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Guidelines and Instructions to Authors i-ii
Population as an impediment in economic development or population as a human resource? Different countries have followed varied examples and become models of development and prosperity, thus raising the living standard of their people.

We unfortunately, messed up pretty badly on the population front, too, and turned what could have been our best asset into our biggest disadvantage. Today, Pakistan is the sixth largest country of the world population is the sixth largest country of the world population wise but our social development indicators are the lowest.

We cannot feed or cloth or educate our population. Any policy initiative faces a daunting challenge of massive number of people and becomes a non starter. Like other areas, we sell this disadvantage to the world and get foreign aid in return. From the United Nations to USAID to DFID, the entire world is keen to help us get our priorities right and for decades now.

But aside from the world of figures and slogans like reproductive health, birth spacing, women empowerment.

Pakistan, world’s sixth largest populated country, is still facing a high growth rate – 2.2 percent and moving quite slow in controlling the increasing population. The progress is described as ‘modest’.

Among the top ten contributors to world population growth during 1995-2000, Pakistan stood third in absolute number, and was on the top in growth rate. According to global projections, Pakistan was at number 13 with 40 million people in the 1950 while it reached at number seven in the world in 1996 with 140 million people.

United Nations’ Population Division projections show Pakistan as the third largest populated country in the world by 2050 with 357 million people, leaving behind America and following India and China.

An effective population policy must address reduction in the rate and incidence of unwanted fertility, reduction in demand for big families, and large investment in adolescents.

Population planning should not be taken as a clinical issue but as a social issue. The current growth rate of Pakistan is 2.2 percent, which ideally should be in one digit. It was five percent in the 1960s. Population planning programme remained neglected in Ziaul Haq’s regime. “We need to learn from Bangladesh.”

Pakistan’s population control framework started in 1965 with the creation of population welfare department at the federal level. This is known as the best days of the programme, from 1965 to 1969, during the era of Ayub Khan.

Religious parties protested against family planning, playing an important role in ending Khan’s rule. Pakistan launched one of the first population control programmes in the late 1950s, yet it has lagged far behind other countries in effective implementation over the past five decades. It never had an effective and comprehensive family planning policy till 2002.

Based on fertility trends of the 1990s, Population Policy 2002 projected to bring down fertility rates by 2020. The National Population Policy 2010 draft, which is yet to be approved by parliament, seeks population stabilization goal through early completion of fertility transition and facilitates realization of demographic dividend by linking fertility transition process with skill promotion and employment generation policies.

The policy repositions family planning from health perspective and focuses on the attainment of Millennium Development Goal of reducing maternal mortality by two third by 2015.

Pakistan started adapting the contraceptives and related surgeries after 1994’s International Conference on Population Development in Cairo. From 2002, the country created provincial level secretariats and ministries for population welfare.

The federal population ministry was devolved after the 18th Amendment in the Constitution, making population a provincial subject. However, the federal government would continue to financially support these departments and ministries by 2015.

“Policies and strategies are not very effective because people are not fully aware of the issue.”

The ratio of contraceptive adoptability is 34 percent at the moment. According to him, low use of contraceptives, shyness to adopt family planning methods, want of a male baby and religious factors are some of the challenges in achieving the targets. “The subject of reproductive health and population should be included in school and college level syllabus,” he suggests, adding, “In Punjab, the population welfare department is running 1500 male and female mobilization centres providing training.

Pakistan obtained demographic dividend” in the 1998 census, which means people who earn are more in number than the beneficiaries. Unfortunately, Pakistan has lost the fruits of this dividend. Population is growing at the rate of 3.2 million every year, according to official statistics.

Pakistan is losing this one-time mothers die in Pakistan every day due to pregnancy complications. “Almost 60 percent couples of Pakistan want family planning while 30 percent are able to meet this task. Pakistan’s drop out ratio of couples for family planning is highest in the subcontinent due to poor services.”
Microalbuminuria in Patients with Essential Hypertension
Salma Kadir, Musarat Jehan Baloch and Nazir Ahmed Memon

ABSTRACT

Objective: To determine the microalbuminuria in patients with essential hypertension.
Study Design: Cross-sectional multidisciplinary study.
Place and Duration of Study: This study was conducted at the Tertiary Care Hospitals and the data was also gained from private clinics for six months during 2018-2019.
Materials and Methods: All the patients of 30-70 years of age and either gender, having hypertension (systolic blood pressure -SBP ≥140 mmHg and/or diastolic blood pressure - DBP of ≥90 mmHg) were recruited and enrolled in the study. Blood pressure was measured two times at 5 minutes interval while the mean arterial pressure (MAP) was also calculated. The urinary examination was done among relevant individuals for microalbuminuria by collection of urine specimen and the micro albumin: creatinine ratio <30mg/g considered as normal albuminuria while between 30-300mg/g was microalbuminuria whereas the frequency / percentages (%) and means ±SD computed for study variables.
Results: During 6 month study period total 120 patients were explored and study. The mean ± SD for age (years) of population was 52.31±6.62. Regarding gender, male 78 (65%) and 42 females (35%), residence as urban 48 (40%) and rural 72 (60%), family history of hypertension 53 (44.2%), diabetes mellitus 84 (70%), obesity 55 (45.8%) and microalbuminuria 79 (65.8%).
Conclusion: The presence of microalbuminuria in hypertensive individuals shows positive association and should be considered as timely screening tool for microalbuminuria in patients with essential hypertension.
Key Words: Hypertension, microalbuminuria and proteinuria.

INTRODUCTION

Hypertension is a disorder that affect majority individuals worldwide and raises the risk for the development of cardiac, cerebral and kidney complications. The majority of individuals have essential hypertension which is defined as increase in blood pressure (BP) of unknown cause despite the widely identified crises related to uncontrolled blood pressure, the disease remains inadequately treated in most individuals mainly due to its asymptomatic appearance even when it progressively involves multiple systems of the body. The term microalbuminuria is defined as urinary albumin excretion (UAE) rate higher than normal, the lowest detection limit of proteinuria as estimated by standard laboratory procedure in the absence of urinary tract infection and illness including acute myocardial infarction. Detection of UAE in the early morning urine sample comprises as an ideal test for screening and overnight urine collection might be the best choice for monitoring urinary albumin. The hypertension and microalbuminuria commonly associated while the mechanism is controversial but is thought to be a kidney manifestation of generalized vascular endothelial dysfunction and strongly related with increased cardiovascular risk. It is well known that both that coexisting hypertension exacerbates and impairs renal function and somehow results in a markedly increased risk of uncontrolled hypertension. It has been recommended that patients with hypertension should be tested for albuminuria at the time of initial diagnosis and yearly thereafter because screening for the earliest stages of renal damage and controlling hypertension can help preventing more severe kidney disease, so the blood pressure monitoring and control is important especially after the onset of kidney impairment. Thus, the present study was conducted to see the correlation between microalbuminuria and hypertension in essential hypertension because early identification and management can save the patient to acquire life threatening complications associated with hypertension.

MATERIALS AND METHODS

Six months’ hospital based cross-sectional multidisciplinary study (2018-2019) was conducted at...
tertiary care hospitals and the data was also gained from private clinics. All the patients of 30-70 years of age and either gender, having hypertension (systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg) were recruited and enrolled in the study. Blood pressure was measured two times at 5 minutes interval while the mean arterial pressure (MAP) was also calculated whereas the known cases of chronic kidney diseases, urinary tract infection, liver cirrhosis, already on hemodialysis and the patients having malignancy and already on immunosuppressive therapy and the pregnant and lactating ladies were considered in exclusion criteria. The urinary examination was done among relevant individuals for microalbuminuria by collection of urine specimen and examination was done among relevant individuals for microalbuminuria. The data was collected on pre-designed proforma and analyzed in SPSS to calculate the frequencies and percentages.

RESULTS
Table No.1: The Demographical and Clinical Profile of Study Population

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Frequency (N=120)</th>
<th>age (%)</th>
</tr>
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<tbody>
<tr>
<td><strong>Age (yrs)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-39</td>
<td>17</td>
<td>14</td>
</tr>
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<td>40-49</td>
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<td>60-70</td>
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<td>21.7</td>
</tr>
<tr>
<td>70+</td>
<td>20</td>
<td>18</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>78</td>
<td>65</td>
</tr>
<tr>
<td>Female</td>
<td>42</td>
<td>35</td>
</tr>
<tr>
<td><strong>Residence</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>48</td>
<td>40</td>
</tr>
<tr>
<td>Rural</td>
<td>72</td>
<td>60</td>
</tr>
<tr>
<td><strong>Family History Of Hypertension</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>53</td>
<td>44.2</td>
</tr>
<tr>
<td>No</td>
<td>67</td>
<td>55.8</td>
</tr>
<tr>
<td><strong>Diabetes Mellitus</strong></td>
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<td></td>
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<tr>
<td>Yes</td>
<td>84</td>
<td>70</td>
</tr>
<tr>
<td>No</td>
<td>36</td>
<td>30</td>
</tr>
<tr>
<td><strong>Obesity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>55</td>
<td>45.8</td>
</tr>
<tr>
<td>No</td>
<td>65</td>
<td>54.2</td>
</tr>
<tr>
<td><strong>Microalbuminuria</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>79</td>
<td>65.8</td>
</tr>
<tr>
<td>No</td>
<td>41</td>
<td>34.2</td>
</tr>
<tr>
<td><strong>Mean ± SD</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP</td>
<td>155.72±8.65</td>
<td></td>
</tr>
<tr>
<td>DBP</td>
<td>99.61±5.72</td>
<td></td>
</tr>
<tr>
<td>HBA1C</td>
<td>8.84±2.86</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>31.25±2.43</td>
<td></td>
</tr>
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</table>

During one-year study period total fifty patients were explored and study. The mean ± SD for age (years) of population was 52.31±6.62. The demographical and clinical profile of study population is presented. Table 1.

