43.1% estimated mortality rate was documented in 2014 Ahmedabad heat wave event by Azhar et al.<sup>23</sup> In this study, 37.3% deaths were noticed which is comparable to the case study by Kalaiselvan et al.<sup>16</sup> A number of complications have been attributable to mortality after heat stroke viz. renal failure, hemodynamic shock, arrhythmias, rhabdomyolysis, and multi-organ failure.<sup>17,24</sup> In this study, mortality was related to shock and multiorgan failure.

The morbidity and mortality related to heat stroke can be preventable by appropriate diagnosis and institution of prompt treatment. The diagnosis is based on identification of precipitating factors with presence of hyperthermia and CNS dysfunction.<sup>11</sup> Early reversal of hyperthermia by cooling, cardiovascular monitoring, and sedation and analgesia are the essential treatment, which in turn, prevent multiorgan failure syndrome.<sup>11</sup> It has been suggested that with appropriate treatment, survival can approach 100%.<sup>12</sup>

## CONCLUSION

Heat stroke is the major disaster which involves mainly older males with co-morbidities. It is associated with

significant derangements in laboratory parameters and carries significant mortality as a consequence of multi-organ failure. To prevent such disasters in future and to establish a uniform strategy we need further and more extensive studies.

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

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# Vitamin Thiamine and Glucose Homeostasis in Alloxan Induced Diabetes Mellitus

Abdul Hafeez Baloch<sup>1</sup>, Iqbal Ahmed Memon<sup>2</sup> and Kashif Rasheed Shaikh<sup>3</sup>

## ABSTRACT

**Objective:** valuating the vitamin B<sub>1</sub> (thiamine) on glucose homeostasis and Glycosylated hemoglobin A1 (HbA1c) in Alloxan induced diabetic rat model.

**Study Design:** Experimental study

**Place and Duration of Study:** This study was conducted at the Animal House, Isra University Hyderabad from September 2014 to March 2015.

**Materials and Methods:** 60 adult albino rats were divided into four groups; Group 1. Controls, Group 2. Rats receiving thiamine added diet, Group 3. Diabetics rats on normal diet and Group 4. Diabetic rats receiving thiamine added diet. Alloxan (120 mg/kg) was introduced intraperitoneally to induce diabetes. Vitamin B<sub>1</sub> was given orally at 1.6 g/kg body weight for 12 weeks. Venous blood was taken from tail vein by small bore cannula at the baseline and after 12<sup>th</sup> week. Blood glucose and HbA1c were detected at baseline and after 12<sup>th</sup> week. Data was saved in proforma and analyzed on SPSS 22.0 using paired student t-test at 95% confidence interval.

**Results:** Blood glucose and HbA1c levels were found statistically significant in groups 1 vs. 3 (p=0.0001), 1 vs. 4 (p=0.0001), 2 vs. 3 (p=0.0001), 2 vs. 4, (p=0.001) and 3 vs. 4 (p=0.024) at the end of experiment period. Significant improvement in blood glucose and HbA1c was noted in the vitamin thiamine treated rats.

**Conclusion:** Vitamin thiamine improved the blood glucose homeostasis and reduced Glycosylated Hemoglobin A1 effectively in experimental rats. It is recommended to supplement diabetic subjects with vitamin thiamine.

**Key Words:** Vitamin thiamine, Glucose homeostasis, HbA1c

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## INTRODUCTION

Vitamin thiamine is also known as the vitamin B<sub>1</sub>. Thiamine functions as a coenzyme in the glucose metabolism and plays pivotal role in glucose homeostasis. Thiamine pyrophosphate co-enzyme catalyzes several steps of glucose and intermediary metabolism. Thiamine is essential for the normal glucose metabolism and homeostasis as it is necessary for the biochemical reactions of glycolysis and Krebs cycle. Diabetes mellitus (DM) is characterized by abnormal glucose homeostasis. Thiamine deficiency causes abnormality of glucose metabolism in DM subjects.<sup>11</sup> Vitamin thiamine deficiency disturbs the glucose homeostasis resulting in hyperglycemia and accelerated microvascular and macrovascular complications.<sup>11</sup>

DM is increasing these days as estimated by the International Diabetes Federation (IDF). IDF estimates show a rise of diabetics of 439 million by the year 2030.<sup>1</sup> Currently, Pakistan is suffering diabetes epidemic and ranks 6<sup>th</sup> position as reported.<sup>2</sup> Previous studies from Pakistan had reported 15% population of country is suffering from DM, and many millions are undiagnosed.<sup>3,4</sup> Crude estimates of Pakistan National Diabetes Survey (PNDS) reported that for each diagnosed case of DM; there are 3 cases of pre-diabetes (impaired glucose tolerance) and 2 cases of undiagnosed DM.<sup>5,6</sup>

Chronic hyperglycemia is the hallmark of DM which damages the vital organs like eyes, kidneys, nerves, blood arteries.<sup>7,8</sup> Thiamine deficiency is linked with damage of these organs in diabetics as reported previously.<sup>9,10,11</sup>

Chronic hyperglycemia, in the presence of thiamine deficiency, activates protein kinase C, accelerated hexosamine synthesis, and formation of advanced glycation end products (AGEs). AGEs are involved in the pathogenesis of micro- and macrovascular complications in diabetics.<sup>11</sup> AGEs synthesis is increased through triose-phosphate intermediates of glycolysis in the presence of thiamine deficiency.<sup>12,13</sup> High doses of thiamine suppresses the AGEs pathways through improved glucose homeostasis, thus reducing the risk of diabetic complications.<sup>9</sup>

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The present study aimed to evaluate the effect of high doses of thiamine on glucose homeostasis and Glycosylated HbA1c in Alloxan induced albino rat model.

## MATERIALS AND METHODS

The present experimental study was carried out at the Animal House, Isra University Hyderabad from September 2014 to March 2015. A sample of 60 male albino rats was selected according to well delineated criteria of inclusion and exclusion. A male albino rat of 200-250g body weight was the inclusion criteria. Female rats, sick rats and rats not feeding were the exclusion criteria. Rats were kept in standard environment of room temperature with normal humidity (55-60%). Normal chow diet and water was freely available. Rats were exposed to 12/12 hour dark-light cycle. Intraperitoneal injection (i.p.) of Alloxan (120mg/kg body weight) was administered to induce diabetes mellitus.<sup>15,16</sup>

Sixty male albino rats were divided into four groups by random selection, containing 15 rats in each group.

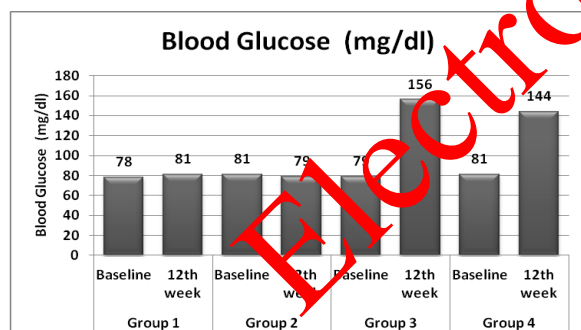
Group 1 Controls (n=15), Group 2 Rats receiving thiamine added diet (n=15), Group 3 Diabetics rats on normal diet (n=15) and Group 4 Diabetic rats (n=15) receiving thiamine added diet. Vitamin B1 was given orally at 1.6 g/kg body<sup>14</sup> weight for 12 weeks. Venous blood was taken from tail vein by small bore cannula at the baseline and after 12<sup>th</sup> week. Blood glucose and HbA1c were detected at baseline and after 12<sup>th</sup> week. Normal blood glucose for rats was taken at 52-105mg/dl. HbA1c range for rats was taken normal as 3-8.8%.<sup>15</sup> Data was saved in proforma and analyzed on SPSS 22.0 using paired student t-test at 95% confidence interval ( $p \leq 0.05$ ).

## RESULTS

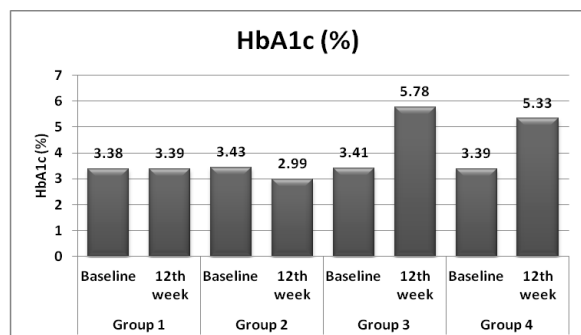
Blood glucose and HbA1c levels were found statistically significant in groups 1 vs. 3 ( $p=0.0001$ ), 1 vs. 4 ( $p=0.0001$ ), 2 vs. 3 ( $p=0.0001$ ), 2 vs. 4, ( $p=0.001$ ) and 3 vs. 4 ( $p=0.024$ ) at the end of experiment period. Significant improvement in blood glucose and HbA1c was noted in the thiamine treated rats. The findings are summarized in table 1 and graphs 1 and 2.

**Table No. I: Blood glucose level and Glycosylated hemoglobin A (HbA1c) in experimental animals (n=60)**

	Group 1 Control group (Normal diet)		Group 2 Control group (Normal diet+ Vit.B <sub>1</sub> )		Group 3 Diabetic group (Normal diet)		Group 4 Diabetic group (Normal diet+ Vit.B <sub>1</sub> )	
	Baseline	12 <sup>th</sup> week	Baseline	12 <sup>th</sup> week	Baseline	12 <sup>th</sup> week	Baseline	12 <sup>th</sup> week
Blood Glucose (mg/dl)	78±4.34	81±3.3	81±0.5	79±4.4	79±1.5	156±17.6	81±3.5	144±12.4
HbA1c (%)	3.38±0.21	3.39±0.2	3.43±0.21	2.99±0.11	3.41±0.4	5.78±0.99	3.39±0.2	5.33±0.69



**Graph No.1: Bar graph showing blood glucose levels in rat groups**



**Graph No.2: Bar graph showing Glycosylated HbA1 in rat groups**

## DISCUSSION

The present study reports on the effect of high dose thiamine intake on glucose homeostasis and HbA1c in Alloxan induced diabetic albino rat model. A search of literature of showed a few studies have been conducted previously, although the topic is of clinical importance as the burden of DM is increasing in Pakistan.<sup>9,15</sup> Previous studies had reported vitamin thiamine deficiency is prevalent in the diabetic subjects.<sup>9,10,15-17</sup> Vitamin thiamine is necessary for the glucose metabolism. The present study reports high dose of vitamin thiamine improved glucose homeostasis and HbA1c in Alloxan induced diabetes model of albino rats. The findings are in keeping with previous reports.<sup>9,10,15</sup> Blood glucose and HbA1c showed statistically significant amelioration in the experimental diabetic rats compared to controls.

Glucose homeostasis and HbA1c showed significant improvement in diabetic rats fed thiamine rich diet (Group 4) compared to controls (Group 1) ( $p=0.0001$ ) (Table I). Group 3 and 4 also showed significant amelioration of blood glucose as shown in table 1 and graph 1 and 2 ( $p=0.001$ ). Glycosylated HbA1 was significantly reduced in the diabetics given thiamine

supplements ( $p=0.001$ ). Significant reduction in HbA1c noted in present study in contradistinction to previous studies.<sup>9,15</sup>

Reason is very logical, that above studies<sup>9,15</sup> used vitamin thiamine therapy just for 4 weeks which is less compared to 12 weeks vitamin supplementation in the present study. It is suggested that the vitamin thiamine be prescribed for long durations for clinical effect to be elicited.

Thiamine supplementations inversely affected the blood glucose levels, has been reported in a previous study,<sup>17</sup> this shows it's positive impact on correcting the blood glucose levels. Above findings are in keeping to present study.

A previous study<sup>18</sup> reported improvement in blood glucose and blood lipid profile in diabetic rats supplemented with vitamin thiamine. The findings of above study support the present study. Above study<sup>18</sup> concluded that the thiamine dependent enzymes transketolase (TK) and pyruvate dehydrogenase (PDH) activities are improved, hence this improved blood glucose regulatory mechanisms.

Another previous study was conducted with thiamine and benfotiamine on blood glucose polyol pathway. The study was conducted on cultured vascular cells. A significant improvement in blood glucose was noted. They concluded that the thiamine and benfotiamine may help to prevent and retard the microvascular complications of diabetes mellitus.<sup>19</sup> Improved blood glucose levels of above study in agreement to the present study. The present study observed amelioration of blood glucose homeostasis and Glycosylated hemoglobin A1 (HbA1c) in thiamine supplemented diabetic rats.