DISCUSSION
The high prevalence of microvascular complications of hypertension means that the number of individuals with end stage renal disease due to hypertension will also increase dramatically. The risk factors related to microalbuminuria were hypertension and poor glycemic control and is now widely appreciated that the excretion of even small amounts of protein in urine may leads to life threatening future complications such as cardiovascular and cerebrovascular disorders and progression in renal dysfunction. The literature has been shown the association between microalbuminuria and high levels of blood pressure and Ahmedani MY, et al reported that microalbuminuric patients have higher systolic and diastolic blood pressure which has been also endorsed by other authors. Similarly Afkhami-Ardehani M, et al and Varghese A, et al also reported correlation between the microalbuminuria and the high blood pressure. Svensson M, et al identified high blood pressure increases the risk of acquiring nephropathy. Our study also observed the significant correlation between hypertension and microalbuminuria and the majority individuals have uncontrolled diabetes mellitus. Thus, the hypertension is probably both a cause and presentation of diabetic nephropathy. The former literature has observed that detecting and monitoring of patients with hypertension is necessary because its timely treatment can prevent nephropathy. The microalbuminuria in hypertensive individuals suggests that high blood pressure is associated with proteinuria. Hence, high prevalence of microalbuminuria in patients with essential hypertension must alert the clinicians regarding the occurrence of sub-clinical chronic kidney disease in our population and the preventive strategies for reduction of the burden of chronic kidney disease should be designed by early identification and timely management of hypertension.

CONCLUSION
The existence of microalbuminuria in hypertensive individuals shows positive association and should be considered a timely screening tool for microalbuminuria is essential for proper treatment and prevention of future cardiovascular or cerebrovascular events by control of hypertension.

Author’s Contribution:
Concept & Design of Study: Salma Kadir
Drafting: Musarat Jehan Baloch
Data Analysis: Nazir Ahmed Memon
Revisiting Critically: Salma Kadir, Musarat
CONFlict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES


Penetrating Trauma in Children, Our Experience
Muhammad Ramzan¹, Abid Hameed Sheikh¹, Sofia Mustafa¹, Faseeh Abid² and Muhammad Zubair¹

ABSTRACT

Objective: To study the characteristics of patients, management, and outcomes of penetrating thoracic and abdominal trauma in children.

Study Design: Descriptive case series study.

Place and Duration of Study: This study was conducted at the Paediatric Surgery Department Bahawal Victoria Hospital Bahawalpur, from April 2016 to April 2020.

Materials and Methods: A total of 93 patients with penetrating to abdomen and thorax were admitted in pediatric surgery department from April 2016 to April 2020. These patients were evaluated with reference to patient’s biodata, their clinical presentation, mode of trauma, management and their outcome.

Results: Out of 93 patients admitted to pediatric surgery department with penetrating thoraco abdominal trauma 37 were due to fall from height especially from trees, 27 due to road traffic accidents, 13 because of stabbing and 16 due to firearm injuries. The mean age was 9.73 ± 4.31 [1–16] years, sixty-four were wounded in abdomen, 19 in thorax and 10 in both the abdomen and thorax. Fifty-six patients underwent some sort of surgical intervention and remaining 37 patients were conservatively managed. The hospital stay on a mean was 2.47± 3.13 days for pts managed conservatively and 7.37±11.43 days for pts with surgical intervention.

Conclusion: The penetrating trauma to abdomen and thorax significantly differ in incidence being more in abdomen, surgical management is the main management option though; conservative may be the other option but with vigilant monitoring. Along with development of management strategies, emphasis on prevention of trauma must be considered.

Key Words: penetrating injury, abdomen, thorax


INTRODUCTION

Trauma is considered the major cause of pediatric morbidity, and mortality¹. The majority (80-90%) of injuries in pediatric patients are because of blunt trauma whereas penetrating injuries are (10 – 20%) very less²,³. However, the penetrating injuries result in increased mortality as compared to blunt trauma among all ages⁴. Recently, the incidence of penetrating trauma is increasing among all age groups and children⁵. As the children has thin body wall and smaller size the injuries to internal organs are more serious⁶. The penetrating injuries to abdomen are more frequent as compared to thorax but the mortality is more in thoracic trauma⁶,¹. The assessment and managing a penetrating trauma is challenging and it needs rapid action in assessing and doing some intervention⁷.

Penetrating injury may be defined as, an injury caused by physical trauma to the skin and tissues by a foreign object like gun, knife or some sharp object by mechanical penetration⁶,⁴,⁵. Penetrating injury to abdomen may involve some breach in peritoneal cavity, like gunshot and stabbing wounds and fall from height and road traffic accidents⁸.

As with the rest of the world, possession of guns and stabbing objects by children is also increasing in Pakistan⁹. A poor socioeconomic status, lack of education, exposure to the exaggerated media, and the increased availability of these objects (motor vehicles especially motor bikes to children) may be the reason for increased number of penetrating injuries⁸.

MATERIALS AND METHODS

After taking approval from hospital ethical committee all the patients with penetrating injuries to abdomen and thorax admitted to pediatric surgery departments were included in the study. Patients with poly trauma and blunt trauma abdomen/thorax were excluded. All patients (both male and female) with age upto 16 years
were included in study. A total of 93 patients met the criteria between April 2016 to April 2020. All the record of patients, mode of trauma, investigations and management plan (conservative / surgical exploration), duration of hospital stay and outcome were noted. After resuscitation and initial management, patients were immediately evaluated by radiological department for X-ray abdomen (supine/ erect), FAST (focused abdominal sonography for Trauma), x-ray chest anteroposterior and lateral view and abdomen / thoracic computed tomography (CT) scan as needed.

Data regarding findings of physical examination, blood tests, and/or results of radiologic study were obtained. If the patient had only superficial injury, means, did not breach peritoneum and pleura, they were managed by wound care and wound closure. Rest of the patients were prepared for exploration. In cases of abdominal trauma exploratory laprotomy was performed. Whereas in thoracic trauma initial tube thoracostomy performed for pneumothorax/ hemothorax/hemopneumothorax. Formal thoracotomy was reserved for ongoing blood loss in thoracostomy tube. Findings of visceral injuries i.e. liver, spleen, pancreas, mesentery bowel (small/large) and stomach were noted and recorded. All patients were monitored post operatively for outcome and duration of hospital stay.

Statistical analysis was done by using SPSS version 11.5 software. Analysis done regarding injuries type, demographic characteristics i.e. age of patients and gender, clinical presentations of patients, their management and outcome the expression of data was as mean ± SD with a confidence interval of 95%. Further analysis done by using t test, Chi square test. P value of ≤ 0.05 considered to be significant.

RESULTS

Data of 93 patients was analyzed. The mean age of patients was 9.73 ± 4.31 [1–16] years. Pts with abdominal injured have a mean age 9.98 ±3.74 (1-16), whereas in thoracic trauma mean age was 9.58 ±3.83(1-16) and in both abdomino thoracic pts age was 9.87 ±4.17(1-16). There was no statistical difference in age group of patients. As regards the gender, male patients were 78(84%) and female were 15(16%) with a significant statistical difference. Stabbing (trauma due to knife, penetrating trauma by sharp devices and falling over some sharp object) was the reason in majority of patients i.e. 64 (69%). Twenty patients (21.9%)were due to accidental injuries i.e. road traffic accidents, and 9 (9%) patients were due to gunshot injuries (table 1). Thirty-seven (40%) patients were managed conservatively and rest 56(60%) patients underwent surgical exploration.

All the patients were investigated as complete blood count, x-ray imaging and cat scan as required among all patients. Cat scan was done in 54% patients among whole study group of thoracic injury, 65% of patients with abdominal injury and 68% of both abdomen and thorax injury. USG imaging were done from 64% of patients among whole study group, 29% of patients with thorax trauma, 57% of patients with trauma to abdomen, and 39% of patients having both thoracic and abdominal trauma.

In patients of thoracic trauma, 10 were managed by tube thoracostomy only, two patients underwent thoracotomy with one having gunshot injury having bleeding, found lung parenchymal injury and 2nd due to foreign body lying inside thoracic cavity. Seven patients managed conservatively having rib fractures, minimal surgical emphysema and a patient with flail segment.

![Figure No. 1: Different cases of penetrating wounds presented at the hospital with and surgical interventions](image)

| Table No.1: The characteristics of penetrating trauma in abdomen and thorax |
|-----------------|-----------------|-----------------|
|                | Abdominal | Thorax | Abdominothoracic |
| Gender          |            |       |                 |
| Male            | 55         | 15    | 8               |
| Female          | 9          | 4     | 2               |
| Age (Year)      | 9.98 ±3.74(1-16) | 9.58 ±3.83(1-16) | 9.87 ±4.17(1-16) |
| Mechanism of Injury |            |       |                 |
| Accidental      | 13         | 4     | 3               |
| Stabbing        | 44         | 13    | 7               |
| Gunshot         | 7          | 2     | 0               |
| Management      |            |       |                 |
| Conservatively  | 27         | 7     | 3               |
| Surgery         | 37         | 12    | 7               |
| Stay at Hospital (Days) | 5.33 ±7.74 (1–23) | 3.63 ±4.11(1-13) | 3.47 ±4.11(1-14) |
In patients of abdominal and abdominothoracic injuries, thirty patients were managed conservatively by wound care, and vital monitoring. Forty-four patients underwent surgical exploration (Figure 1).

Stabbing (trauma due to knife, penetrating trauma by sharp devices and falling over some sharp object)

Among these 11 were having intestinal perforations with mesenteric bleed, 7 liver injuries, 4 spleens, 1 gallbladder and 1 with intraperitoneal urinary bladder injury and 1 patient with diaphragm rupture (Table 2). Nineteen patients had no visceral injuries, only hemoperitoneum and peritoneal breach.

Table No. 2: Frequency of organs affected

<table>
<thead>
<tr>
<th>Organs affected</th>
<th>No. of Patients</th>
</tr>
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<tbody>
<tr>
<td>Liver</td>
<td>7</td>
</tr>
<tr>
<td>Bowel</td>
<td>11</td>
</tr>
<tr>
<td>Gall bladder</td>
<td>1</td>
</tr>
<tr>
<td>Spleen</td>
<td>4</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>1</td>
</tr>
<tr>
<td>Diaphragm</td>
<td>1</td>
</tr>
<tr>
<td>Unaffected organs</td>
<td>19</td>
</tr>
</tbody>
</table>

Table No. 3: Duration of hospital stay

<table>
<thead>
<tr>
<th>Duration (days)</th>
<th>Conservative</th>
<th>Surgical Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.47± 3.13</td>
<td>7.37±11.43</td>
<td></td>
</tr>
</tbody>
</table>

The mean duration of hospitalization was 4.77± 6.84 (1–23) days for whole study patients, 3.63 ± 4.11(1-13) days for thoracic trauma, 5.33 ± 7.4 (1–23) days for abdominal trauma. And 3.47 ± 4.1114 days for both abdomino thoracic trauma. There was no statistical difference in hospital stay among different groups however when compared to hospital stay among conservative and surgical intervention the findings were as under i.e. with conservative treatment 2.47± 3.13 days and surgical intervention was 7.37±11.43 days which was quite significant(P<0.013) table 3. the study group with operation had a longer hospitalization as compared to conservative group.

DISCUSSION

Though a lot is being done to educate masses regarding children protection from trauma, still trauma is the main cause of mortality and morbidity. The majority (80-90%) of injuries in pediatric patients are because of blunt trauma whereas penetrating injuries are (10 – 20 %) very less, with increased number of motor vehicles and heavy traffic in use the road traffic accidents has increased.

In our study male population was more affected than female. Same is the case in a study conducted by Abri B et al and Bolekon ME et al i.e. the incidence due to penetrating injuries was found to be six fold greater in males than that in females. This shows that boys are more indulged in such activities like violence and other such activities resulting in injuries. Most of the fatal cases are due to children, mainly males, below 16 years of age.

Penetrating abdomen / thorax trauma is commonly seen among teenagers and adolescent and is mostly intentional (e.g., gunshot /knife wounds). In our study it is a bit different which show stabbing due to fall from height and accidental trauma are more common (70 %). While bowel was most often traumatised in our study, Abri et al. reported liver, and spleen were injured more often by Bryan A Cotton et all in his study noted the bowel affected the most followed by liver and spleen. CT scan was done in most of the patients in our study to find the solid organ injury. Similarly, Bryan A Cotton stated in his study that CT scan was advised the most often for evaluation of wounds in the hepatic region to decide about exploration. Forty percent of patients in our study was managed conservatively. Similarly, a study conducted showed successful management by conservative approach in thoracic and abdominal trauma in majority of patients. The hospital stay was very less in conservative approach as compared to surgical intervention with significant p-value in our study. This approach was in accordance with another study showing shorter hospital stay.

CONCLUSION

The penetrating trauma to abdomen and thorax significantly differ in incidence being more in abdomen. surgical management is the main management option though; conservative may be the other option but with vigilant monitoring. Alongwith development of management strategies, emphasis on prevention of trauma must be considered.

Author’s Contribution:
Concept & Design of Study: Muhammad Ramzan
Drafting: Abid Hameed Sheikh, Sofia Mustafa
Data Analysis: Faseeh Abid, Muhammad Zubair
Revisiting Critically: Muhammad Ramzan, Abid Hameed Sheikh
Final Approval of version: Muhammad Ramzan

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

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3. Sandler G, Leishman S, Branson H, Buchan C, Holland AJ. Body wall thickness in adults and
To Determine the Frequency and Pattern of Common Electrolyte Abnormalities in Children Presenting with Acute Gastroenteritis

Irfan Ullah¹, Irfan Khan¹, Muhammad Shafiq¹, Farida Sherazi², Khalid Khan¹ and Khalil Ahmad³

ABSTRACT

Objective: To Determine the frequency and pattern of common electrolyte abnormalities in children presenting with acute gastroenteritis.

Study Design: Cross sectional study.

Place and Duration of Study: This study was conducted at the pediatric department Qazi Hussain Ahmad medical complex Nowshera from July 2019 to December 2019.

Materials and Methods: In this study 109 children were included. About 5 ml Blood was taken and sent to the laboratory for assessment of electrolyte abnormalities including hypo- & hyper-natremia, hypo- & hyper-kalemia.

Results: In our study, the mean age of children was 4 ± 5.57 years. There were 56% male and 44% female children. The frequency of pattern of common electrolyte abnormalities like hyponatremia was 28%, hypernatremia was 19%, hypokalemia was 12%, hyperkalemia was 7% among children presenting with acute gastroenteritis.

Conclusion: Our study concludes that frequency of pattern of common electrolyte abnormalities like hyponatremia was 28%, hypernatremia was 19%, hypokalemia was 12%, hyperkalemia was 7% among children presenting with acute gastroenteritis.

Key Words: Pattern of common electrolyte abnormalities, children, acute gastroenteritis.

INTRODUCTION

Acute gastroenteritis in pediatrics is the global health concern. It happens to occurs in 1.5 billion diarrhea episodes and 3 million deaths every year.¹ A wide range of intestinal bacteria can cause acute pediatrics diarrhea.² The main pathogens and protozoan isolated from stool samples of children aged <5 years are diarrhea genic Escherichia coli, Salmonella spp., Shigella spp., Yersinia spp. & Campylobacter spp., and Giardia intestinalis, Entamoeba histolytic & Cryptosporidium spp., respectively. Additionally, the representatives of four viral families i.e. rotaviruses (Reoviride), noroviruses & sap viruses (Caliciviride), human astroviruses (Astroviride) and adenoviruses subgenus F (Adenoviride), are mostly isolated in childhood acute gastroenteritis.³ Dehydration, electrolyte imbalances and renal failure are major complications of acute gastroenteritis. Since an oral rehydration therapy program has been initiated by WHO, the mortality rate has substantially declined. Apart from dehydration, electrolyte abnormalities are one of the major concerns in patients with acute gastroenteritis. Disorders in the electrolyte composition can have serious consequences and are associated with morbidity and mortality. Many pediatricians believe that laboratory studies, including Blood Chemical Analysis (BCA), are not usually necessary to assess children with acute diarrhea. However, it has been reported that serum electrolyte panels were useful in children receiving intravenous (IV) fluid therapy for their dehydration. On the other hand, other pediatricians express contradictory comments on the aforementioned finding.⁷⁹

They believe that many electrolyte abnormalities would resolve if children with acute gastroenteritis are appropriately rehydrated. The common cause of hospitalization of pediatrics age group due to acute gastroenteritis is greater gradations of dehydration severity supplemented by social factors. The accurate assessment of dehydration degree among infants
&children is essential for appropriate diagnosis and treatment. Under-estimation of dehydration raises morbidity & mortality, while over-estimation may cause unsuitable care and financial expenses. In one previous study on children with acute gastroenteritis 50% of children presented with moderate dehydration, 28.3% with mild and 22.6% with severe dehydration. Metabolic acidosis was recorded in 54.7%, hyponatremia in 17%, hypernatremia in 9.4%, hypokalemia in 22.6%, hyperkalemia in 3.8% and azotemia in 22.6%. In another study conducted by Ahmad MS the frequencies of the various patterns of electrolyte abnormalities were recorded as 26.9% hyperkalemia, 17.3% hypernatremia, 10.6% hyponatremia and 7.7% hypokalemia. This study was designed to estimate the frequency and pattern of electrolytes abnormalities in pediatrics presenting acute gastroenteritis. As mentioned above, blood analysis is generally avoided in children with acute gastroenteritis and chemical including electrolyte abnormalities if present can play a crucial role in the management plan and determine the overall morbidity and mortality of children who develop acute gastroenteritis. This study will provide us with local data and the findings will be shared with other pediatricians in local community and suggestions will be made regarding future research and implementation. Further recommendations will be made regarding screening of electrolytes level in pediatrics.

MATERIALS AND METHODS

This Cross sectional study was done at Qazi Hussain Ahmad medical complex Nowshera from July 2019 to December 2019. Duration of study was six months. Sample Size109 cases was estimated keeping confidence level of 95%, and proportion of hypokalemia 7.7% in children with acute gastroenteritis, and adjusting 5% margin of error. Sampling technique used was Non-probability, consecutive sampling. All children presenting acute gastroenteritis were included. It was defined as Passage of three or more loose or watery stools in a 24 hours period for less than 14 days. A loose stool being one that would take the shape of the container as given by history both genders (male & females) and age between one month and five years were included in the study. Children with History of use of steroids in the last one month and five years were included in the study. This study was done after taking authorization from the hospitals’ ethical & research committee. Children aged less than 5 years, both gender, with acute gastroenteritis fulfilling the selection criteria were recruited for the study. Main aim and benefits of research project were clarified to all the parents and the informed written consent taken from them. All children were evaluated for complete history and clinical examination. A 5 ml venous blood sample was taken from all the children and sent to the laboratory of the hospital to detect electrolyte abnormalities including hyponatremia (sodium concentration < 135 meq/L), hypernatremia (sodium concentration > 150 meq/L), hypokalemia (potassium concentration < 3.5 mmol/L) and hyperkalemia (potassium concentration > 5.5 mmol/L). Data was stored and analyzed later on via SPSS version 20. The mean & SD were calculated for variables like age, serum analyses. Frequency (%) was calculated for variables like gender, electrolyte abnormalities (hyponatremia, hypernatremia, hypokalemia, hyperkalemia).

RESULTS

In this study, the mean age of patients was 4 ± 5.57 years. There were 12(11%) children of age between 1 month to 1 year, 48(44%) had age between 2 to 3 years and 49(45%) had age between 4 to 5 years. Out of 109children, 61(56%) children were male while 48(44%) children were female. (Table no 1). Regarding serum analyses, the mean serum sodium concentration was 145 ± 12.12 meq/L while mean Serum potassium concentration was 4.7 ± 3.84 mmol/L. (Table no 2). Patterns of electrolyte abnormalities among 109 patients were analyzed as 31(28%) patients had hyponatremia, 21(19%) patients had hypernatremia, 13(12%) patients had hypokalemia, 8(7%) patients had hyperkalemia.

<p>| Table No 1. Age &amp; gender Distribution (n=109) |</p>
<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>4 ± 5.57</td>
</tr>
<tr>
<td>1 month to 1 year</td>
<td>12 (11%)</td>
</tr>
<tr>
<td>2-3 years</td>
<td>48 (44%)</td>
</tr>
<tr>
<td>4-5 years</td>
<td>49 (45%)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>61 (56%)</td>
</tr>
<tr>
<td>Female</td>
<td>48 (44%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table No 2: Serum analyses (n=109)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
</tr>
<tr>
<td>Serum sodium(meq/L)</td>
</tr>
<tr>
<td>Hyponatremia ≤135 meq/L</td>
</tr>
<tr>
<td>Normal sodium 135-150 meq/L</td>
</tr>
<tr>
<td>Hypernatremia &gt;150 meq/L</td>
</tr>
<tr>
<td>Serum potassium (mmol/L)</td>
</tr>
<tr>
<td>Hypokalemia &lt;3.6 mmol/L</td>
</tr>
<tr>
<td>Normal potassium 3.5-5.5 mmol/L</td>
</tr>
<tr>
<td>Hyperkalemia &gt;5.5 mmol/L</td>
</tr>
</tbody>
</table>

DISCUSSION

Our study shows that the frequency of pattern of common electrolyte abnormalities like hyponatremia was 28%, hypernatremia was 19%, hypokalemia was 12%, hyperkalemia was 7% among children presenting with acute gastroenteritis. Similar results were observed
in another study done by Ukarapol et al., in which 50% of children presented with moderate dehydration, 28.3% with mild and 22.6% with severe dehydration. Metabolic acidosis was recorded in 54.7%, hyponatremia in 17%, hypernatremia in 9.4%, hypokalemia in 22.6%, hyperkalemia in 3.8% and Azotemia in 22.6%.