## CONCLUSION

Vitamin thiamine improved the blood glucose homeostasis and reduced Glycosylated Hemoglobin A1 effectively in experimental rats. It is recommended to supplement diabetic subjects with vitamin thiamine.

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

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# To See the Work Related Musculoskeletal Disorders among College Teachers

Shahab Uddin<sup>1</sup>, Abbas Memon<sup>2</sup>, Asif Shaikh<sup>1</sup> and Hina Badar<sup>1</sup>

## ABSTRACT

**Objective:** To determine the prevalence of work related musculoskeletal disorders among college teachers of Karachi and Hyderabad.

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

**Place and Duration of Study:** This study was conducted at the Department of Physiotherapy & Orthopaedic, Liaquat University Hospital Hyderabad from January 2013 to June 2013.

**Materials and Methods:** We selected college teachers from both gender by convenient sampling. Those selected, were subjected had a work experience of about one year in teaching. Nordic questionnaire was used to determine the work related musculoskeletal disorders. The questionnaires were sent to 400 intermediate teachers and 342 completely filled questionnaires were returned back. Analysis was done through SPSS.

**Results:** The highest prevalence of work related pain was found neck, shoulder, lower back, and knees and pain starts when they perform their work. 50% participants responded that they keep their neck in bending position and shoulders elevated while using black board.

**Conclusion:** The results concluded that neck, shoulder, lower back, and knees are mostly affected regions. The use of ergonomically rules can help to alleviate the problem.

**Key Words:** Prevalence, Work related Musculoskeletal Disorders, Teachers, Postural training.

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## INTRODUCTION

Musculoskeletal Disorders due to work (WMSD) [also known as Repetitive Strain Injury (RSI) or Cumulative Trauma Disorder (CTD)] are the musculoskeletal disorders that have been developed due to work related issues. It may involve different regions of body like upper extremity, lower extremity, cervical, back regions etc. The onset of these problems need to be known where as it is a common belief that it is caused by overuse.<sup>1</sup> According to WHO musculoskeletal disorders are major cause or reason of absenteeism from the job or work. Also a considerable amount of money is spent because of these disorders. These disorders may involve different body regions. The severity of their symptoms varies from ache to severe pain.<sup>2</sup> WHO defined WMSDs as follows WMSD results from a number of causes and issues. In these issues, the environment of work and performance both contribute, but the amount of influence on the cause may vary.<sup>3</sup>

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WMSDs are the conditions that involve musculoskeletal structures like tendons, muscles, ligaments etc. and the cause of these conditions are not of acute nature. They develop when the physical demands of the working place or occupation causes damage to any & body part. WMSD may be develops by frequent acquiring of bad postures or forceful or again and again repeating the movements which exert pressure or demand more energy. The risk of developing WMSD increases with frequent exposure to such conditions.<sup>4</sup> According to Occupational Health & Safety Centre of Canada, WMSDs are disorders that are painful and they involve muscles, nerve & tendons. The causes may include frequency of repetition, acquiring bad postures. These disorders are painful at rest as well as at work place. As upper limb is involved in almost all the works so upper extremity is mostly involved in WMSDs, whereas lower extremity & back can also be involved where they are utilized during the work. WMSDs do not develop due to a single trauma. They result from repetitive episodes of trauma. They gradually & slowly come into existence.<sup>5</sup> WMSDs are among the leading reasons of work related disabilities and being absent from work.<sup>6</sup> According to a paper by Hogg-Johnson 50% to 80% of the population in developed countries have had back pain during their whole life span. Also 30% of all the lost time claims are due to back disorders.<sup>7</sup> WMSDs are very common among many occupations as well as teachers. Its incidence is quite high among the



school teachers. A study shows that teachers are prone to develop the WMSDs because of the awkward postures they acquire during their job.<sup>8</sup> Other study says that teachers in physical education are more prone to acute or chronic injuries due to their work and this leads to retirement before time and age.<sup>9</sup> There are some ergonomically issues also associated with the causation of WMSD among the teachers. In China a study showed that WMSD prevalence is very high among teachers. It may develop in neck, shoulder, low back, wrist/hand, elbow & knees.<sup>10</sup>

If we talk about the causing factors of WMSDs among the teachers the causes may include age, gender and BMI. Also working under pressure situations may also contribute in causing WMSDs.<sup>11</sup> If we talk about teachers dealing nurseries the cause may be lifting kids & carry them.<sup>12</sup> The studies also show that the cause of premature retirement among teachers is WMSDs.<sup>3</sup> Beside this studies show that back was the region mostly affected by WMSDs among the teachers of Malaysia and China.<sup>7</sup> The study also shows that the older i.e. experienced teachers are more prone to develop WMSDs. Also female teachers show high prevalence of WMSDs than male teachers.<sup>8</sup> The study also shows that psychosocial issues can also contribute in the causation of WMSDs among the teachers.<sup>13</sup> Ergonomically issues like furniture selection for classes and laboratories can also play important role.<sup>14</sup>

WMSDs can be prevented if good ergonomically procedures are employed. It includes maintain the work surface according to height, adjusting the chair and use of appropriate furniture.<sup>15</sup> The objective of this study was to determine the prevalence of work related musculoskeletal disorders among the college teachers. By knowing this, helpful strategies would become easy to make as when we know the issue we can solve it better. They can make strategies to cope up with these problems and in turn this will help to enhance their skills. (No disorder no absenteeism).

## MATERIALS AND METHODS

400 participants were randomly selected in different colleges of Karachi and Hyderabad. The duration of the study was six months from January 2013 to June 2013. The participants were randomly selected, who were teaching in different colleges of Karachi and Hyderabad and Nordic questionnaire with consent form were distributed to all participants. Participants were asked to complete the questionnaire and returned to the researcher or the person who gave it to them after one week of time. The targeted population of this study was both gender and had a work experience of about one year as college teacher were included in this study. Lab assistants and administrative staff were excluded from this study. Those teachers who had a history of severe trauma, such as a fracture, neurological injury involving the spine, shoulders or head, or a recent

whiplash injury (i.e. less than two years ago) were also excluded from the study. Nordic questionnaire was used as a data collection tool as it is useful method of covering a large population in a relatively short time and economically it is a cheap method rather than any other type of methods. This method is useful for straight forward questions and Nordic provide more ease to the participants as participants can answer the questionnaire in their free time which may also helpful for them to consider each question carefully. First section of the questionnaire contained questions related to age, gender, weight, height, BMI working hours and sleeping hours. Second section contained questions regarding WMSDs in different regions of body. The questionnaire was based on close ended questions as close ended type of questions are easy to answer and this format of questions is more easy to understand for the researcher as well as for the respondents as there is no language problem in close ended type of questions as they require very little or no explanation. All the data was entered SPSS (version 20.0)

## RESULTS

342 teachers were selected from different colleges of Karachi with a mean value of age (mean 33), and having a standard deviation of (S.D  $\pm$  11.57). Ratios of female respondents were greater (61.4%) as compared to males (38.6%). Table 1:

**Table 1: Demographic Details (N=342)**

Variables	Frequency	Percent
<b>Age</b>		
25-34 years	114	33.3
35-44 years	78	22.8
45-54 years	96	28.1
55 & above	54	15.8
<b>Gender</b>		
Male	132	38.6
Female	210	61.4
<b>Years of experience</b>		
1-5 years	60	17.5
5-10 years	90	26.3
10-15 years	48	14.0
more than 15 years	144	42.1
<b>Daily work hours</b>		
1-5 hours	30	8.8
6-10 hours	312	91.2
<b>BMI</b>		
b/w 18 and 23	162	47.4
above 23	180	52.6

Those participants who were working from 1-5 years were 17.5% participants, 26.3% participants were working from 5-10 years, 14% from 10-15 years whereas 42.1% participants were working from more than 15 years. 52.6% participants were lying in the BMI category of overweight. Table 1:

Prevalence rate of musculoskeletal disorders in different body parts during 12 months, most of the participants had problem in neck, Rt. Shoulder, lower back, upper back & knees statistically 57.9%, 43.9%, 29.8%, 22.8% respectively. Figure: 1:

The results prevalence of musculoskeletal disorders in different body regions during last 7 days showed that most of the participants complaint of trouble in neck, rt. Shoulder, lower Figure: 2:

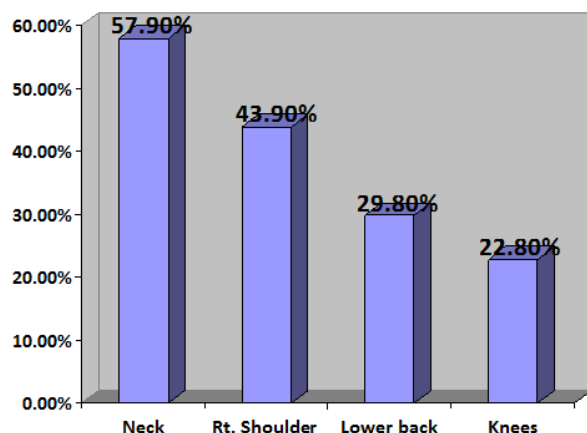


Figure No.1: Pain during last 12 months (N=342)



Figure No.2: Trouble during Past 7 days (N=342)

## DISCUSSION

All the musculoskeletal disorders that develop due to any sort of problem related to work or job that the affected person is doing is called Work Related Musculoskeletal Disorders or WMSD. Here we discussed about teachers. Teachers may be teaching students at different levels and each level has their own responsibility and liabilities. Teachers teaching at intermediate level the teachers not only have to teach their respective subjects but they also have to prepare different notes for their subject also at this level the students have many issues so the teachers also have to work to do counseling of these students to solve the issues. Beside this when it comes to teaching and dedicated teaching, the teachers have to search for best

known knowledge to convey to their students. For this purpose they may have to read a lot or sit on computer for long periods to search for accurate and appropriate information.

If we look at the working procedures that the teachers may employ to convey the knowledge to their students they may have to stand or sit for long hours. When we study on the prolong sitting or standing it is known that prolong acquiring of a certain posture may lead to increased pressure on intervertebral discs and when this pressure is increased, this increased pressure may lead to disorders associated with intervertebral discs i.e. it may cause neck or back pain.<sup>15</sup>

This study showed that the activity level of teachers may be low due to which they gain weight and their BMI increases as their weight increases. Also we can associate this with the prolong durations of work that the teachers have to do. This shows that the activity level of teachers may be low because of their prolong work durations.

If we look at the 12 month prevalence of musculoskeletal disorders among teachers of intermediate level we found that neck has high prevalence i.e. 57.9%. This can be associated with a previous study done in China which showed 12 month prevalence for neck pain as 48.7% among teachers.<sup>9</sup>

The reason for this high prevalence may be head down posture for prolong durations.<sup>7</sup> as discussed earlier, teachers have to acquire certain postures for prolong durations. The responses to 12 months prevalence of shoulder joint was found to be 2<sup>nd</sup> highest i.e. 43.9% for right shoulder. This may be associated with neck pain or it may also be due to prolong use. This prevalence may be associated with previous study by Lawrence I. This study's results showed 55% problem in shoulders, this study was done on nurses.<sup>11</sup>

The responses to 7 days prevalence of neck pain were found to be 47.4% & that for shoulder was found to be 36.8%. The 3<sup>rd</sup> highest & 4<sup>th</sup> highest 12 month prevalence was found to be for lower back and upper back respectively. Again the cause may be repetitive movements or awkward postures. The results show that 42.1% & 29.8% of teachers reported pain at lower back & upper back respectively. These can be associated with previous study done by Beyen et al in Ethiopia.<sup>3</sup> This study showed L.B.P. in 57.5% of participants. If we look at the 7 days prevalence we found that 29.8% & 28.1% of participants showed problem in lower back and upper back respectively. If we discuss the reason of this prevalence, the reason may be awkward posture. As discussed earlier, teachers have to sit or stand for prolong duration, this may cause discomfort and if despite of discomfort the same posture remains the condition may get worst.<sup>3</sup>

The fifth highest 12 month prevalence was found to be for knees. The results showed that 22.8% of participants had knee problems. This can be associated with the

results of previous study done in China in 2012. This study showed that 22.6% of the participating teachers had knee pain.<sup>9</sup> When we look at 7 days prevalence we found that knee problem was present among 22.8% of the participants.

The results showed that the teachers had high prevalence of musculoskeletal disorders. These disorders also had prevented many of the participants to perform their daily routine work. These postures and movements may limit the activities of the suffering person.<sup>16</sup> As we have seen that highest prevalence was found to be for neck and shoulder among the intermediate teachers so this prevention from activity may be associated with their high prevalence. Beside this we can say that if the persisting problem remains for long period it may lead to prevent the sufferer from performing his or her daily activities.

The study done in 2009 by Rahman S et al had showed that obesity was associated with low back pain.<sup>17</sup> In 12 month prevalence, those who had knee pain, 18 had normal BMI & 60 had high BMI. Same was the result found for 7 days prevalence. In 12 month prevalence for Ankle pain 12 had normal whereas 30 had high BMI. In 7 days prevalence 6 had high BMI. The study done in 2006 by Adamson J. et al. had shown that high BMI is associated with hip, knees, ankle & feet pain. So we can say that those participants who complaint of pain of knee, ankle or hip may be because of their high BMI.<sup>18</sup> High BMI itself is dangerous for health. Obesity is said to be a cause of many diseases so if a person is having high BMI that person may develop many diseases. If we talk about the musculoskeletal disorders they can also develop if a person has high BMI. High BMI means that a person is over weighted or obese and if a person has high BMI over all mass of that person would be increased. This means that a person with high BMI has to do more effort to do the same work which a normal BMI person can do with little effort. More effort means more energy consumption and more muscle work. If the musculoskeletal system of this person having high BMI is weak or incapable to perform the work this can lead to injury and resulting into musculoskeletal disorders.

Ergonomics is a field which makes the environment individual friendly. If the correct use of ergonomics is employed in the working environments the injuries can be minimized. Also if the valuable rules of ergonomics are applied in the working environment of the teachers this can minimize the injuries and disorders caused by work related issues.

## CONCLUSION

This study was conducted to evaluate the prevalence of WMSDs among intermediate teachers. The results concluded that neck, shoulder, lower back, and knees are mostly affected regions. The use of ergonomically rules can help to alleviate the problem. This study has

proved that there is high prevalence of WMSDs among intermediate teachers, looking at this I may recommend that awareness programs related to posture awareness and ergonomics should be conducted. Also it should be made essential that good ergonomically designed furnishes may be used to minimize this high prevalence.

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

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# Functional Outcome of External Fixator in Grade II & III Open Fractures of Tibia in Children

Abbas Memon, Mehtab Ahmed Pirwani and Shakeel Ahmed

## ABSTRACT

**Objective:** To assess the functional outcome of external fixator in children with open tibial fracture in the department of Orthopaedics Surgery of LUH Hyderabad/ Jamshoro

**Study Design:** Observational / descriptive study.

**Place and Duration of Study:** This study was conducted at the Orthopaedic Department of LUMHS from June 2014 to March 2015.

**Materials and methods:** In this study, 60 children (younger than 12 years) suffering from Gustilo grade II and III open fracture of tibia were admitted at the emergency department of the center and evaluated. All the cases were treated with external fixation, after complete counseling their parents or their attendants. While the children were admitted at the emergency department of the hospital, they underwent prophylaxis using antibiotic. All patients underwent washing and primary debridement operation at the emergency department. According to the attending surgeon, the patients were treated either using external fixator after hospitalization. After management union of the fracture was assessed through clinical examinations such as lack of pain, tenderness, and radiography of both lateral and anteroposterior (AP) views during the follow-up period.

**Results:** In this study mean age was found  $10.3 \pm 3.6$  years, male were found in majority 42(80.67%). Road traffic accident was the most common cause of mechanisms of injury was in 35(61.31%). Cases with grade III type of fracture found in majority 57.69%. union after management was achieved 98.8% of the cases, superficial infection was found in 06(11.53%) cases, while deep infection, Malunion and delayed union were found 03(5.76%), 07(13.46%) and 05(9.61%) respectively. While non-union was found only in one case.

**Conclusion:** External fixator is very safe, insignificant invasive, got short surgical time, following by short hospital duration as well as can be applicable as unequivocal & effective administration of open fractures of tibia among children.

**Key Words:** Open Fracture, external fixators, Tibia, Children

**Citation of article:** Memon A, Pirwani MA, Ahmed S. Functional Outcome of External Fixator in Grade II & III Open Fractures of Tibia in Children. Med Forum 2016;27(6):44-47.

## INTRODUCTION

Tibial fractures have been 3<sup>rd</sup> commonest pediatric long-bone fracture after forearm & femoral fractures. About half of pediatric tibial fractures take place among distal 3<sup>rd</sup> of tibia,<sup>1</sup> it is followed by as; midshaft fractures of tibia (39%), and least frequently of the proximal 3<sup>rd</sup> of tibia is engaged.<sup>1</sup> Fractures of tibia in the skeletally undeveloped patients can be managed without surgical treatment but tibial fractures resulting from high energy traumas are of special importance considering type of the selected treatment method affecting the children future.<sup>2,3</sup> Manipulation and casting are regarded as definite treatments for children tibial fractures.<sup>4</sup>

Tibial Open fractures in pediatric populace can be correlated with prominent morbidity, including however not restricted to nonunion, deep infectivity, compartment syndrome, and even amputation.<sup>5-7</sup> Though a few clinicians profess that these traumas can possibly behave in same pattern in adults & children, others consider that these traumas are tolerated better among children, specially young ones.<sup>6</sup> In most of accessible literature appears to exhibit that higher Gustillo type fractures (among children & adult) likely comprises few expected outcomes and more complications.<sup>5-7</sup> Though, most of these studies having less numbers, in this way, it is not easy to demonstrate a statistically significant variance even if one undeniably exist. Tibial open fractures management in young kids is a challenging issue. Conventional techniques to manage these fractures, for instance closed treatment through plaster casts, have came out from casting, debridement & open irrigation, either segregated or via plaster & pins and, newly; internal or external fixation techniques.<sup>8</sup> External fixators are applied at open complex fractures, as a result of high energy traumas plus cases of numerous damages.<sup>9</sup>

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Early administration via external fixation is well recognized however, additional alternative comprises internal fixation by plates, immobilization in cast or intramedullary nailing.<sup>10</sup> The best stabilizing technique of Gustillo level II&III fracture is uncertain. External fixator is widely preferred by the majority of surgeons as an option for treatment of category III of open fracture of tibia.<sup>11</sup> External fixators propose numerous benefits in managing open fractures of tibia. This study aims at evaluating the functional outcome of external fixator within children having open fractures of tibia at the department of Orthopaedics LUH Hyderabad/Jamshoro.

## MATERIALS AND METHODS

This cross sectional study was conducted at orthopaedic department of LUMHS, with duration of time from June 2014 to March 2015. In this study, 60 children (younger than 14 years) sobering from Gustilo grade A and B III open fractures of tibia, were admitted at the emergency department of the center and evaluated. Children having Gustilo II,III grade of tibial open fractures were selected. Children with history of lower extremities fractures, systemic and metabolic diseases, and skeletal congenital diseases were excluded. The children were matched considering age, gender, damage mechanism, and open fracture type (grade III) and associated damages as well as complications were recorded for all patients. All the cases were treated with external fixation, after complete counseling their parents or their attendants. While the children were admitted at the emergency department of the center, they underwent prophylaxis using antibiotic. All patients underwent washing and primary debridement operation within the first 6 hours of admission at the emergency department. According to the attending surgeon, the patients were treated either using external fixator after hospitalization. After management union of the fracture was controlled through clinical examinations such as lack of pain, tenderness, crepitation at the fractured area as well as using radiography of both lateral and anteroposterior (AP) views during the follow-up period. Delayed union was regarded as non-union for more than 6 months.

## RESULTS

In this study mean age was found  $10.3 \pm 3.6$  years, male were found in majority 42(80.67%) as compare to females 10(19.33%). Road traffic accident was the most common cause of mechanisms was in 35(67.31%) following by fall and machine injury with the percentage of 12(23.07%) and 05(09.62%) respectively. Table:1

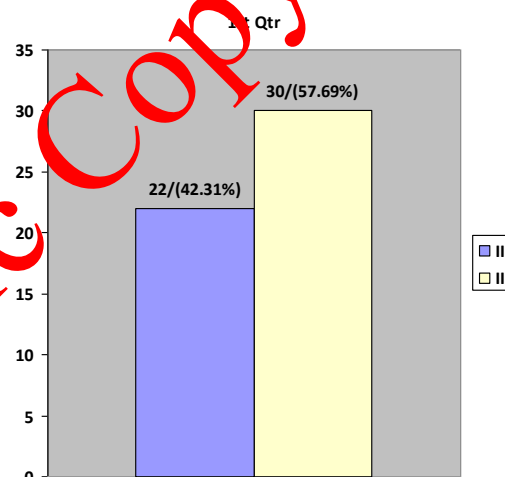
Cases with grade III type of fracture found in majority 57.69% while grade II were found 42.31%. Figure: 1.

According to the complications superficial infection was found in 06(11.53%) cases, while deep infection, Malunion and delayed union were found 03(5.76%), 07(13.46%) and 05(9.61%) respectively. While non union was found only in 1 case Table:2

According to the followup 7 cases were not comes, while in the remaining 45 cases mean time of the bone healing was found in grade II fractures 10.4 weeks, while in grade III it was found 12.5 weeks. Table:3.

**Table. No.1. Demographic variables (n=52)**

Variables	No. of patients /(%)
<b>Age (mean<math>\pm</math>SD)</b>	10.3 $\pm$ 3.6 years
<b>Gender</b>	
Male	42(80.67%)
Female	10(19.33%)
<b>Mode of Injury</b>	
RTA	35(67.31%)
Fall	12(23.07%)
Machine injury	05(09.62%)



**Figure No.1: Fracture distribution according to grades (n=52)**

**Table No.2: Complications after management (n=52)**

Variables	No. of patients /(%)
Superficial infection	06(11.53%)
Deep infection	03(5.76%)
Malunion	07(13.46%)
Delayed union	05(9.61%)
Non union	01(1.92%)

**Table No.3: Fracture Healing Time (n=45)**

Fracture Type	Mean Time of Bone Healing
Type II	10.4 Weeks
Type III	12.5 Weeks

## DISCUSSION

A complex span of tibia in relation to the randomness of open fracture (soft tissue traumas as well as fractures themselves are influencing factors of fractures therapy, union duration as well as impediments) made fractures of this category tricky to treat.<sup>12</sup> Tibia is the

commonest affected bone among open fractures as well as correlated with considerable economic, social, and psychological repercussion. In administration of these fractures, external fixator is applicable as an ultimate pattern of fixation to deal with the mutual trauma of soft tissues as well as bone.<sup>13,14</sup>

In this study mean age was found  $10.3 \pm 3.6$  years, male were found in majority 42(80.67%) as compare to females 10(19.33%). Similarly, Hossein Aslani et al.<sup>15</sup> proposed that mean age of the children having open tibial fracture was  $10.5 \pm 3.2$  in the external fixator group. Furthermore, Hossein Aslani et al.<sup>15</sup> mentioned male were in the majority 55.5% and female 44.5%. It can possibly be because of the variance among life style for instance: male children are concerned highly in outdoor activities (playing outdoor games, bicycle and schools away from house) in contrast with female children; therefore, they are additional susceptible to risk concerning open fractures.

Outcome of this study exhibited that RTA is widespread reason of fractures in 35(67.31%) out of total cases. Mirjat AH et al,<sup>16</sup> reported that RTA is general affect of open fracture relating tibia, as 65.0%. This may due to ignorance traffics regulations, rough driving, deprived roads states of society. Likewise, a few authors stated alike observations for instance, C.M. Brown et al<sup>17</sup> observed TRA within 90% of cases as well as Sultan Set al<sup>18</sup> came across with 87.6% of RTA cases.

In this study according to the complications superficial infection was found in 06(11.53%) cases, while deep infection, Malunion and delayed union were found 03(5.76%), 07(13.46%) and 05(9.61%) respectively. Mean time of the bone healing was found in grade II fractures 10.4 weeks, while in grade III it was found 12.5 weeks. In this study non union was found only in one case. Similarly in some other studies also found comparable results as : Hulle et al<sup>19</sup> evaluated diaphyseal fractures of femur & tibia administered via external fixation during 1987-1991 among 48 children. The signs of external fixation comprise failed conservative administration, manifold traumas, open fractures, as well as unstable fracture patterns. All fractures cured without additional surgical involvement, as well as the frequency of critical complications had been low, though pin track sepsis has been widespread. Myers et al<sup>20</sup> mentioned the application of external fixation among thirty tibial fractures of high energy (11 closed, 19 open) among children having a mean age of 11.9 years, followed 60 weeks. The mean duration of union was 4.8 months, while the fixator was reserved in situ for 3.2 months. A high incidence of complications has been observed: with delayed union 4/30 (13%), nonunion 2/30 (6.7%), following malunion as 3/30 (10%), and leg length discrepancy 3/30 (10%), after that with pin track contamination 8/30 (27%), and with

wound infection 3/30 (10%) as well as 2/30 (6.7%) developed osteomyelitis.