Similar results were also observed in another study done by Ahmad MS in which the frequencies of the various pattern of electrolyte abnormalities were recorded as hyperkalemia (26.9%), hypernatremia (17.3%). Hyponatremia (10.6%), hypokalemia (7.7%). Similar findings were observed in another study conducted by Okposio MMIN which dehydration due to hyponatremia was the commonest cause of dehydration among children, accounting in about 60.5% children. Metabolic acidosis was diagnosed in about 59.5% children while hypokalemia was diagnosed in 44.3% children. But concentration of serum bicarbonates was disturbed considerably by the degree of dehydration (p = 0.001). In children age > 1 year and the presence of vomiting were significantly related to the hyponatremia (p = value < 0.05), while age of ≤ 1 year while the absence of vomiting was significantly related to the metabolic acidosis (p = value < 0.05).11,14

Such findings were also observed in a study by Shah et al., i.e. 56% children had electrolyte imbalance in Nepalese children. But, Ukarapol et al., found isotonatremic dehydration as more common. The reason in this difference was due to the variation in the reference range that was used as cut-off value in several studies. While the serum sodium concentration < 136 mmol/L was considered as hyponatremia. In one study, conducted by Ukarapol et al., who defined hyponatremia as serum sodium concentration < 130 mmol/L, a significant relationship was observed in hyponatremia & children aged >1 year, male children and also presence of vomiting. While Effiong et al., found frequency of hyponatremia was high with increasing age but insignificant for male gender. Dehydration because of hyponatremia occurs mostly in children less than five years old with gastrointestinal tract infections. Such cases are normally prescribed liquids containing less sodium concentration like water, juices, ginger ale, soda, or tea.15-19

Shah et al., also found similar results and reported 46% electrolyte imbalance and also high as 37.1% reported by Majeed et al. In our study, hypokalemia was observed was possibly because of greater loss of potassium through loose stool i.e. ≤100 meq/L potassium might be wasted in stools. Other risk factor for hypokalemia was malnutrition, but in our study, insignificant association was observed between hypokalemia and children weighed< 2 SD for age. The most description for this was that few children may have been misdiagnosed as having malnutrition; however, this may be because of acute diarrhea along with the dehydration which may cause the acute weight loss. The altered weight that was reinstated after the rehydration might be marginally higher than before diarrhea and perhaps do not meet the criteria for malnutrition i.e. < 2SD weight for age.15,20-22

The commonest clarifications of development of the metabolic acidosis among pediatric acute diarrhea are: reduced level of bicarbonate via stool, ketone production due to hunger, and production of lactic acid from reduced tissue perfusion in hypovolaemia. Reduced renal perfusion might also cause the reduced glomerular filtration rate that consecutively, leads to reduced excretion of hydrogen ions. However, few more studies found insignificant difference in level of serum bicarbonate in association with degree of dehydration.23-25

CONCLUSION

Our study concludes that frequency of pattern of common electrolyte abnormalities like hyponatremia was 28%, hypernatremia was 19%, hypokalemia was 12%, hyperkalemia was 7% among children presenting with acute gastroenteritis.

Author’s Contribution:
Concept & Design of Study: Irfan Ullah
Drafting: Irfan Khan, Muhammad Shafiq
Data Analysis: Farida Sherazi, Khalid Khan, Khalil Ahmad
Revisiting Critically: Irfan Ullah, Irfan Khan
Final Approval of version: Irfan Ullah

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

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Effect of Nuchal Cord on Perinatal Outcome and Relationship with Mode of Delivery

Seema Gul Salman¹, Maria Rafiq¹, Khalil Ahmad², Khalid Khan³, Irfan Khan³ and Irfan Ullah³

ABSTRACT

Objective: To compare perinatal outcome with mode of delivery in patients without Nuchal cord and those with Nuchal cords including single, double and multiple loops.

Study Design: Retrospective study

Place and Duration of Study: This study was conducted at the Gynae Department Gaju Khan Medical College Sawabi, Pakistan from January 2019 to June 2019.

Materials and Methods: This was a retrospective study of 303 single gestation term pregnancies with spontaneous labor. Patients were grouped as without Nuchal cord and those with Nuchal cord including single, double and multiple turns. These were compared with perinatal outcome and delivery mode.

Results: This study showed that Nuchal cord was not associated with neonatal death, a bad Apgar score (<7) at 1 and 5 min. However, cases with multiple cords were shown to be associated with meconium-stained liquor, neonatal admission in Intensive care, fetal distress and emergency C-section.

Conclusion: Nuchal cord with multiple turns was associated with fetal distress but without affecting Apgar scores. Nuchal cord was not associated with adverse outcomes and prenatal ultrasound for this purpose is not required.

Key Words: Nuchal cord, Perinatal outcome, Multiple loops, Apgar scores, Caesarian section.


INTRODUCTION

Nuchal cord is clinically controversial. The incidence can vary from 15–34%.¹ ² ³ It has been traditionally believed that it can cause compression of cord, bradycardia in the fetus, meconium-stained liquor and frequent lower Apgar scores at 1 and 5 minutes, respectively.² ³ However, it has been shown that it is not associated low Apgar scores at 5 minutes, increased caesarean sections, and admission to neonatal intensive care unit or perinatal mortality.³ ⁴ With wide availability of color Doppler Nuchal cord is increasingly being diagnosed but consensus guidelines have not been achieved regarding the management and counseling of such patients.² Additionally, the differences that may arise from variations in the number of Nuchal cord turns and their effect on management have also not been studied thoroughly.

This study was therefore carried out to compare perinatal outcome with mode of delivery in patients without Nuchal cord and those with nuchal cords including single, double and multiple loops, respectively.

MATERIALS AND METHODS

A retrospective study was carried out at Gynae Department Gaju Khan Medical College Sawabi, from January 2019 to June 2019 after approval from the Hospital’s Ethics Committee. Data regarding occurrence of Nuchal cord and the number of turns is recorded in the wards register for each patient. All patient data was reviewed from the register and they were grouped as no Nuchal cord, Nuchal cord one, two and multiple turns respectively. Inclusion criteria were all term (37 week of gestation) pregnancies and spontaneous labor. Exclusion criteria were based on preterm infants, multiple pregnancies and patients without active labor who had elective caesarean section. Other data recorded for the purpose of the study included fetus distress that would require emergent caesarean section or assisted delivery, neonatal intensive care admission and fetal death. Statistical analysis was done with SPSS version 23 using Chi-square, T test and Fisher’s exact test where appropriate. Results were considered statistically significant at p ≤0.05.

RESULTS

Overall incidence of nuchal cord was 20.8 %. Its incidence in terms of loop turns for 1, 2 and multiple
turns was 53 (17.5%), 8 (2.6%) and 2 (0.7%), respectively as shown in Table-1. Overall maternal age was 25.27 ± 0.141 years. Maternal age was statistically significant with p value 0.001 between the groups without nuchal cord and those with 1, 2 and multiple turns. Mean maternal age for the group without nuchal cord was 25.06 years and that for 1, 2 and multiple turns was 25.47, 29 and 29.5 years respectively. Parity was statistically significant with a p-value 0.001. Nulliparous women among the group without Nuchal cord were 89 (29.4%) and those with 1, 2 and multiple turns of cord were 53 (17.5%), 4 (1.3%) and 1 (0.3%), respectively. There were 151 (49.8%) multiparous women in the group without nuchal cord compared to 0, 4 (1.3%) and 1 (0.3%) women in the 1, 2 and multiple turns of cord groups respectively. Although fetal death was statistically significant at p-value 0.001 however there were a total of only 3 fetal deaths, 1 (0.3%) in the no nuchal cord group and 2 (0.6%) in the nuchal cord group with one each in the 1 and multiple turn groups respectively. Meconium stained liquor was statistically significant at p-value 0.024 with 57 (18.8%) patients in the group without nuchal cord and 11 (3.6%), 4 (1.3%) and 2 (0.7%) patients in the 1, 2 and multiple turn groups respectively. However, analysis within 1, 2 and multiple loops showed that greater loops were associated with presence of meconium stained liquor at the statistically significant p-value of 0.014. Apgar score <7 was statistically insignificant at 1 minute (p-value = 0.075) and 5 minutes (p-value0.286). There were 3 (1%) patients in the no cord group and 0, 4 (1.3%) and 1 (0.3%) patients in the 1, 2 and multiple turn loops groups respectively. This distribution for the 5-minute group was 3 (1%), 1 (0.3%), 0 and 1 (0.3%) patients for the cordless group and groups with 1, 2 and multiple turns respectively.