We found union in 98.8% of the cases and non union only in 1.92% of the cases. As well as NE Gougoulas et al<sup>21</sup> stated that external fixation has been applied in total fractures of 536 cases out of this figure 82% had grade-3 open traumas. In each fracture, soft-tissue coverage was delay for above 72 hrs. Union was observed as a mean of 37 weeks with high union rate (94%). The occurrence of delayed union, (union following 6 months), was 24% like among an overall 392 fractures.

## CONCLUSION

External fixator may efficiently be applied as fixation definitive mean in open tibial fractures in children with general injury to soft tissue. External fixator is very safe, insignificant intrusive, get short surgical time, following by short hospital duration as well as may be applied as explicit as well as effectual management of open fractures of tibia in children.

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

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# Novel Role of Topical Diltiazem in Reducing Raised Intraocular Pressure in Rabbits

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## ABSTRACT

**Objective:** The objective of the current study was to evaluate the IOP lowering of topical diltiazem which is a calcium channel blocker.

**Study Design:** Observational / descriptive study

**Place and Duration of Study:** The study was conducted at the Department of Pharmacology, Khyber medical college Peshawar, KPK-Pakistan from November 2015 to February 2016.

**Materials and Methods:** 40 healthy rabbits of a local strain weighing 1.50 to 2.00 kgs were obtained and kept at the animal house of the department of pharmacology, BMC Bannu. The study was conducted on both eyes of conscious rabbits. Three sets namely X, Y&Z were made. Topical diltiazem was injected to set X(made ocular hypertensive and glaucomatous through weekly injecting sub-conjunctival betamethasone suspension). Ocular hypertensive control set Y was also established which gets synthetic tears for a period of 28 days through the whole project. Set Z received no treatment during research and it act as normotensive control.

**Results:** Our results indicated that topical diltiazem can reduce the intraocular pressure very efficiently and quickly. Topical diltiazem wielded IOP reducing outcome in a much transitory time period. Marvelous animal's survival was also related to it.

**Conclusion:** In future, topical diltiazem might be incorporated as a substitute anti-glaucoma drug in order to manage optical hypertensive crisis, provided its safety in human.

**Key Words:** Glaucoma, Optical Hypertension, CCB, IOP

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## INTRODUCTION

Man is borne with a nature which is non-satisfying and inquiring. That is why he is always been involved in newer researches. A worldwide research in the same background, is ongoing to expand the management of glaucoma. To make improvement in the treatment of glaucoma and to explore the causes being involved in its onset, researchers are making extensive work on the same<sup>1</sup>. A no of drugs are made which have vasodilating and intraocular pressure lowering tendencies<sup>2</sup>. As per Glaucoma Range, medical scenario of the disease is fairly terrible and capricious.

CCB or Calcium channel blockers are assorted collection of drugs<sup>3</sup>. Keeping in view the therapeutic values of CCB's, many boulevards are still need to be discovered in order to completely understand salutary effectiveness of CCB's. In coming years, research will expectantly discover their variety in numerous therapeutic arenas additionally with ophthalmology.

CCBs are in use since 70's for their role in lowering IOP. An abundant research articles are accessible about IOP upsetting possessions of CCB's. Although more than a few contradictory information existing concerning the CCB's role on IOP<sup>4,5,6</sup> but the overall propensity is in the direction of a reduction in IOP<sup>7,8,9</sup>. Potential applications are reported about CCBs for their role in glaucoma including vasodilatation and thus refining optic nerve blood flow and neuro protection<sup>10</sup>. The technique to increase IOP through using steroids (suspension) was as described by<sup>11</sup>. The current work done is envisioned to notice the usefulness of topical diltiazem on steroid persuaded elevated intraocular pressure in rabbits. The result of the study will lead to an addition in the existing conflicting data.

## MATERIALS AND METHODS

It was an experimental study which was conceded on rabbits in two phases including phase-A& phase-B.

**Phase-A:** During this phase, ocular hypertension was created in the animals of sets X & Y excepting the standard/control set Z. The phase was continued for 3 weeks i.e. twenty one days (range 0-21).

**Phase-B:** A two days gap was given before the start of phase-B, to acquire a completely established elevated IOP (day 22 & 23).

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Through phase B, animals of set X (made ocular hypertensive during phase A), were provided a treatment with topical diltiazem ( $8.9 \times 10^{-2}$  M) solution. Set Y was in still mock tears. 4 weeks i.e. 28 days (day 24-51) were consumed during this phase. Infusion of the drugs was a single drop throughout the week.

**Animals Used:** 40 rabbits were brought for the study. The experiment was conducted on both eyes of standard and cognizant rabbits. Animals of either sex (male and female) or species (albino and colored strains) were incorporated. Their average weight was between 1500–2000 gms and their age was in between 1-2 years. Two weeks observation was done before the onset of the experiment. The animals were retained in the “Animal House, Khyber Medical University, Peshawar”. Feeding was done on fodder, wheat grains ad libitum. Fresh and nutritious water was also provided.

**Grouping of Animals:** Rabbits were organized in three sets.

**Set X:** This set contained 10 rabbits which were steroid treated and ocular hypertensive. The animals of this set were infused with topical diltiazem ( $8.9 \times 10^{-2}$  M for four weeks).

**Set Y:** 20 rabbits were included in this set. Ocular hypertension was created within this set of animals. The set worked for ocular hypertensive control. It got mock tears for a period of four weeks.

**Set Z:** 10 rabbits were retained within this set. It was aimed to serve as normal control or normotensive. No treatment was given to this set of animals.

**Chemicals:** Various chemicals were used during the study including Diltiazem HCl powder, Proparacaine HCl 0.5%, Inj. Betamethasone suspension, Fluorescein sodium 2% and artificial tears drops.

**Equipments:** Tonometer and rabbits containers were used in the study.

**Initiation of Glaucoma:** 1. Set X & Y animals were made ocular hypertensive (n = 30). A sub conjunctival suspension of betamethasone (betamethasone sodium phosphate & betamethasone acetate 3mg/ml each)/week (0.7ml) was infused in both eyes.

2. Infusion of Betamethasone was given for three weeks.

3. Injections were given at day zero, 1, 2 & 3.

**Procedure for Injecting Beta Methasone:** Specially manufactured wooden boxes were used to keep the rabbits within them. The rabbits were infused. 5% proparacaine HCl, to persuade local anesthesia, was used. Sooner after some time, betamethasone was administered in sub conjunctival pouch of the animals. Insulin injects were incorporated to achieve the same.

**Procedure of Determining IOP:** 1. All the rabbits were tested for their IOP using tonometer for two weeks (Before the start of the study). Four readings were noted during this time. Animals showed variations more than 5mm Hg in their intraocular pressure were omitted (n = 5) and newer animal's set was involved to swap the omitted ones.

2. To evade diurnal difference of the IOP, readings were taken at a fix time during the entire study (Ocular Pharmacology Text Book 1997).

3. Measurements of the IOP in both eyes were taken twofold in a week. Corneal epithelial damage was protected by doing this (Kanski 2004). Thursday and Monday were selected for these practices.

4. Through phase-A, 1<sup>st</sup> reading was noted prior to injecting weekly Betamethasone (Thursday) and 2<sup>nd</sup> was recorded after 3 days (Monday).

5. Base line pressure was considered after infusing 1<sup>st</sup> injection of Betamethasone. It was designated as “zero time”.

6. Before taking readings, the animals were provided with topical local anesthesia followed by fluorescein that causes stain in cornea.

7. Animals immobilization was done by placing them in specially designed wooden boxes.

8. IOP was recorded with the help of tonometer.

9. In phase-B, steroids infusion was ceased but IOP measurement was still continued. IOP was noted prior to the infusion of the drugs.

10. 2<sup>nd</sup> phase IOP readings were well-thought-out to be the initial pressure.

**Preparation of Diltiazem:** The only available form of diltiazem is the tablet form. Its ophthalmic solution is not readily available.

A strength of  $8.9 \times 10^{-2}$  M is known to possess intraocular pressure lowering effects (Juan Santafe 1997). We took the same solution and preceded our work.

**Process for Drug Therapy:** 1. Infusion of diltiazem & artificial tears was remained in progress during 2<sup>nd</sup> phase (day 24<sup>th</sup>).

2. It was completed in both eyes at a specific time.

3. Readings of the IOP was noted down prior to the infusing the drug.

## RESULTS

Readings (IOP) were taken. Similar readings of both eyes were observed. (Right eye readings mentioned only). The readings shown as \*, \*\* and NS

\* = Significant ( $P < 0.05$ ), \*\* = Highly significant ( $P < 0.05$ ), NS = Non significant ( $P > 0.05$ )

**Table No.1: Set Y and Z mean IOP during 1<sup>st</sup> and 2<sup>nd</sup> phase**

Time Interval (Weeks)	Set Y (Ocular hypertensive)	Set Z (Normotensive control)
0	19.63±0.64	20.00 ±0.31
1	22.04±0.65*	21.63± 0.60
2	22.65±0.25**	21.60±0.30
3	24.02±0.58**	22.86±0.46
4	24.64±0.24**	21.84±0.46
5	26.56±0.33**	21.80±0.56
6	26.60±0.26**	22.02±0.52
7	26.45±0.40**	22.05±0.50
8	25.45±0.30**	21.09±0.40

**Table No. 2: Sets X&Y mean IOP differences during 2<sup>nd</sup> phase**

Time Interval (Weeks)	Set X (Topical diltiazem)	Set Y (Artificial tears)
0	25.36± 0.30	25.50± 0.22
1	25.55 ±0.26**	26.54 ±0.32
2	21.29 ±0.70**	26.55± 0.25
3	21.04 ±0.80**	26.40± 0.42
4	20.52 ±0.64**	25.38 ±0.32

**Table No.3: Week wise mean IOP difference of diltiazem treated ocular hypertensive rabbits**NB: 2<sup>nd</sup> measurements of IOP has been mentioned only

	Time Interval (Weeks)	Set X (Diltiazem treated)	Mean difference
0	Starting IOP	25.40±0.32	0.91±0.22
	Week 1 / Value 2	24.40±0.26	
1	Week 1 / Value 2	25.43±0.26	3.20±0.60**
	Week 2 / Value 2	20.26±0.70	
2	Week 2 / Value 2	20.24±0.71	0.30±0.40NS
	Week 3 / Value 2	20.00±0.78	
3	Week 3 / Value 2	20.20±0.79	0.51±0.60*
	Week 4 / Value 2	19.45±0.60	

## DISCUSSION

CCB's are known to be under use for more or less than 30 years for their IOP sinking properties. Sufficient facts are accessible regarding IOP lowering potency of ccbs. Its effects are testified in man as well as in animals. Contradictory reports are there but still, there is no consensus on the same<sup>12-15</sup>.

Above all, even then, CCB's are considered to be important for the researchers due to their probable effect in glaucoma patients in lowering IOP as well as providing vasodilatation and neuro protection<sup>16-19</sup>. AGS (American Glaucoma Society) has connected the usage of iron and calcium augmentation in glaucoma victims (22<sup>nd</sup> annual meeting)<sup>20</sup>.

The aforesaid work was conceived to validate IOP dropping tendency of diltiazem topically. The results substantiate that diltiazem can lesser intraocular pressure, consequently, resulting in an aid in the current information which shows CCB's role in managing glaucoma/ocular hypertension.

Steroid headed to a fast increase in IOP of set X & Y. The improvement in IOP was established statistically momentous after 2<sup>nd</sup> dose of betamethasone showing a P value <0.05 as shown in table 1. After 4<sup>th</sup> injection, the progression became extremely significant statistically (P<0.05).

The normotensive control set Z, did not display any statistically noteworthy alteration in their IOP'S throughout the work done (P>0.05).

After interpreting the results of phase-B, it was noticed that topically smeared diltiazem abridged the IOP efficiently as shown in table 2. Set X result are highly statistically significant (P<0.00) in comparison with the control set Z (ocular hypertensive).