Table No.1: Details of incidence of nuchal cord

<p>| N (%) | Maternal age (Years) | Parity | Fetal Death | Meconium stained Liquor | Apgar score &lt;7 | Neonatal ICU admission | Fetal distress | Mode of delivery |
|-------|----------------------|--------|-------------|-------------------------|---------------|------------------------|---------------|-----------------|-----------------|
|       | 25.27 ± 0.141        |        |             | [p = 0.001]              | [p = 0.024]   | [p = 0.075]            | [p = 0.347]   | [p = 0.128]     | [p = 0.471]     |
|       | [p = 0.001]          |        | [p = 0.001] | [p = 0.001]              | [p = 0.024]   | [p = 0.075]            | [p = 0.347]   | [p = 0.128]     | [p = 0.471]     |</p>
<table>
<thead>
<tr>
<th>N (%)</th>
<th>No nuchal Cord N (%)</th>
<th>Nuchal cord 1 turn N (%)</th>
<th>Nuchal cord 2 turn N (%)</th>
<th>Nuchal cord 2 turn N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>25.06</td>
<td>25.47</td>
<td>25.47</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>53 (17.5%)</td>
<td>63 (20.8%)</td>
<td>63 (20.8%)</td>
<td>63 (20.8%)</td>
</tr>
<tr>
<td></td>
<td>2 (0.7%)</td>
<td>1 (0.3%)</td>
<td>1 (0.3%)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>8 (2.6%)</td>
<td>4 (1.3%)</td>
<td>4 (1.3%)</td>
<td>1 (0.3%)</td>
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<tr>
<td></td>
<td>1 (0.3%)</td>
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<td>1 (0.3%)</td>
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</tr>
<tr>
<td></td>
<td>115 (38%)</td>
<td>29 (9.6%)</td>
<td>29 (9.6%)</td>
<td>29 (9.6%)</td>
</tr>
<tr>
<td></td>
<td>18 (5.9%)</td>
<td>3 (1%)</td>
<td>3 (1%)</td>
<td>3 (1%)</td>
</tr>
<tr>
<td></td>
<td>13 (4.3%)</td>
<td>3 (1%)</td>
<td>3 (1%)</td>
<td>3 (1%)</td>
</tr>
<tr>
<td></td>
<td>138 (46.7%)</td>
<td>46 (15.4%)</td>
<td>46 (15.4%)</td>
<td>46 (15.4%)</td>
</tr>
<tr>
<td></td>
<td>178 (58.7%)</td>
<td>45 (14.9%)</td>
<td>45 (14.9%)</td>
<td>45 (14.9%)</td>
</tr>
<tr>
<td></td>
<td>178 (58.7%)</td>
<td>53 (17.5%)</td>
<td>53 (17.5%)</td>
<td>53 (17.5%)</td>
</tr>
<tr>
<td></td>
<td>49 (16.2%)</td>
<td>17 (5.7%)</td>
<td>17 (5.7%)</td>
<td>17 (5.7%)</td>
</tr>
<tr>
<td></td>
<td>13 (4.3%)</td>
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<td></td>
<td>13 (4.3%)</td>
<td>3 (1%)</td>
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</table>

<table>
<thead>
<tr>
<th>Mode of delivery</th>
<th>Spontaneous NVD</th>
<th>Emergent Cesarean</th>
<th>Instrumental</th>
</tr>
</thead>
<tbody>
<tr>
<td>p-value</td>
<td>0.098</td>
<td>0.09</td>
<td>0.836</td>
</tr>
<tr>
<td>as whole group</td>
<td>178 (58.7%)</td>
<td>49 (16.2%)</td>
<td>13 (4.3%)</td>
</tr>
<tr>
<td>p-value</td>
<td>0.471</td>
<td>0.09</td>
<td>0.836</td>
</tr>
<tr>
<td>Spontaneous NVD</td>
<td></td>
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</tr>
<tr>
<td>Emergent Cesarean</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Instrumental delivery</td>
<td>13 (4.3%)</td>
<td>3 (1%)</td>
<td>0</td>
</tr>
<tr>
<td>p-value</td>
<td>0.836</td>
<td>0.09</td>
<td>0.836</td>
</tr>
</tbody>
</table>
Neonatal ICU admission was not statistically significant as the p value was 0.347. A total of 115 (38%) neonates were admitted to ICU in the cordless group where 29 (9.6%), 3 (1%) and 2 (0.7%) patients were admitted to ICU in the 1, 2 and multiple turn loops groups respectively. Fetal distress was statistically insignificant with a p-value of 0.128. There were 18 (5.9%) patients with fetal distress requiring emergent C-section or instrumental delivery in the cordless group compared to 3 (1%), 1 (0.3%) and 1 (0.3%) patients in the 1, 2 and multiple loop turns groups, respectively. However, within turn loops statistical significance was achieved as more of the turn loops i.e. 3 was associated more with requirement for emergent treatment with p-value of 0.001. Mode of delivery was statistically insignificant as the p-value for groups without cord and that with nuchal cord as a whole was 0.22. Patients that delivered with spontaneous NVD in the cordless group were 178 (58.7%) compared to 45 (14.9%), 7 (2.3%) and 1 (0.3%) patients in the 1, 2 and multiple turn groups respectively. The group with nuchal cord was associated with more spontaneous vaginal deliveries than the group without nuchal cord, p-value 0.001. However, 1 and 2 turns were associated with greater spontaneous NVDs 45 (71.4%) and 7 (11.1%) whereas multiple turns sub group was associated with less spontaneous NVDs 1 (1.6%). Emergent C-section was performed in 49 (16.2%) patients in the cordless group compared to 5 (1.7%), 1 (0.3%) and 1 (0.3%) patients in the 1, 2 and multiple turn groups respectively. The group with nuchal cord was associated with fewer Emergent C-sections than the group without nuchal cord, p-value 0.001. Lastly Instrumental delivery was performed only in 16 patients with 13 (4.3%) in the cordless group and 3 (1%) patients in 1 turn of loop group respectively.

DISCUSSION

The incidence of nuchal cord in the present study was 63 (20.8%) which is less than that in comparable international studies. Nuchal cord as a whole was not associated with low Apgar scores (<7) at 1 or 5 minutes, admission to the neonatal ICU or emergency caesarean section and this is in accordance with similar findings reported in international literature. Schaffer et al. and Assimakopoulos et al. showed that nuchal cord was associated with lower Apgar scores (<7) at 1 minute but this was not supported by our data which is also in accordance with Kong et al. and other international studies. Comparison of Nuchal cord as single turn and its absence was compared by Schaffer et al. and Larson et al. Schaffer et al. showed that multiple cords were associated more frequently with meconium-stained liquor without any rise in low Apgar (<7) at 5 minutes or admission to Neonatal ICU. Their study did not show any change in the delivery mode. Larson et al. showed that meconium-stained liquor and operative vaginal deliveries was associated more with multiple nuchal cords but low Apgar score <7 at 5 minute was not associated with it. Narang et al. showed that presence of nuchal cord was associated more frequently with meconium-stained liquor without any difference between the number of loops. In our study we compared in various ways absence of nuchal cord with nuchal cord as a whole and where there were clear clinical implications with nuchal cord as single, double and multiple loops of the cord. This has been previously studied by Kong et al. as well but we are of the opinion that such a stratification is more helpful regarding clinical implications and management. Among variables associated with greater loops of nuchal cord were meconium stained liquor, admission to neonatal ICU, emergent caesarean section and fetal distress requiring a caesarean or instrument delivery. This was greatest for multiple turns however there were only 2 (0.7%) such patients in the whole study group which is a very small cohort. Multiple turns of the cord are fetuses that more likely require greater monitoring and care including admission to neonatal ICU and prevention of complications such as aspiration of meconium. The clinical implication which arises here is that if such a condition is detected antenatally on an ultrasound pre-emptive preparation for handling with such and related counselling can be provided in advance.

In our study association of multiple turns of the cord was statistically significant for low (<7) Apgar scores at 1 and 5 minutes thereby recommending avoiding a vaginal delivery in such cases. This is in contrast to Kong et al. where this was not statistically significant and the authors recommended vaginal deliveries. The present study however lacks the cohort size of Kong et al. and a larger study population will clarify this further. Multiple turns were however associated more frequently with meconium stained liquor, fetal distress and emergent C-section or delivery with instruments which is in accordance with international studies. Nuchal cord is diagnosed antenatally either by an ultrasound or suspicion such as a non-engaged fetal head or meconium-stained liquor. In this regard Tamrakar et al. recommended that a non-engaged fetal head should serve as the basis for referral to a tertiary hospital and confirmation with an ultrasound. In the present study we found that among the variables associated more frequently with 1 or 2 turns of the cord are low (<7) Apgar scores at 5 minutes (p=0.035), meconium stained liquor (p=0.008) and fetal death (p=0.003). This is in contrast to Kong et al. who showed that 1 and 2 turns were not associated with poorer outcomes. We still recommend that based on suspicion screening should be performed for safety and any medico legal concerns.

Nuchal cord of multiple turns is rare with incidence almost 0.4% in some studies.
therefore recommended disregarding screening as a routine for early labor as this is not cost-effective. Instead they recommended meconium-stained liquor as the basis for suspecting fetal distress and using this for pre-emptively considering other interventions such as emergent caesarean or instrumental deliveries. Nuchal cord of multiple turns is specifically associated with more frequent adverse fetal effects but no consensus guidelines have been reached so far as for their management. Individual center preferences have led to using nuchal cord as an indication for elective caesareans. Kong et al. still recommended that before an elective C-section in such instances a repeat ultrasound should be performed.

Nuchal cord especially single or double turns has not been consistently shown to be associated with adverse fetal outcomes in international literature. Therefore, a routine Caesarean should not be recommended in every case. The adverse effects of such a policy are obvious. Uterine rupture, subsequent adherence of placenta in further pregnancies, placenta previa and frequent respiratory complications in the fetus.

We plant to include a larger cohort in the future to add to the other literature on the subject. These and other studies should serve as the basis for consensus. These can then be used to reach guidelines and management protocols which will help establish algorithms for dealing with nuchal cords, clarify counselling strategies and prevent avoidable cesareans. A clear antenatal approach towards nuchal cords will go a long way towards relieving mother and attendant anxiety associated with cases.

CONCLUSION

Nuchal cord with multiple turns was associated with fetal distress but without affecting Apgar scores. Nuchal cord was not associated with adverse outcomes and prenatal ultrasound for this purpose is not required.

Author’s Contribution:

Concept & Design of Study: Seema Gul Salman
Drafting: Maria Rafiq, Khalil Ahmad
Data Analysis: Khalid Khan, Irfan Khan, Irfan Ullah
Revisiting Critically: Seema Gul Salman, Maria Rafiq
Final Approval of version: Seema Gul Salman

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

REFERENCES

Antibiotic Resistant Pseudomonas Aeruginosa Causing Nosocomial Infection in Burn Patients of Quetta, Pakistan

Ashiq Hussain1, Bezan Baloch2, Masroor Ahmad3, Shafee Muhammad Khosa4, Muhammad Tahir5 and Nazeer Ahmed Sasoli2

ABSTRACT

Objective: This study was planned to estimate the possible risk factor of burn wound infection, frequency and antibiotic resistant to pseudomonas aeruginosa in burn patients.

Study Design: Descriptive study.

Place and Duration of Study: This study was conducted at the Department of Microbiology Bolan Medical Complex Hospital Quetta from November 2018 to November 2019.

Materials and Methods: A total of 270 Swab samples were collected from 137 burn wound infected patients from BMC Hospital Quetta. Samples were then subjected to culture on different microbiological media along with Gram staining different biochemical tests and antimicrobial sensitivity was done with disc diffusion procedure.