Looking at table 2, the alteration in IOP of set X as compared to set Y became highly significant statistically from the first 7 days of treatment (P<0.00). Topical diltiazem substantiated to be effective in sinking IOP. Topical diltiazem has the tendency to drop the IOP very energetically, predominantly between 1<sup>st</sup> and 2<sup>nd</sup> week. A constant level in IOP was observed between 3<sup>rd</sup> and 4<sup>th</sup> week. Adiredrip in the IOP noticed was 5.10±0.61 between week 0 and 2. In the last week of treatment, it showed statistically non-significance (P>0.05), when its IOP lowering effect was compared week wise (Table 3).

After steroids cessation, some natural IOP lowering effect was also seen in set Y. The IOP dip was found significant statistically (P>0.05) in comparison with the values perceived at the termination of betamethasone therapy (Week 3). After termination of steroids treatment, the IOP was checked for additional 4 weeks in both sets.

This study does not shelve mechanism of action of diltiazem & any related drug related harmfulness except steroids. In conclusion, we recommend additional laboratory and animal models studies to discover its IOP sinking action and validate any systemic or local untoward effects. Diltiazem should be tested in human volunteers and then in glaucoma/ocular hypertension patients. Topical diltiazem effect on vasodilatation and nerve protection obviously needs more high profile research work.

## CONCLUSION

It is evident that topical diltiazem is helpful to treat acute ocular hypertensive crisis because of its quick IOP dropping properties, contributing to a reduction in glaucoma related morbidity and economic costs. Dose adjustment must be mandatory on individual basis.

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

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# Reasons for Negligence of Oral Health Care

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## ABSTRACT

**Objective:** The purpose of this study is to evaluate factors responsible for negligence of oral health care in our population.

**Study Design:** Observational / descriptive study.

**Place and Duration of Study:** This study was conducted at the Jinnah Medical and Dental College, Karachi from August 2015 to September 2015.

**Materials and Methods:** A questionnaire was structured which was based to evaluate, the background, including age, gender, social and educational level, dental habits and the reasons responsible for them. The data was stored in excel worksheet and was analyzed using SPSS.

**Results:** The major factors responsible for people neglecting oral health care was found out to be the high cost prices of dental treatments by 36%, followed by lack of care seeking attitude by 28% and time management by 23% of people. Socio-Economic status and educational background also had a significant relationship. People from lower socio economic and educational background were seen to be never visiting the dentist. No significant relationship was found with relation to age, marital status, availability of dentist, and dental misconceptions.

**Conclusion:** People are neglecting oral health care mainly due to the high cost price of dental treatments. Care seeking attitude is seen to be absent in our population. Dental health comes last in the set of priorities by the majority of people. Time is another area people find difficult to manage. These areas can be worked upon to decrease the prevalence of dental disease in our population.

**Key Words:** Dental health negligence, Oral health care, Care-seeking attitude, Time management, Socio-economic status, Dental treatment charges.

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## INTRODUCTION

Around 5 billion people all around the world suffer from oral diseases including tooth decay, dental erosion, periodontal and gingival disease.<sup>1</sup> In our part of the world the prevalence of oral diseases is also seen to be high. In general population many individuals have some unresolved dental issues. Regardless of their age, gender, social status or educational background, few seek elective dental treatments other than emergency. High cost, dental phobia or anxieties are among key issues in not having regular dental visits.<sup>2,3,4</sup> This study is being conducted to help us identify the factors that may be related to lack of interest in seeking dental treatment despite high prevalence of oral diseases in our population.

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## MATERIALS AND METHODS

The study was conducted at Jinnah Medical and Dental College (JMDC) from August 2015 to September 2015. A 15 item questionnaire was used to collect the data including age, gender, social and educational level, dental habits and the reasons responsible for them. The purpose of the study patients was told to all patients. The data was stored in excel worksheet and was analyzed using SPSS.

## RESULTS

The study sample consisted of 115 adults seen in JMDC. There were 39% females and 61 % males. The age range of the sample was between 18 to 65 years with 32 years being the mean age with a SD of 12.65 (Figure 1).

In our study 36% of the people never visited a dentist due to high cost of treatment, 28% had an attitude of neglect to oral care while 23% of people had time constraints for visiting a dentist (Figure 2).

The data also showed significant relationships between the dental care negligence with socio-economic status. People from low socioeconomic status who never visited the dentist were highest, comprising of 74%,

while people from the middle socio-economic status who never visited the dentists were 26% (Figure 3).

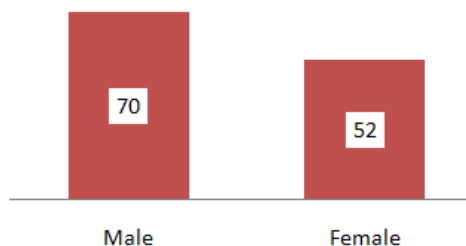


Figure No.1: Gender Distribution

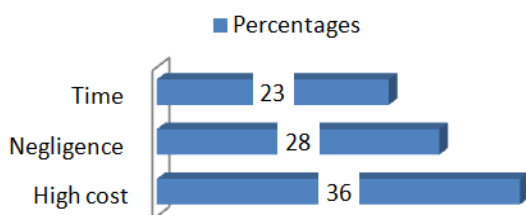


Figure No.2: Reasons for negligence

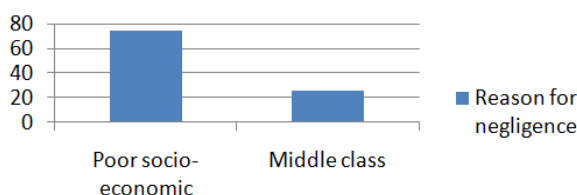


Figure No.3: Socio-economic Status

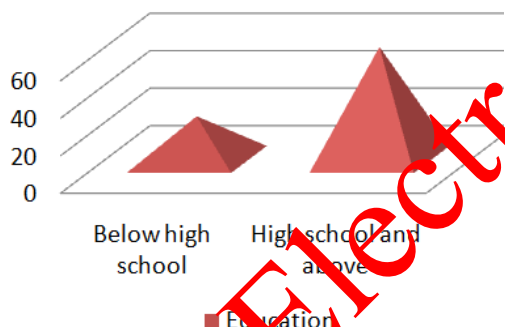


Figure No.4:

Educational level was also seen to be playing significant role as the data indicated that 23% of people who had education up to high school had not once visited the dentist, while people with educational level above high school who visited the dentist at least once a year were 60%. (Figure 4).

## DISCUSSION

According to the results the main reasons for neglecting oral health care was regarding the high cost of treatment associated with the dental procedures as 36 % of patients referred to it in all social classes. However 74 % of patients from low socio economic status never visited a dentist. This is in accordance with the studies

that show Financial limitations are an important reason for inability to see a dentist. In a study it is reported that one out of five patients are being unable to afford needed dental care.<sup>5</sup> Another study highlighting on the oral health status of adults in the age group between 18 to 64 years found that in 2008, among seven given reasons that one may skip a dental visit for an oral health issue, the primary reason was “could not afford/no insurance.”<sup>6</sup> It was also shown that financial affordability of the patient in the dental sector remains low, relative to other parts of the healthcare sector.<sup>7,8</sup>

The second most common reason that came out to be responsible for keeping patients away from seeking dental treatments is the absence of care seeking attitude as 28% of patients fall in this category. This trend is in contrast to the results of the study done by Zhu et al.<sup>9</sup> in China where only 68% of 35-44 years old subjects had made at least one dental visit in their lifetime. The probable reason may be that people in our community mainly rely on home remedies for ailments before consulting a doctor or a dentist. In a study conducted by Newman and Gift it was reported that 53% of people in USA regularly visit dentist even when there is no problem. This vast disparity may be attributed to the lack of awareness of the study population regarding the role played by regular dental visits in preventing dental diseases.<sup>10,11</sup>

• People in general have a much laid back and lazy attitude regarding their health, in particular oral health. There is no national index of oral health available in Pakistan but studies conducted at different centers refer to lack of interest in oral health as also indicated by concept of regular dental checkups is hardly seen. The only thing that brings the patients to a dentist is excruciating pain or disturbed aesthetics. 23% of patients reported time constraints as a reason for neglecting oral health as timing for appointments were found to be inconvenient for these patients. This also had a direct relationship with socio economic status as more patients of lower economic status found timing to be a constraint when it came down to oral health maintenance. This is in line with results in a study done in UK, where also 24% respondents agree to a similar statement.<sup>12,13</sup> This indicates the laid-back attitude of respondents in the present study toward the time scheduling of dentists. The number of patients visiting dental clinic seemed to improve with the level of education as 60% of patients with education above high school level were found to be visiting a dentist at least once a year for check-up/ treatment.

## CONCLUSION

People are neglecting oral health care mainly due to the charges as they find them unjustified. Care seeking attitude is seen not very often particularly the dental health comes last in the set of priorities by the majority of people. Time management is another area people

complained about at both ends, the dentist's as well as for the patients. These areas can be worked upon to decrease the prevalence of dental disease in our population by highlighting the importance of oral health care to the people.

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

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# A Survey of Cross-Infection Control: Knowledge, Attitude and Practice among Dental Students

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## ABSTRACT

**Objective:** The objectives of this study were to investigate various infection control methods and amenability with infection control procedures experienced by undergraduate dental students in their clinical years and house officers at Jinnah Medical & Dental College.

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

**Place and Duration of Study:** This study was conducted in one of the private sector college, Jinnah Medical & Dental College in Karachi from 15<sup>th</sup> January 2016 to 20<sup>th</sup> February 2016

**Materials and Methods:** This study was carried out in one of the private sector college, Jinnah medical & dental college in Karachi. The study set comprised of 3<sup>rd</sup> and 4<sup>th</sup> year dental students and house officers (n=80). A 24 item questionnaire was used to collect data related to knowledge about cross infection, barrier techniques, vaccination status, infection control practices and awareness. The questionnaire used was de novo. It was distributed to all the students and house officers. The self-administered questionnaires were collected immediately after completion on the same day. The responses of the questionnaire were coded for data analysis. Results obtained from different individuals were analyzed using SPSS.

**Results:** In this present study, majority of the students were well aware of cross infection in the first two years of medical/dental college studies whereas the remaining 20% came to know about it in their last two years. Regarding barrier techniques, it was found that (77%) students were well aware of all 4 components of PPE. When enquired whether the students were immunized against hepatitis B, 89% had an affirmative response. In our study there was a low prevalence of needlestick injury (30%). This indicates that our students have substantial knowledge and understanding about handling of sharp objects and are adequately practicing them.

**Conclusion:** The knowledge about cross infection in students was found to be adequate but application of prevention protocols need to be emphasized.

**Key Words:** Cross-infection control, knowledge, attitude, practices, needle stick injury

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## INTRODUCTION

Dentistry is a field of high priority regarding the risk of cross infections, therefore, the dental students have to consider every patient potentially infected since many carriers are not aware of their infection.<sup>1</sup> Cross-infection is the clinical transmission of infectious agents from one individual to another. Students, dentists, auxiliary staff and patients have risk of cross infection each time they attend the dental clinic/OPD.<sup>2</sup> In order to prevent infections, it is important to ensure that the dental students are well aware of hygienic protection

and are educated regarding cross-infection control measures.<sup>1</sup> These practices are important to reduce the risk of hospital acquired infections thereby ensuring a safe and healthy hospital environment for students, patients, dentists, staff and visitors.<sup>3</sup>

Dental teaching institutions have the obligation to protect patients and take protective measures for the students, as they have not yet developed the set of skills essential for practice and are in direct contact with the patients and so may be at a greater risk of exposure to infections. Observing the students infection control practices and reviewing the circumstances involved in their exposures will guide us to introduce safer practices and provide them with better protection.<sup>4</sup>

The guidelines related to cross infection control measures in a dental setting have been updated by the Centers for Disease Control in 2003.

The major aim of these guidelines is to provide an environment with all standard safety precautions in addition to prevention of transmitting infections among dentists, dental students and their patients.<sup>5</sup>

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Studies monitoring infection control practices among students are necessary to assess the efficiency of infection control training. In addition it facilitates the development of educational programs to improve adherence to guidelines and reduce injuries.<sup>6</sup>

There is need of further research to evaluate the current knowledge, attitude and practice of dental students regarding infection control and understand the nature of injuries during dental practice. Moreover, appropriate training should be provided regarding infection control to safeguard patients as well as the well-being of undergraduates to ensure a safer work environment.<sup>5</sup>

The objectives of this study were to investigate various infection control methods and amenability with infection control procedures practiced by undergraduate dental students in their clinical years and house officers at Jinnah Medical & Dental College. This initial cross-sectional study will serve as a needs-based assessment for the development of programs and workshops to develop better infection control practices at this institution.