Results: Revealed 220 out of 270 (81.48%) sample were contaminated with in different microorganism. Out of these positive culture n=125 (57%) strains of pseudomonas aeruginosa were isolated. The most common cause was flame burns n=57 (41.59 %), followed by scalds burns 38 (27.72 %), electric burns 23 (16.77 %) and chemical burns 19 (13.87 %), respectively. A total 125 isolates of Pseudomonas aeruginosa were recovered from burn patients and the most resistance 100% antibiotic was ampicillin and doxicillin. And least resistant of drugs are azithromycin and imipenem.

Conclusion: Increased trend of antimicrobial resistance is an alarming in infections in the area. Moreover, majority of burn patients were male aging above 20 years with flame burn the main cause of accident and incident.

Key Words: Antimicrobial resistance, Burn, Pseudomonas aeruginosa, Nosocomial infection.


INTRODUCTION

Burn patients have a higher threat of nosocomial infection for numerous of reasons, Immuno-compromised impacts of burn, prolonged hospitalization, delayed of diagnosis and treatment method of burns patient1. Burns infections are serious common public health problem worldwide. The Burn injuries vary among different age groups, gender and geographical region of the country2. About half of the total global burn cases occur in South Asian region alone. Public health is a global disquiet due to injuries and demises, with an expected 265,000 deaths yearly according to the World Health Organization.

1 Department of Microbiology / Surgery2 / Plastic3 / Hematology4 / Pediatric Medicine5, Bolan Medical College Quetta.

Correspondence: Dr. Ashiq Hussain, Assistant Professor of Microbiology Bolan Medical College Quetta.
Contact No: 0334-2467552
Email: dr.shah73@gmail.com

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Most are found in low- and middle-income nations, and practically half happen in the South-East Asia Region3. Burn injury is a significant yet under-investigated zone in Pakistan. According to Global Burden of Disease in 2010 investigation appraises that the age-standardized death rate for injury brought about by fire, heat, and hot substances is 5.8 per 100,000 populace in Pakistan4. Overn0.3 Million deaths are reported from Burns and fires each year throughout the world. Although this rate have been declined in recent years due to strict vigilance and establishment of state of the art modern burn centers5. The presence of dead and denatured burn scar, the suppression of the cellular immune and antibody mediated immune system reduce chemical mediator and exposed skin surface may favor microbial growth6. Generally, deaths in burn patients attributed to complication of the infection with multiple organisms and also the involvement of maximum body surface area5. Although Gram-negative organisms are the most common to cause serious infection in burn patients. However, in most of the cases Staphylococcus aureus has also notable figure in burn wounds. In extensive burn cases, when the organisms proliferate in the scar and the number of organisms reaches in millions per
gram of tissue, it leads to systemic infection and lethal bacteremia. The most common isolated microorganisms from the burn shin surface are Staph aureus and Pseudomonas aeruginosa. Others may include, Klebsiella spp, coagulase negative Staphylococcus, Escherichia coli, Enterobacter spp and Candida spp etc. However, P. aeruginosa is opportunistic human pathogen causing around 9-10% of hospital acquired nosocomial infections. The organism has great potential of developing resistance to commonly used antibiotics. This resistance is due to many factors such as, efflux pump, ability and production of antibiotic deactivating enzymes etc. Resistance to Penicillin and Cephalosporin may be due to enzymes Cephalosporinas with its hyper production or suppression. Similarly, Porins protein channels also allow the uptake of nutrients and other constituents such as antimicrobial substances into cell.

MATERIALS AND METHODS
The Descriptive study was conducted at the Department of Microbiology Bolan Medical Complex Hospital Quetta from November 2018 to November 2019. Multiple samples were collected from different site of burnt patients n= 137 (Male n= 80; Female n=57) with sterile swabs and were immediately transported to the Microbiology laboratory of BMC Hospital. Patients with burn cases from outpatient department and indoor patients both were recruited with no age restriction. All the samples were inoculated on different microbiological media and were then incubated at 37°C for 24 hours in an aerobic condition. The organisms were gram stained and various biochemical tests (oxidase, catalase, citrate, indole and carbohydrate utilization test) were performed. Isolates of Pseudomonas aeruginosa were identified on the basis of colony characters and growth pattern on Cetrimide agar and various biochemical tests. While antimicrobial susceptibility screening was done on Mueller-Hinton agar by agar disc diffusion method. Data collected were entered in SPSS. Version.18.0 and demographic data were analyzed using standard protocol.

RESULTS
A total of 137 patients admitted in different ward (Burn ICU 48 and Burn ward 89) in BMC Hospital, Quetta were consented for samples and 270 samples were collected from these patients. Those samples collected from patients were culture onto different media and 220 (81%) out of 270 samples were positive for bacterial culture growth, while 125/220 (56.81%) growth were positive for Pseudomonas aeruginosa. In this study 80 (58.39%) and 57 (41.60%) patients were male and female, respectively as shown in figure 1.

Figure No. 1: Gender wise distribution of burn wound infected patients

Table No.1: Demographic characteristics of burn patients

<table>
<thead>
<tr>
<th>Age (Years)</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>01-20</td>
<td>19</td>
<td>17</td>
<td>36</td>
</tr>
<tr>
<td>21-40</td>
<td>37</td>
<td>22</td>
<td>59</td>
</tr>
<tr>
<td>41-60</td>
<td>24</td>
<td>18</td>
<td>42</td>
</tr>
</tbody>
</table>

Total 80 (58.39%) 57(41.60) 137

The most common cause recorded were flame burn 57/137 (42%), followed by 38/137 (27%) by scalds as shown in Fig.2

Figure No.2: Frequency of different factors for burn in both age groups

Risk factor related to burn wound infection: The degree of burn with 3rd and 4th degree burn was more common in female than male patients, 31 (22.62%),65 (47.44%) and 41 (30.00%) patients were with 1st degree, 2nd degree and 3rd,4th degree respectively. Total body surface area (TBSA) were also evaluated and 78/137 (56.93%) 39/137 (28.46%) and 20/137 (14.59%) patients were with 20%, 40% and 60 % respectively of TBSA as shown in Table.2 Stay at hospital were recorded and 90 (65.69%) and 39 (28.46%) patients were with 2 week and 2-4 weeks stay in hospital for treatment as shown in table.2.
Table No. 2: Risk factor related to burn wound infection

<table>
<thead>
<tr>
<th>Degrees</th>
<th>Male</th>
<th>Female</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st degree</td>
<td>19</td>
<td>12</td>
<td>31 (22.62%)</td>
</tr>
<tr>
<td>2nd degree</td>
<td>45</td>
<td>20</td>
<td>65 (47.44%)</td>
</tr>
<tr>
<td>3rd and 4rt degree</td>
<td>16</td>
<td>25</td>
<td>41 (30.00%)</td>
</tr>
<tr>
<td>Total</td>
<td>80</td>
<td>57</td>
<td>137 (100%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total Body Surface Area (TBSA)</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 to 20 %</td>
<td>78 (56.93%)</td>
</tr>
<tr>
<td>21 to 40 %</td>
<td>39 (28.46%)</td>
</tr>
<tr>
<td>41 to 60 %</td>
<td>20 (14.59%)</td>
</tr>
<tr>
<td>Total</td>
<td>137 (100%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hospital stay (days)</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 to 14 days</td>
<td>90 (65.69%)</td>
</tr>
<tr>
<td>15 to 30 days</td>
<td>39 (28.46%)</td>
</tr>
<tr>
<td>&gt; 30 days</td>
<td>8 (5.83%)</td>
</tr>
<tr>
<td>Total</td>
<td>137 (100%)</td>
</tr>
</tbody>
</table>

Antimicrobial resistance pattern
The result of antimicrobial resistance to P. aeruginosa isolated from wound swab culture of burn infected patients against 16 antimicrobial agents is presented (Fig.2). The most resistance 100% antibiotic was ampicillin and doxicillin. And least resistant of drugs are azithromycin and imipenem as shown in figure 3.

![Antibiotic resistance pattern % of the p a urengiosa](image)

Fig No. 3: Antibiotic sensitivity pattern (%) of the wound isolates

DISCUSSION

Thermal injuries are considered as a major health problem especially in low income countries. It generally occurs due to fire, chemicals, exposure to hot liquid and contact surface. Naked necrotic tissues can be commonly seen in burnt patient and are considered major site of microbial contamination. Malfunctioning of neutrophils, cellular and humoral immune response leads to immuno-suppression leading to enhanced chance of wound colonization by microorganisms.

The overall, environment of burn unit is prone to be easily contaminated by organisms which have the ability to transfer from one patient to other. Pseudomonas aeruginosa is well-known opportunistic organism. It colonizes burn wounds and gains access to burnt patients through cross contamination. Due to emergence of resistance the mortality rate due to pseudomonas is rising.

In the present study, male patients were more than female in burn centers. This might be due to the fact that males in Pakistan are more concerned than females and responsible for the majority of duties outside home that may increase risks of burn accidents. This finding is in line with similar studies in Palestine. In this study, more patients were from fire burn followed by scalds and were supported by previous studies (Fig.2). These findings corroborate with study from Karachi, Pakistan, in which scald and fire were reported the leading causes of burn. Similarly, flame burn was the most common cause of burns followed by scalding, in a study from Iran. Similarly, 30-50 years were the most common age of the patients. Our findings corroborate with findings from Karachi, Pakistan. In this study, body surface area burn varied from 6 - 60 %. In n=78 (56.93% patients, it ranged from 1-20 %, TBSA. 21-40 % category included the percentage of patients n=39 (28.46%) and 41%-60 % burns category showed the lower percentage of patients n= 20 (14.59%). Our results were in conflict with a study in which 11 -30 % body surfaces of 35 patients and 31 % -60 % of 46 patients had burns while 19 patients had 61 -92 % burns.

Pseudomonas aeruginosa were isolated 125 strains from 220 positive culture samples (56.81 %) from burn patients in this study. This finding was in consistent to other studies. Some other previous studies have reported higher occurrence of P. aeruginosa along in patients with 59 %, 57 %, and in Quetta 37%. Antimicrobial resistance pattern of different antibiotics was checked against P. aeruginosa. Our results revealed high level resistance against cloxacillin, Piperacillin, Ceftazidime and low-level resistance against Imipenem (Fig-3). Nikokar et al., (2013) studied antibiotic sensitivity and resistivity pattern of P. aeruginosa isolates and reported similar results as of our findings.

Pseudomomas aeruginosa remains an opportunistic culprit that causes most of the hospital acquired infections and has developed resistance to various common antimicrobial drugs. Similarly, Ali et al., (2015) also reported the resistance of different isolates of P. aeruginosa to commonly used drugs such as, Ofloxacin, Ciprofloxacin, Gentamycin and Imipenem etc. It exploits great potential of organism to develop MDR.

In this study, we found that during prolong hospitalization (2-4 weeks) of the patient, P. aeruginosa more common in such cases. It is obvious that satisfactory and better attention of the burned patient is
necessary to shorten the patient stay in hospital. The early detection of isolates and its antibiotic sensitivity is recommended for quick and early recovery of patient.

CONCLUSION

Burn injuries are traumatic with adverse effects long lasting effects on patient life. Male patients were more prone to burn wounds predominantly caused thermal flame with 31-50 years most common age. Patients with 21-40 % TBSA and long hospital stay were mostly infected with P. aeruginosa. The most common susceptible antibiotics were Imipenem, Cefotaxime, Tobramycin and Amikacin. Rational use of antibiotics may be discouraged and proper in vitro screening of complicated cases against commonly used antibiotics will surely help in the better management of multi-drug resistant in burn patients.

Author’s Contribution:
Concept & Design of Study: Ashiq Hussain
Drafting: Bezan Baloch, Masroor Ahmad Shafee
Data Analysis: Muhammad Khosa, Muhammed Tahir, Nazeer Ahmed Sasoli
Revisiting Critically: Ashiq Hussain, Bezan Baloch
Final Approval of version: Ashiq Hussain

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

REFERENCES

Frequency of Complications of Open Omental Patch Repair for Perforated Duodenal Ulcers

Bezan Baloch¹, Ashiq Hussain², Nazeer Ahmed Sasoli¹, Muhammad Tahir³, Masroor Ahmad⁴ and Shah Wali⁵

ABSTRACT

Objective: This study was conducted to determine the frequency of post-operative complications of omentoplasty in patients with perforated duodenal ulcers.

Study Design: Descriptive Study.

Place and Duration of Study: This study was conducted at the Department of General Surgery, Bolan Medical Complex Hospital Quetta from September 2018 to February 2020.

Materials and Methods: A total number of 261 patients with diagnosis of duodenal peptic ulcers having age 18 to 60 years were included in this study. Closure of perforated duodenal ulcers was done by giving a midline laparotomy incision. Following identification of the perforation area, extensive peritoneal toilet was performed using warm saline. Patch repair was then done in standard fashion. Mass closure of fascia was performed using omental patch with 1/0 suture and interrupted closure to skin incision subsequently with proline sutures. Diagnosis of post-operative complications of omentoplasty e.g. organ space infections, sepsis and death rate were noted in the post-operative period.

Results: Mean age of patients was 40.42±9.61 years. There were 144 (55.17%) male and 117 (44.83%) female patients. Mean duration of symptoms of patients was 9.49±4.38 hours. Organ space infections occurred in 16 (6.13%) patients, sepsis in 10 (3.83%) patients and mortality in in 23 (8.81%) patients.

Conclusion: Omental patch repair is simple to perform and yet reliable for closure of much large perforations. Only Patch closure is sufficient for duodenal perforations considering low complications rate. In present study frequency of complications was comparable as mentioned in previous studies.

Key Words: Perforated peptic ulcers, omental patch repair, mortality.

INTRODUCTION

Structurally the duodenum is C shaped segment part of the the gastrointestinal tract and limited to the pylorus. Duodenal perforation is an occasional but fatal illness.¹ Perforated duodenal ulcer was first described by Muralto in 1688 and reported by Lenepneau.² There after Dean presented the first case in 1894 which successfully surgical closure of a perforated duodenal ulcer.³ Perforated duodenal ulcer disease is associated with a 2% to 10% mortality rate, with septicaemia being the most common cause of death. Preoperative shock, perforation for greater than 24 hours prior to surgical intervention, and concurrent significant illness have consistently been shown to be predictive of mortality, and the presence of all three risk factors carries a near 100% mortality.⁴ Perforation and fistulas of the gastrointestinal tract may occur after endoscopic/surgical procedures and disease states perforated peptic ulcer.⁵ Iatrogenic gastrointestinal tract perforation rates proportionally increase as more GI endoluminal procedures are performed.⁶ For almost three decades now, the standard of care to treat perforated foregut ulcers has been by simple closure with or without an omental patch (OP) and long-term proton pump inhibitor (PPI) therapy, with antibiotic treatment for Helicobacter pylori eradication if present.⁷ ⁸ The expected high morbidity and mortality from such surgical procedures raises a question about the need for less invasive procedures.⁹ Despite advancements in therapeutic techniques regarding the management of perforated duodenal ulcers, all procedure are still associated with inherent technical and logistic complexity. Clipping of the duodenal ulcers by using an omentum patch has been advocated for sealing larger defects.¹⁰ ¹¹ Very little data is published regarding the complications of usage of omental patch
for closure of duodenal peptic ulcers. Sepsis, organ space infections and death are common devastating complications of omentoplasty. A study found organ space infection rate of 4.6%, sepsis rate of 4.6% and death rate also 4.6%. The wound infections organ space rate of 6.0%, sepsis in 2.0% patients and death rate of 8.0% in patients of perforated duodenal ulcers. Very little work has been done regarding the complications of omentoplasty in patients of perforated duodenal ulcers and no data has been published from Pakistan regarding the complications of omentoplasty (omental patch) in patients of duodenal ulcers. The results of this study will help us to determine frequency of complications of omentoplasty in patients of duodenal perforations and will help us to recognize what are the most frequent complications in these patients. By knowing most frequent complications we will be able to adopt preventive measures so that we can reduce the frequency of these complications.

**MATERIALS AND METHODS**

This is Descriptive Study was completed at Department of Surgery, Bolan Medical Complex Hospital, Quetta from September 2018 to February 2020. First of all, approval was taken from the ethical committee of the hospital. After approval, a total number of 261 patients who presented in department of emergency surgical unit of Bolan Medical Complex Hospital Quetta fulfilling the inclusion criteria were included in this study. Besides, non-probability, Consecutive sampling were used for sample collection. Both male and female patients with diagnosis of duodenal peptic ulcers having age 18 to 60 years also included. Patients planned to undergo re-do operations for perforated duodenal ulcers were excluded. Closure of perforated duodenal ulcers was done. Diagnosis of post-operative complications of omentoplasty e.g. organ space infections, sepsis and death rate were made according the criteria given in the operational definitions. Data regarding age, and gender of patients was also calculated.

Data was analyzed using SPSS v17. Frequency and percentage were used to present gender, organ space infections, sepsis and operative mortality. While age, and duration of symptoms was presented as mean ± standard deviation. Effect modifiers such as age, gender of patients and duration of symptoms were controlled by stratification. Post-stratification Chi-square test was applied to determine the effect of these effect modifiers on complications of omentoplasty e.g. organ space infections, sepsis and operative mortality. P-value <0.05 was considered as significant effect.

**RESULTS**

Mean age of patients included in this study was 40.42±9.61 years. Minimum age was 18 years and maximum age was 60 years (Table 1).

<table>
<thead>
<tr>
<th>Age (Years)</th>
<th>Mean</th>
<th>Maximum</th>
<th>Minimum</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-40 Years</td>
<td>40.42</td>
<td>60</td>
<td>18</td>
</tr>
<tr>
<td>41-60 Years</td>
<td>40.42</td>
<td>60</td>
<td>18</td>
</tr>
</tbody>
</table>

Mean duration of symptoms of patients was 9.49±4.38 hours. Minimum duration of symptoms was 02 hours and maximum duration of symptoms was 24 hours. There were more males as compared to the females. There were 144 (55.17%) male and 117 (44.83%) female patients. Figure. 1 is demonstrating the organ space infections occurred in 16 (6.13%) patients and remaining 245 (93.87%) patients has no organ space infection.

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

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-40 Years</td>
<td>40.42</td>
</tr>
<tr>
<td>41-60 Years</td>
<td>40.42</td>
</tr>
</tbody>
</table>

Table No.2: Stratification of Age to Determine the Association of Age with Organ Space Infections, Sepsis and Mortality

<table>
<thead>
<tr>
<th>Age Group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-40 Years</td>
<td>0.42</td>
</tr>
<tr>
<td>41-60 Years</td>
<td>0.33</td>
</tr>
</tbody>
</table>

Regarding frequency of Sepsis, there were 10 (3.83%) patients who were diagnosed with sepsis and remaining 251 (96.17%) patients did not suffered from sepsis. Mortality occurred in 23 (8.81%) patients out of 261 patients. Stratification of age was performed, in patients having age 18-40 years, organ space infections occurred in 10 patients and in patients having age 41-60 years, organ space infections occurred in 06 patients with significant p-value of 0.42. In patients having age 18-40 years, sepsis occurred in just 03 patient and in patients having age 41-60 years, sepsis occurred in 07 patients with insignificant p-value of 0.33. In patients having age 18-40 years, mortality occurred in 13 patients and in patients having age 41-60 years, mortality occurred.
in 10 patients with insignificant p-value of 0.64 (Table 2).

Stratification of gender was performed, in male patients, space organ was occurred in 10 patients and in female patients, space organ infections occurred in 06 patients with statistically insignificant p-value of 0.543. In male patients, sepsis occurred in 05 patients and in female patients, sepsis occurred in 05 patients with statistically significant p-value of 0.737. Regarding mortality, mortality occurred in 12 male patients and in 11 female patients with statistically insignificant p-value of 0.762 (Table 3).

Table No.3: Stratification of Gender to Determine the Association of Gender with Organ Space Infections, Sepsis and Mortality

<table>
<thead>
<tr>
<th>Gender</th>
<th>Organ Space</th>
<th>Sepsis</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>10</td>
<td>05</td>
<td>12</td>
</tr>
<tr>
<td>Female</td>
<td>06</td>
<td>11</td>
<td>11</td>
</tr>
</tbody>
</table>

Stratification of duration of symptoms was performed, in patients having duration of symptoms 02-09 hours, organ space infections occurred in 12 patients and in patients having duration of symptoms 10-24 hours, space organ infections occurred in 04 patients. This difference was statistically insignificant with p-value of 0.067. In patients having duration of symptoms 02-09 hours, sepsis occurred in just 04 patients and in patients having duration of symptoms 10-24 hours, sepsis occurred in 06 patients. This difference was statistically insignificant p-value of 0.406. In patients having duration of symptoms 02-09 hours, mortality was occurred in 13 patients and in patients having duration of symptoms 10-24 hours, mortality was occurred in 10 patients. This difference was also statistically of 0.714 (Table 4).