## MATERIALS AND METHODS

This study was conducted in one of the private sector college, Jinnah medical & dental college in Karachi. The study set comprised of 3<sup>rd</sup> and 4<sup>th</sup> year dental students and house officers (n=80). A 24 item questionnaire was used to collect data related to knowledge about cross infection, barrier techniques, vaccination status, infection control practices and awareness. The questionnaire used was de-novo. It was distributed to all the students and house officers. The self-administered questionnaires were collected immediately after completion on the same day. The responses of the questionnaire were coded for data analysis. Results obtained from different individuals were analyzed using SPSS.

## RESULTS

The Questionnaire was distributed among 110 dental students (including 3<sup>rd</sup> year, 4<sup>th</sup> year and house officers), out of which 80 of them responded.

Age	Gender	Study year
Mean Age - 23	Male - 17	3 <sup>RD</sup> Year - 11
Minimum - 21	Female - 63	4 <sup>TH</sup> Year - 41
Maximum - 26		House Officers - 28

In response to our first question in the questionnaire, 52% respondents reported they got well aware of the knowledge about cross-infection control in their first year of dental education (28% in 2<sup>nd</sup> year, 14% in 3<sup>rd</sup> year and 6% in the 4<sup>th</sup> year).

Among these respondents, 97% of them answered taking medical history of patients regarding infectious diseases is important. When inquired about infectious diseases that have highest rate of transmission via blood, 46.3% answered Hepatitis B, 41.3% Hepatitis C and only 10% answered AIDs.

In order to prevent infectious diseases, it is important to educate the dental students. 25% reported there are programs taking place in their surroundings related to cross-infection control, but 75% of the respondents answered that there aren't much of the educational programs taking place.

All the participants of this questionnaire think that not just the students, dentists or the auxiliary staff but the whole population should be immunized against Hepatitis B. Further, the questionnaire contained questions about vaccination status, in which we figured 89% of them were vaccinated against Hepatitis B and unfortunately 11% were not.

When inquired about familiarity with the barrier techniques 77% of the respondents showed knowledge about all four techniques (Figure 1) whereas, 15% did not know about protective eyewear.

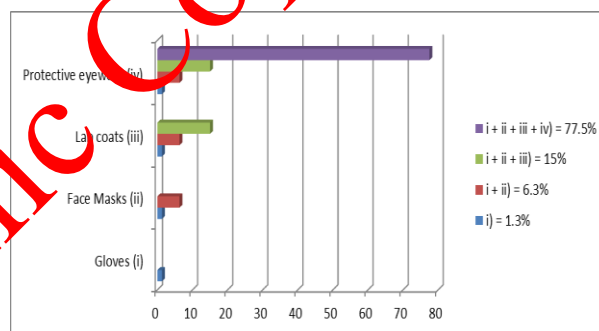


Figure No.1: Barrier Techniques

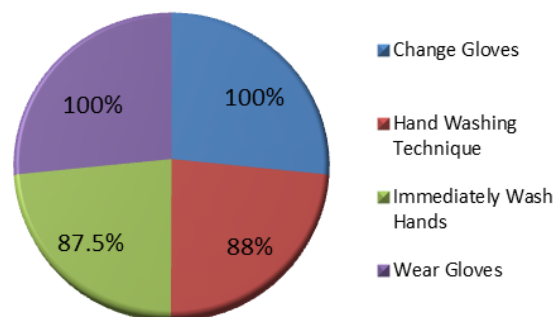
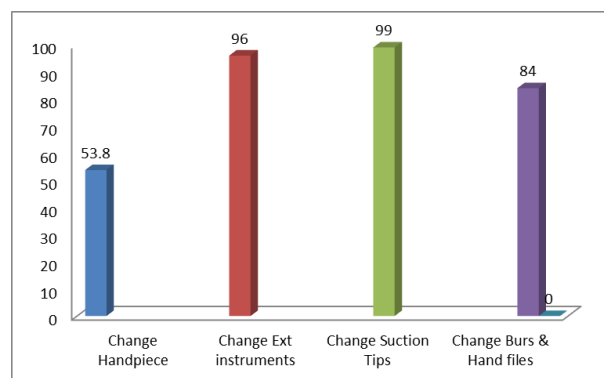


Figure No.2: Protective Measures

All the students (100%) wear gloves and change them after each patient, but 87.5% of them wash hands immediately after the procedure while the remaining 25% did not. When asked about the disposal of gloves, 80% reported they throw them in dustbin. (Figure 2). Regarding the hand washing technique 88% of the students were familiar with it and 47.5 % of them preferred the use of oral mouthwash prior the procedure (Figure 2).

About instrument usage following results were reported (Figure 3). 82.5% respondents reported that, disinfection of dental chair, dental clinic is as necessary as of instruments. 83.8% responded positively for the use of plastic wrappings or otherwise the instruments are kept in a closed container.

Prior to any procedure, 58.8% reported they use plastic gloves for handling of instruments and if an instrument gets accidentally dropped 62.5% of the students will ask the assistant to pick it up and take it away. Regarding disposal of sharp objects 62.5% responded negatively about the presence of separate containers.



**Figure No.3: Instrument usage**

When asked about experiencing Needle stick injury, 30% responded yes, whereas the remaining 70% did not have such exposure.

When inquired regarding the management in case of an exposure 41.3% reported they will apply disinfectant, 25% wash it with water and 22.5% immediately report it. When asked about whether the students were willing to treat patients with cross infection, 63.8% reported an affirmative response. On the other hand, 62.8% of the respondents said that cross-infection does affect their career choice.

## DISCUSSION

In today's era infection control is a major issue of concern among health care providers. Dental practitioners in general and students in particular are very much prone to such hazards due to lack of experience and knowledge. In this present study, majority of the students were well aware of cross infection in the first two years of medical/dental college studies whereas the remaining 20% came to know about it in their last two years.

Among the respondents 97% of them took medical history regarding infectious diseases whereas a similar survey carried out at DIKIOHS reveals the oral history taking scheme is adopted by 76.5% of the practitioners.<sup>2</sup> Detailed history taking has a pivotal role when it comes to cross infection control. Assuring that the patient is in good health relieves the nervousness and unwillingness of the students and allows them to treat patients adequately and confidently.

Regarding barrier techniques, it was found that (77%) students were well aware of all 4 components of PPE (masks, gloves, eye wear and scrubs). Emir et al in their study reported that 96.3% of the dentists demonstrated the habit of using masks, gloves and eye wear.<sup>7</sup> In a different study, authors in Kuwait reported 90% of practitioners used gloves; masks were used by 75% and 52% used protective goggles.<sup>8</sup> Treasure and Treasure indicated 42% of dentists used gloves, 64.8% used masks and 66.4% used protective spectacles in New Zealand.<sup>9</sup> McCarthy and MacDonald revealed that 91.8% of practitioners in Ontario, Canada, always used gloves, 74.8% always used masks and 83.6% used protective spectacles.<sup>10</sup> This reflects inclinations throughout the world where gloves and masks are favored as part of personal protective equipment while scrubs and protective eye wear are not in common use.<sup>11</sup> It is imperative to increase their use as in variety of procedures like scaling, endodontic procedures etc. as the dentist is exposed to a high number of pathogens.<sup>12</sup> Also students in particular incorrectly consider contamination from splashes not a major source of cross infection. Failure to change gloves in between patients is another major cause of cross infection. When asked about usage of gloves, 100% of students stated that they treat single patient with a pair of gloves as in contrast to an Iranian study which reports that 25% of its respondents do not always wear gloves during procedures.<sup>13</sup> When enquired whether the students were immunized against hepatitis B, 89% had an affirmative response. Other studies showed higher responses of 95.8%<sup>14</sup> and 90.8%.<sup>15</sup> McCarthy and Britton's study showed 100% immunization among all the final year undergraduate students at the University of Western Ontario, Canada.<sup>16</sup> On the other hand, Singh et al<sup>17</sup> stated that 61.2% of students in a Dental School in Central India were not vaccinated for HBV despite it was mandatory. He concluded a positive attitude but poor compliance of cross infection control practices amongst students. Immunization of dental students prior to their start of interaction with patients remains the most effective in dental health care. Immunizations not only considerably decrease the incidence but also reduce the transmission of the diseases. Vaccinations must be made mandatory for all students before they are exposed to clinical practice. The dentist should not bank on single protective strategy and masks, gloves, and eyewear should be considered as only the first line of protection in reduction of infectious agents such as aerosols. The second layer of protection is formed by the use of chlorhexidine mouthwash prior to procedure. 47.5% of our study participants said they did prefer the use of oral mouthwash prior to commencing procedures which was slightly lower when compared to another study revealing an oral mouth rinse was preferred 55.5% of the students.<sup>18</sup>

All sharp items must be collected in properly marked containers. In the present study, 62.5% of the respondents said that there were no separate containers available for disposal of sharp objects which is alarming as these sharp objects are a major source of cross infection. In another study, 37.80% of participants reported the use of marked containers to dispose of sharp objects. In previous studies, 72% and 56.20% of practitioners used separately marked containers.<sup>19</sup>

In our study there was a low prevalence of needle stick injury (30%). This indicates that our students have substantial knowledge and understanding about handling of sharp objects and are adequately practicing them. One of the studies suggested of recapping needles has 70% incidence of needle stick injury.<sup>20</sup> Other studies also report a higher fraction of needle stick injuries to students in the early phases of clinical training.<sup>21</sup> When asked whether the students would be willing to treat patients with cross infection, 63.8% of them responded affirmatively, whereas, the same percentage of students (63.8%) said this might affect their choice of career which seems a bit surprising. The concern is mainly against hepatitis B and C and tuberculosis, the reason being the transmissible nature of these diseases and high prevalence in our part of the world. In a similar study carried out in Columbia, USA, only 8.2% showed unwillingness to perform procedures on such patients.<sup>22</sup> The same study reported that a majority of students expressed concerns while treating patients with infection but it made them to modify the treatment plan. Students expressed concerns about treating patients with HIV which is highly prevalent in the western world. In this period of widespread implementation and standard precaution, this unwillingness likely produces the continuing bias towards patients with infectious diseases and underlines the need for additional attempts to educate the students to practice cross infection protocols rather than depriving this population of treatment. This study has some limitations as firstly it is limited to just one hospital and the other is that our study is of cross sectional design so we could not oversee the individual practices and had to rely on their responses. Therefore, the answers might not have correctly reflected the true knowledge and attitude in practice. But when provided with the information and opportunities to work, it promotes healthy changes in attitude and increases the sense of responsibility, thereby preparing them for professional life.

## CONCLUSION

The knowledge about cross infection in students was found to be adequate but application of prevention protocols need to be emphasized.

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

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# Short Term Outcome of Single Stage Anterior Sagittal Anorectoplasty in the Management of Rectovestibular Fistula in Female Children

Muhammad Ramzan, Asif Qureshi, Farasat Majid and Sofia Mustafa

## ABSTRACT

**Objective:** The objective of the study was to assess the short term outcome of single stage anterior sagittal anorectoplasty for the management of rectovestibular fistula in female children.

**Study Design:** Descriptive, Case Series study.

**Place and Duration of Study:** This study was conducted in the Department of Neonatal & Pediatric Surgery, Bahawal Victoria Hospital, Bahawalpur from November 2010 to November 2013.

**Materials and Methods:** Total 151 female children from 1 month to 13 years with the diagnosis of recto vestibular fistula undergoing primary ASARP were selected. No covering colostomy was done in any case. All the patients who were previously operated for RVF, or colostomy done for RVF, and those with septicemia were excluded. All the cases were managed in the ward and short term outcome was assessed in terms of post-operative wound infection (noted at 72 hours after surgery), vaginal tear (assessed during surgery), hospital stay and operative time.

**Results:** There were a total of 151 female patients with mean age of  $17.53 \pm 27.12$  months. Mean operative time in our study was  $85.76 \pm 16.49$  minutes and mean hospital stay was  $5.31 \pm 2.33$  days. All the patients were examined regularly till discharge from ward and looked for any wound infection and vaginal tear. Wound infection was seen in 24 (15.89%) and vaginal tear in 21 (13.91%) patients. Wound infection was managed by daily wound wash with normal saline and povidone iodine solution. Vaginal tear managed during surgery by repair with vicryl 5/0.

**Conclusions:** This study concluded that the short term outcome in terms of mean operative time, hospital stay, wound infection and vaginal tear after single stage anterior sagittal anorectoplasty is satisfactory in recto vestibular fistula treatment in female children.

**Key Words:** Anorectal anomalies, anorectoplasty, hospital stay, wound infection.

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## INTRODUCTION

Anorectal malformation (ARM), one of the common congenital anomalies, may present with a wide spectrum of defects.<sup>1</sup> Anorectal malformations can affect boys and girls, and involve the distal anus and rectum as well as the urinary and genital tracts. It has been found that there is not only an increased incidence of ARM in patient with trisomy 21 (Down's syndrome), but that 95% of patients with trisomy 21 and ARM have imperforate anus without fistula, compared with only 5% of all patients with ARM.<sup>2</sup> Despite better understanding of embryology, anatomy of anorectal malformations and physiology of continence, the management of children with anorectal

malformation has always been a surgical challenge and still poses too many complications. Vestibular fistula and perineal ectopic anus are the commonest anorectal malformations in female children.<sup>3</sup> Recto-vestibular fistula being the commonest type seen (27%), followed by ano-perineal fistula (20%).<sup>4</sup>

The early management of a newborn infant born with an anorectal anomaly is crucial and two important questions must be answered during the first 24 to 48 hours of life. First; are there associated anomalies that threaten the baby's life and should be dealt with right away? And second, should the infant undergo a primary procedure and no protective colostomy or a protective colostomy and a definitive repair at a later date? For babies born with persistent cloaca, the surgeon must also determine whether a dilated vagina is present and if it should be drained, as well as determining whether urinary diversion will be required. These maneuvers are intended to prevent sepsis or metabolic acidosis.<sup>5</sup>

The decision to perform an anoplasty in the newborn period or to delay the repair and to perform a colostomy is based on the infant's physical examination, the appearance of the perineum, and any changes that occur over the first 24 hours of life.<sup>6,7</sup>

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Previously, anorectal malformations (ARM) were treated in multiple stages for fear of disturbed wound healing and subsequent damage to the anal sphincter complex.<sup>8</sup> A covering colostomy was made followed by anorectoplasty in the past. With the ongoing advancement and improvement in the field of medicine the trend is shifting, and single stage procedures are being preferred.

The anterior sagittal approach is another technique devised for managing these lesions.<sup>9</sup> It was first reported by Zanotti in 1988.<sup>10</sup> The first reported series appeared in 1992,<sup>11</sup> with all cases showing satisfactory results. In this approach, patient is placed in lithotomy position, sphincter muscles are entered under direct vision and puborectal muscle is preserved.<sup>9</sup> The advantages reported with this approach include convenient position of patient, good exposure of operative field, adequate mobilization of rectum, and near normal reconstruction of perineal body.<sup>12</sup>

Now most surgeons prefer a single staged primary anterior sagittal anorectoplasty (ASARP). Primary ASARP has the advantages of decreased social, psychological and economic burden on the pediatric patient and her relatives. In primary ASARP, stoma (colostomy) is not required so the disadvantages and complications related to stoma and its management does not occur. As it is a single staged definitive procedure, the outpatient visits and inpatient hospital stay is less as compared to multi staged procedures.

A previous study shows mean operation time for single stage ASARP was  $81.2 \pm 4.8$  minutes and mean hospital stay was 6 days.<sup>13</sup> Vaginal tear occurred in 10%.<sup>14</sup> The cosmetic outcome was satisfactory.<sup>13</sup>

The rectovestibular fistula is not an uncommon problem but there is no local study and only one study was conducted in Pakistan.<sup>14</sup> This study would help us in comparing the outcome with other studies conducted elsewhere.

## MATERIALS AND METHODS

After taking approval from hospital ethics committee, all the admitted patients in pediatric surgery department and from outpatient department of Bahawal Victoria Hospital Bahawalpur having recto vestibular fistula were included in the study. All those patients who were previously operated for RVF or had colostomy done for RVF were excluded from study. Also premature patients or patients with septicemia were excluded.

Informed written consent from parents/guardians was taken. They were informed of the risks and benefits of operation and asked to sign a detailed informed consent in their respective native language. Confidentiality of all information of subjects was maintained. Hence all questionnaires were kept in lock and key.

All patients were undergone dilatation of the fistula with simple rubber catheter of size 8-10 Fr. and rectal washouts with normal saline four times in a day and on

clear fluids, beginning 48 hours pre-operatively or earlier in the presence of constipation and abdominal distension. Investigations including CBC, renal function tests, serum electrolytes, ultrasonography of abdomen and pelvis to rule out genitourinary anomalies and X-ray lumbosacral spine to rule out vertebral abnormalities were done in all the patients.

In anterior sagittal anorectoplasty (ASARP), Patient in lithotomy position, the anterior portion of sphincter muscles was cut through a midline perineal skin incision, rectum was separated from the vagina & then rectum was pulled through the center of these muscles. The perineal muscles were approximated in the midline between the rectum and vagina thus reconstituting the perineal body. The suturing began from the deepest part of the wound and progressed superficially.

The anoplasty was completed with mucocutaneous sutures of polygalactin (Vicryl) usually 4/0. Anteriorly the vaginal fourchette and the vestibule were reconstituted and the perineal skin sutured. Dressing was done with povidone iodine ointment.

Short term outcome was assessed in terms of post-operative wound infection (was assessed clinically and defined as erythema, fluctuation and purulent discharge from wound site after 72 hours to 6 days of operation). Vaginal tear (breach in the wall of vagina more than 0.5cm while separating the wall of rectovestibular fistula from the vaginal wall), hospital stay (from the day of operation to the day of discharge) and operative time (starting from incision to the last skin stitch) was noted by the operating surgeon (supervisor and consultant with more than 5 years' experience in the field).

## RESULTS

Age range in this study was from 1 month to 13 years with mean age of  $17.53 \pm 27.12$  months. Majority of the patients 111 (73.51%) were between 1 month to 1 year of age as shown in Table 1. Mean operative time in our study was  $85.76 \pm 16.49$  minutes and mean hospital stay was  $5.31 \pm 2.33$  days as shown in Table 2.

**Table No.I: %age of patients according to Age distribution (n=151).**

Age	No. of Patients	%age
1-6 months	62	41.06
>6 months-1 year	49	32.45
>1 year-<6 years	33	21.85
>6 years-13 years	07	4.64
Total	151	100.0

➤ **Mean  $\pm$  SD =  $17.53 \pm 27.12$  months**

All the patients were followed regularly till discharge from ward and looked for any wound infection and vaginal tear. Wound infection was seen in 24 (15.89%) and vaginal tear in 21 (13.91%) patients as shown in Table 3. Stratification of age with respect to operative time and hospital stay is shown in Table 4 & 5 respectively which have shown only significant

statistical difference with respect to hospital stay between age groups. Table 6 & 7 have shown stratification of age with respect to wound infection and vaginal tear respectively and showed no statistically significant difference between age groups.

**Table No.2: Descriptive statistics of operative time and hospital stay (n=151).**

	Minimum	Maximum	Mean	SD
Operative time (in minutes)	11	133	85.76	16.49
Hospital stay (in days)	2	12	5.31	2.33

**Table No.3: Frequency of wound infection and vaginal tear**

Variables	Frequency (%)	
	yes	No
Wound Infection	24 (15.89%)	127 (84.11%)
Vaginal Tear	21 (13.91%)	130 (86.09%)

**Table No.4: Stratification of age groups with respect to operative time.**

Age groups	Operative time (in minutes)	
	Mean	SD
<1 year (n=111)	86.25	17.87
>1 year (n=40)	82.59	16.43
P-Value	0.2587	

**Table No.5: Stratification of age groups with respect to hospital stay.**

Age groups	Hospital Stay (in days)	
	Mean	SD
<1 year (n=111)	5.92	2.23
>1 year (n=40)	3.59	1.66
P-Value	0.000	

**Table No.6: Stratification of age groups with respect to wound infection.**

Age groups	Wound Infection	
	Yes	No
<1 year (n=111)	19 (17.12%)	92 (82.88%)
>1 year (n=40)	05 (12.5%)	35 (87.5%)
P-Value	0.4935	

**Table No.7: Stratification of age groups with respect to Vaginal tear.**

Age groups	Vaginal Tear	
	Yes	No
<1 year (n=111)	18 (16.22%)	93 (83.78%)
>1 year (n=40)	03 (7.5%)	37 (92.5%)
P-Value	0.172	

## DISCUSSION

Anorectal malformations (ARM) are well known congenital entities that comprise a spectrum of

anomalies. Rectovestibular fistulas with a normal anus, also known as H-type fistulas<sup>15, 19</sup> or double termination of the alimentary tract<sup>16, 17, 18, 19</sup> are an uncommon subtype comprising about 2.4 % to 3.2% of all anorectal malformations in the Western Countries.<sup>17, 18</sup>

Due to its rarity, consensus about preoperative management, surgical options and postoperative care have not been established.<sup>15, 19</sup> This anterior approach for anovestibular fistulas in female patients had been in use since 1988.<sup>20</sup> Many studies have shown good anatomical exposure to operative field and minimizes the sphincter and other important structures damage with this approach.<sup>21, 22</sup>

Although most of the patients reported in neonatal period in western countries as they are easily recognized<sup>23</sup> but in our study, majority of patients presented were >6 months of age with mean age of 17.53 ± 27.12 months. The reason behind this may be due to lack of awareness regarding the anomaly or not easily approachable health care facilities in our country and surgical consultation is usually taken when patient develops severe constipation or abdominal distention. Similar findings were also observed in a study done in Pakistan by Zaman et al.<sup>14</sup>

In our study, mean operative time in our study was 85.76 ± 16.49 minutes and mean hospital stay was 5.31 ± 2.33 days. All the patients were followed regularly till discharge from ward and looked for any wound infection and vaginal tear. The most frequent intra-operative complication is vaginal injury, especially during separation of the fibrous part of the fistula. Vaginal tears are repaired with interrupted polygalactin sutures and usually heal uneventfully. Wound infection was seen in 24 (15.89%) and vaginal tear in 21 (13.91%) patients. A study by Aziz MA et al<sup>12</sup> has shown mean operative time for single stage anterior sagittal anorectoplasty as 81.2 ± 4.8 minutes and mean hospital stay as 6 days. After therapeutic antibiotics (2-5 days), 11% had some degree of wound infection.<sup>8</sup> Vaginal tear occurred in 10%.<sup>14</sup> Wound infection and dehiscence (usually following a hematoma) are seen occasionally and are treated by Sitz Baths and povidone iodine ointment application. If the rectum has been sufficiently mobilized and the dehiscence is minor healing is uneventful. In major dehiscence a proximal colostomy is performed and revision surgery may be required.<sup>12, 14</sup>

Harjai MM et al<sup>24</sup> in his study reported wound infection and vaginal tear after anterior sagittal anorectoplasty in 20% patients each. He also concluded that there is no difference in outcome on comparison of complications of ASARP versus PSARP. Similarly, Shehata, in his recent series, also observed no statistical significant difference in cosmetic and functional outcome between the two.<sup>25</sup> Wakhlu A et al<sup>26</sup> in his study has shown good result in 95% patients in a single-stage anterior sagittal anorectoplasty. Kulshrestha S et al<sup>27</sup> in his study on 107

patients concluded that single stage anterior sagittal anorectoplasty reduces hospital stay and the cost of treatment in patients.

In another study, Waheeb SM et al<sup>28</sup> has also found many advantages of anterior sagittal anorectoplasty in the treatment of rectovestibular fistula. He reported only 0.48% wound infection, shortened hospital stay and excellent cosmetic results with this technique. Chaudhary RP et al<sup>6</sup> in his study has shown vaginal tear in 6.25% patients and no wound infection with single stage anterior sagittal anorectoplasty. Zamir N et al<sup>14</sup> in his study has found same results with primary anterior sagittal anorectoplasty as that staged with colostomy especially in younger patients. So, initial colostomy followed by ASARP should be reserved only for cases with inflamed perineal skin and severe constipation. He reported short term good (meant nearly normal appearance of perineum with minimal wound scarring) cosmetic results in 63% patients while acceptable (mild wound infection resulting in wide scar) results in 20% patients.

## CONCLUSION

It was concluded from this study that short term outcome in terms of mean operative time, hospital stay, wound infection and vaginal tear after single stage anterior sagittal anorectoplasty is satisfactory in rectovestibular fistula treatment in female children and should be opted routinely in our practice.

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

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# Correlation between Obesity and Severity of Cholecystitis

Ahmed Raza, Saleha Anjum Khan and Shahid Mahmood

## ABSTRACT

**Objective:** The aim and objective of this study is to assess the relationship between obesity and severity of Cholecystitis.

**Study Design:** Observational / descriptive study.

**Place and Duration of Study:** This study was conducted in the Punjab Employees Social Security Hospital Rawalpindi & Azmat Rasheed Hospital Rawalpindi from 1<sup>st</sup> January 2015 to 31<sup>st</sup> Dec 2015.

**Materials and Methods:** 84 patients of symptomatic gall stone disease were included in the study. BMI was calculated & recorded at the time of admission. Patients having BMI > 25kg/m<sup>2</sup> were put in category of overweight/Obese & those having BMI < 25kg/m<sup>2</sup> were considered to be of normal weight.

**Results:** In males proportion of complicated acute cholecystitis was significantly higher in non-obese patients and was around (21%) as compared to obese (7%) with significant statistical difference. On the other hand no significant statistical difference was found between female non-obese & obese patients.

**Conclusion:** Contrary to common belief, complication rate in obese males is less as compared to males of normal weight. While in females, no such difference is noted in complication rate of gall stone disease between obese and non-obese females.

**Key Words:** Obesity, gall stones, cholecystitis.

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## INTRODUCTION

Whether or not obesity should be considered a disease on its own it is an important risk factor for many chronic physical and mental illness. These include cardiovascular diseases like angina, myocardial infarction<sup>1</sup>, congestive cardiac failure<sup>2</sup>, high blood pressure, abnormal cholesterol levels<sup>3</sup>, deep vein thrombosis, pulmonary embolism<sup>4</sup>, dermatological problems like acanthosis nigricans, lymphedema, cellulitis, hirsutism, and intertrigo<sup>5</sup>, endocrine problems like diabetes, polycystic ovaries<sup>6</sup>, complications of pregnancy, birth defects<sup>7</sup>, gastroesophageal reflux disease, cholelithiasis<sup>8</sup>, neurological problems like stroke, migraine, dementia, carpal tunnel syndrome & neuralgia paresthetica<sup>9</sup>, malignancies like breast, ovaries, colorectal, gall bladder, liver, pancreas, stomach, endometrial, cervical, prostate, kidney & non-Hodgkin's lymphoma<sup>10</sup>, psychiatric illnesses like depression, social stigma like 20% decrease chances of marriage in obese females<sup>11</sup>, chronic lung disease and complications during general anaesthesia<sup>12</sup>, sleep apnea syndrome, rheumatology like back pain, osteoarthritis and gout, sexual dysfunctions like erectile dysfunction, hypogonadism, Urological like urinary incontinence and chronic renal failure<sup>13</sup>.

The prevalence of overweight and obesity were highest in the WHO regions of the North America (62% for overweight in both sexes, and 26% for obesity) and lowest in the WHO Region for South East Asia (14% overweight in both sexes and 3% for obesity). Obesity is more common a problem in females as compared to males.

Gallbladder disease (GBD) one of the commonest surgical disorder and is major cause of morbidity, hospital admission, surgical intervention and economic burden and is caused by gallstones<sup>14</sup>. Its prevalence however, varies amongst different populations. In American adults, the prevalence of cholelithiasis is about 10% while in Western Europe the prevalence ranges from 5.9% to 21.9%<sup>15</sup>. Prevalence rates of 3.2% to 15.6% have been reported from Asia<sup>16</sup>. Over 70% of patients with gallstones are asymptomatic<sup>17</sup>. The risk of developing symptoms or complications related to gallstones varies and is approximately 1–4% per year. The most common complications of gallstone disease are acute cholecystitis, gallstone pancreatitis and obstructive jaundice<sup>18,19</sup>. Obesity is one of established risk factors in Gall-stone disease<sup>20</sup>. Five Fs related to gall stone disease are fat, fertile, flatulent, female of forty. Relationship of body weight to gallstone disease has been studied thoroughly but there are very few studies showing the effect of body weight on intensity of cholecystitis. We have conducted a study to see the relationship between Obesity and severity of Cholecystitis.

## MATERIALS AND METHODS

This is a prospective study carried out on 84 patients of cholecystitis whose weight and height measurements

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had been recorded & BMI calculated at the time of admission. Patients having BMI > 25kg/m<sup>2</sup> were put in category of overweight/Obese & those having BMI < 25kg/m<sup>2</sup> were considered to be of normal weight. Patients identified with symptomatic Gall-stone disease were enrolled in study and were classified as –(a) chronic cholecystitis (b) uncomplicated acute cholecystitis (c) complicated acute cholecystitis. Acute cholecystitis was defined when the patient had 2 or more of the following clinical and operative findings- fever >37.5c, right upper abdominal pain with tenderness, (positive Murphys Sign) continuous symptoms > 48 hours despite medical treatment. Ultrasound feature showing wall thickness greater than 4mm and Operative findings included –adhesions to adjacent organs, gross inflammation of gall bladder serosa. Complicated acute cholecystitis refers to the development of life threatening complications such as empyema, peri-cholecystic abscess, gangrene and perforation. The patients with chronic cholecystitis were electively operated on, and those patients with acute cholecystitis were either operated on during their initial admission when they were stabilised or at a later date by performing interval cholecystectomy. The severity of inflammation for cholecystitis was prospectively graded as chronic, acute or complicated according to operative findings.

Data was analysed using SPSS 17 and compared using the Chi-Square test and a p value of < 0.05 was considered statistically significant.

## RESULTS

Total number of patients in our study was 84. Out of the 84 patients 52(62.91%) were females & 32(38.09%) were males. Generally, gall stone disease is considered to be female dominant disease.

**Table No.1: Percentage of Male to female ratio.**

Total	84
Male	32 (38.09%)
Female	52 (62.91%)

Gall stone disease is considered to be a disease of overweight and fatty females of middle age. People of BMI less than 18.5 are under weight, 18.5 to 25 are of normal weight and having BMI above 25 are overweight. Only people with BMI 30 and above are labeled as obese. 54(64.28%) patients were Obese/overweight. 30(35.71%) patients were Non-obese and having BMI calculated less than 25.

**Table No.2: Percentage of overweight patients.**

Total	84
Obese	54 (64.28%)
Normal	30 (35.71%)

58 cases (69.04%) were diagnosed to have chronic cholecystitis and 26 as acute cholecystitis. Out of 26 cases of acute cholecystitis, complications were seen in 7 patients (10%). Among the complicated cases, empyema was noted in 4 patients and peri-cholecystic abscess in 2 patients and one with mucocele.

**Table No.3: Presentation of patients.**

Total	84
Chronic cholecystitis	58 (69.04%)
Acute cholecystitis	19 (20.06%)
Acute cholecystitis with complications	7 (10%)

Surprisingly, in males, proportion of complicated acute cholecystitis was significantly higher in non-obese patients (21%) as compared to obese (7%) with significant statistical difference. According to our study, complicated acute cholecystitis seen in a much lower percentage in males. It seems to be that obesity in males act as some sort of barrier to cause complications. On the other hand there was no significant statistical difference between female non-obese & obese patients. The rate of complicated acute cholecystitis is almost equal in obese and non-obese females.

## DISCUSSION

Obesity is on rise like an epidemic in developed world. Its prevalence is increasing in developing countries due to westernisation of lifestyle and change in dietary habits. The common perception in this part of the world is that obesity is characteristic of the developed countries. Recent research has revealed an alarming rise in the incidence of obesity globally including Asia and Africa. 2001 WHO report reveals obesity has reached almost epidemic proportions globally, with more than 1 billion adults overweight and at least 300 million of them clinically obese and is considered to be bigger health problem than smoking. It has become a major contributor to the health system globally. In developing countries, it coexists with under-nutrition, obesity is considered as a complex condition, with serious social and psychological dimensions, effecting virtually all ages, sex and socioeconomic groups. Increase in weight of a person is the result of several interrelated factors; these include environmental, genetic, and behavioral factors. Modern life has significantly affected daily life, by making both living and working conditions more relaxed. People tend to spend more hours sitting in front of televisions or computers as compare to outside, burning fewer calories, instead of engaging in healthy physical activity<sup>21</sup>. Common belief of many common people as well as health professionals that obesity is simply the result of a lack of will power and an inability to change eating habits is no longer defensible. Obesity and over weight is a result of more complex interaction of environmental and genetic factors. Now days,

popular current hypothesis is that in most people, obesity is the interaction of the environment and a genetic predisposition to accumulate excess adipose tissue. Usually, both the environmental factors and genetic factor must be present for obesity to occur. Recent evidence shows that animals infected with certain viruses develop obesity. This also challenged the hypothesis that obesity is almost always a product of a genetic predisposition. One or more of these viruses may contribute to obesity in humans, but additional research must be done<sup>22</sup>.

Body Mass Index (BMI) is a simple criterion of weight-for-height that is commonly used to classify underweight, overweight and obesity in adults. It is defined as the weight in kilograms divided by the square of the height in metres ( $\text{kg/m}^2$ ). There are different criteria to determine weight abnormalities and obesity using BMI as tool. According to WHO classification BMI from 18.5 to 24.9 is considered normal, from 25 to 29.9 is considered overweight, from 30 to 34.9 is class 1 obesity, from 35 to 39.9 is class 2 obesity and 40 and above are considered as class 3. 66.7 percent of American population are considered overweight or obese, 34.3 percent were considered obese, and 5.7 percent were considered to have extreme obesity. Excess weight, especially obesity affects almost every aspect of health, from mood, memory, reproductive to respiratory system. Obesity increases the risk of several debilitating and deadly diseases like cardiac disease, diabetes and some malignancies. It does this through a variety of mechanisms; some are straightforward as the mechanical stress of carrying extra weight and some involving complex hormonal and metabolic changes. Obesity has a negative effect on the length and quality of life. Weight loss can reduce some obesity-related risks. Losing as little as 5 to 10 percent of body weight offers meaningful health benefits to people who are obese even if they never achieve their "ideal" weight<sup>23</sup>. Obesity is one of the risk factors of Gall-stone disease. The most common, and the only type associated with obesity, is the cholesterol gall-stone which consists mainly of accretions of cholesterol crystals around a nucleus. The other gallstone type, the pigment stone, is less frequently seen, contains larger amounts of calcium, and is usually associated with chronic haemolytic states and bacterial infections rather than with obesity<sup>24</sup>. Although obesity is an established risk factor for cholesterol gallstones in both genders, the association of gallstone disease with obesity tends to be found less consistently in men than in women<sup>25</sup>. Similarly, in our study, more than 62 percent patients were females. Obesity is a significant risk factor for gallbladder disease, particularly in women. In an early study, the mean gallstone prevalence in moderately obese Caucasian American women was 31 percent compared with 10 percent in the normal weight control group<sup>26</sup>. Several studies that

found a positive relation between body mass index (BMI; in  $\text{kg/m}^2$ ) and gallstone disease in women failed to show such an association in men<sup>27</sup> which raises the possibility that men may be less liable to gallstone formation associated with obesity because they may have more lean body mass than women<sup>28</sup>. The supersaturated bile in the gall bladder of obese subjects may account for this phenomenon<sup>29</sup>. Obesity increases the biliary secretion of the cholesterol, by increasing in the HMG CoA reductase activity<sup>30</sup>. In our study 54(64.28%) patients were Obese/overweight 30(35.71%) were Non-obese. Although there is increased incidence of Gall-stones in obese people but there is no such correlation between severities of cholecystitis with obesity. This was the outcome of our study as well. There was increased incidence of complicated Gall stone disease in non-obese male patients as compared to obese males, although this difference was insignificant in females. A possible explanation is that the body fat may have a protective effect on the inflammatory process of cholecystitis.

## CONCLUSION

Gall stone disease is associated with obesity. Contrary to common belief, complication rate in obese males is less as compared to males of normal weight. While in females, no such difference is noted in complication rate of gall stone disease between obese and non-obese males.

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

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Emphasize the new and important aspects of the study and conclusions that follow from them.

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**RECOMMENDATIONS**

When appropriate may be included.

**ACKNOWLEDGMENTS**

List of all contributors who do not meet the criteria for Authorship, such as a person who provided purely technical help, writing assistance or department chair who provided only general support. Financial & Material support should be acknowledged.

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