Table No. 4: Stratification of Duration of Symptoms to Determine the Association of Duration of Symptoms with Organ Space, Sepsis and Mortality

<table>
<thead>
<tr>
<th>Duration of Symptoms</th>
<th>Organ Space</th>
<th>Sepsis</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-9 Hours</td>
<td>12</td>
<td>04</td>
<td>12</td>
</tr>
<tr>
<td>10-24 Hours</td>
<td>126</td>
<td>119</td>
<td>11</td>
</tr>
</tbody>
</table>

DISCUSSION

Since the introduction of the management of perforated duodenal ulcers by omental (Graham) patch plication in 1937, the surgical technique has been evolved with the introduction of different modifications and approaches which often used the same principle of closure of the perforation combined with extensive peritoneal lavage.\textsuperscript{14} The approach of open repair of perforated duodenal ulcers remained the gold standard treatment. It was simple and effective and provided long-term regression of the disease when combined with eradication of H. pylori and recess of nonsteroidal anti-inflammatory medication. In these patients, mortality is frequently associated with underlying sepsis and inflammatory response, which correlates with patient risk factors rather than surgical technique or complications.\textsuperscript{15} In present study, we evaluated the complications rate of omental patch repair for management of perforated peptic ulcers. In present study, most common complication was organ space infections occurred in 6.13% patients, followed by sepsis that was diagnosed in 3.83% patients. And mortality occurred in 8.81% patients. A study conducted by lee et al.\textsuperscript{12} on outcomes of omental patch repair including 108 patients who underwent open omental patch repair. They reported organ space infections in 4.6% patients, sepsis in 4.6% patients and death also, in 4.6% patients. In another study conducted by Vakayil et al.\textsuperscript{16} involving 1846 patients who underwent open omental patch repair for management of perforated peptic ulcers, reported organ space infections in 6.2% patients, sepsis in 11.8% patients and mortality in 5.8% patients. In a study conducted in Pakistan by Unar et al.\textsuperscript{17} on postoperative complications of omental patch repair reported intra-abdominal abscess in 6.2% patients, reoperations in 3.6%, renal failure in 4.1%, post-operative leakage in 3.6% patients and mortality in 5.1% patients after surgery. Etonyeaku et al.\textsuperscript{18} also reported similar outcomes they reported organ space infections in 8.9% patients, and mortality rate of 13.3%.

Moreover, the factors that can contribute to increased frequency of complications are advanced age, cigarette smoking and delay in surgery after the onset of symptoms.\textsuperscript{19} In present study we included only those patients who had duration of symptoms <24 hours to minimize the effect of delay in treatment on surgical complications. We did not find any significant association of age, gender and duration of symptoms on post-procedural complications.

CONCLUSION

Omental patch repair is simple to perform and yet reliable for closure of much large perforations. Only Patch closure is sufficient for duodenal perforations considering low complications rate. In present study frequency of complications was comparable as mentioned in previous studies.
Author’s Contribution:
Concept & Design of Study: Bezan Baloch
Drafting: Ashiq Hussain, Nazeer Ahmed Sasoli
Data Analysis: Muhammad Tahir, Masroor Ahmad, Shah Wali
Revisiting Critically: Bezan Baloch, Ashiq Hussain
Final Approval of version: Bezan Baloch

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

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Umbilical Artery Blood Acid-Based Status in Fetal Growth Restriction with Normal and Abnormal Doppler Studies

Isma Rauf¹, Talat Nelofer¹, Yasir Arfat² and Adnan Rauf³

ABSTRACT

Objective: The objective of this study was to determine and compare the acid-base status of the umbilical artery blood in growth restricted fetuses having normal and abnormal Doppler studies at the time of C-Section via Doppler velocimetry.

Study Design: Descriptive / Cross-sectional study.

Place and Duration of Study: This study was conducted at the Department of Obstetrics & Gynecology, Women Medical College, Abbottabad, and Women & Children Hospital Abbottabad from June 2019 to December 2019.

Materials and Methods: Patients attending the antenatal OPD Clinic, with singleton pregnancy were enrolled for the study and patients with structural anomalies were excluded. Consents from the patients were obtained and history was recorded. IUGR fetuses were divided into two groups; group A (normal Doppler flow) and group B (abnormal Doppler flow). These patients were followed up till delivery and at the time of C-section umbilical artery sampling was done. The data was scored and analyzed statistically.

Results: Doppler Studies results indicated that the mean pulsatility index of Group A was 0.622 ± 0.148 and that of group B was 0.862 ± 0.120 which is statistically significantly different. Acid Base study Patients with abnormal Doppler had significantly more frequent abnormal acid base status. The abnormal ABGs in patients with abnormal Doppler was 6.231 (95% CI 2.351–16.513). The mean pH of the patients in the normal doppler group was 7.14±0.98 and that in the abnormal Doppler group was 7.03±0.14. This difference in pH was statistically significant, the abnormal Doppler group having significantly more acidosis. APGAR score. 1min in the abnormal ABG group 15 (34.9%) babies had an APGAR score of > 7 at 01 minute as opposed to 22 (59.4%) in the normal ABG group. In the abnormal ABG group 28 (65.1%) babies had an APGAR score of 0-6 at 01 minute as opposed to 15 (40.5%) in the normal ABG group. The mean APGAR score at 05 minute in the abnormal Doppler flow group was 6.901±2.23 and the mean APGAR score at 05 minute in the normal Doppler flow group was 7.55±0.75. The differences in 05 minute APGAR score was statistically significant between the two groups; p=0.006

Conclusion: Babies with abnormal umbilical artery Doppler had significantly more frequent chances of having abnormal blood gas status on cord umbilical artery blood analysis. Therefore, acid-base at the time of birth help to improve fetal surveillance.

Key Words: umbilical artery blood, acid-based status, fetal growth restriction, doppler studies, fetal surveillance.

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INTRODUCTION

IUGR is a sonographic predictable of fetal weight that is less than 10th percentile of the gestational age. Increased risk of perinatal mortality, morbidity, and impaired neurological development is associated with growth restricted fetuses. IUGR fetuses are prone to intrauterine death & asphyxia at birth stage. The main objective of antenatal care is rightly estimation of compromised IUGR fetuses for timely intervention. Doppler ultrasound plays an important role in the management of IUGR fetuses. The rate of growth of the restricted fetuses with reversed or absent blood circulation speed in the umbilical artery are at respiratory distress, higher risk of cesarean section, chronic lung disorder, necrotizing enterocolitis, acute renal failure and ultimately death. There are ample of evidence in obstetric patients that Doppler index of fetal circulation can reliably identify future perinatal consequences. Growth restricted fetuses with abnormal and normal PI of umbilical artery causes 15% and 34% incidence of acidosis respectively by authors.¹,³ Assessment of fetal growth and wellbeing is important key objectives of antenatal care. In human pregnancies,
placental inadequacy is the driving reason for asymmetrical IUGR. There are various methods of surveillance of fetal growth restriction4-6 i.e. clinical assessment, fetal biometry, estimated fetal weight, biophysical profile, and Doppler velocimetry. The positive predictive value of clinical assessment, abdominal circumference and fetal weight are lower as compared to that of Doppler or blood gas analysis results in detecting fetal growth restriction once diagnosed and severity of risk predicted, the neonatal outcome can be improved.

Estimates of fetal acid-base balance and oxygenation are not shown in fetuses with restricted growth if the velocimetry is normal. Abnormal velocimetry, on the other hand, causes fetal blood sampling, which can only be recognized from hypoxia and acidosis by growth retardation. Several authors have reported, the important role of Doppler sonography in predicting risk for poor neonatal outcomes in IUGR fetuses9-15. Umbilical cord pH has long been used, as a surrogate measure of fetal oxygenation, with most authors agreeing that severe acidosis at birth is associated with an increased incidence of neonatal complications. The present study was carried out using fetal umbilical artery Doppler examination on a cohort of fetuses suspected of having fetal growth restriction and then followed their acid base status and subsequent antenatal courses to assess early neonatal outcomes. The purpose of this research work was to understand umbilical artery Doppler precisely predict acid-base status at birth stage to enhance fetal surveillance.

MATERIALS AND METHODS

This was a descriptive case study conducted in the Department of Obstetrics & Gynecology, Women Medical College, Abbottabad, and Women & Children Hospital Abbottabad from June 2019 to December 2019. Sample size was 80 patients with IUGR calculated by using WHO Sample Size Calculator for studies. Prior to the investigations, all patients informed consents were taken. Patients attending the antenatal OPD Clinic, with singleton pregnancy and small for gestational age were enrolled for the study. Patients with structural anomalies on anomaly scan were excluded from the study. Detailed history and examination of each patient was performed. Patient’s gestational age was calculated by their last normal menstrual period, urine pregnancy test and first trimester dating scan. Patient’s symphysis fundal height was measured by tape. Measuring tape was placed on the symphysis pubis and with the centimeter marks face down, measure to the previously noted top of the fundus. The patients in which symphysis fundal height was corresponding to gestational age were evaluated for IUGR by ultrasound. Ultrasound measurements, femur length, biparietal diameter, abdominal perimeter, head circumference, amniotic fluid content, and placental maturity were measured for the confirmation of IUGR. Gestational age was confirmed by ultrasound results on the first day of the final menstrual period and 20 weeks before pregnancy. The heads and abdominal perieters of these fetuses measured by ultrasound were less than 5th percentile of standard values for fetuses of same ages. Less than 10th percentile neonatal weight was considered growth retardation according to standard birth weights and gestational age criteria. Patients diagnosed as IUGR fetuses was referred for Doppler flow studies for umbilical artery pulsatility index (PI), resistance index (RI), and systolic to diastolic ration (S/D ratio) then study patients were distributed into two groups, in group A (IUGR with normal Doppler flow studies) and group B (IUGR with abnormal Doppler flow studies). Blood circulation from fetal umbilical artery was performed prior to the Doppler fetal test and coaxial pulsed Doppler velocimeter having a sample volume of 5 mm and high pass filters were set at 100 Hz for testing. Three consecutive wave forms were used for each reading to measure results on hard copies by utilizing computerized planimeter. The simplified gosling formula was applied for computing the pulsatility index (PI) as shown in equation 1.

\[
Pulsatility \text{ Index} = \frac{\text{systolic velocity} - \text{diastolic velocity}}{\text{mean velocity}} \text{ Eq1}.
\]

Decrease diastolic velocity of quantified PI was accepted as an indication of placental impedance to blood flow, however, the absence of end diastolic flow showed the presence of severe placental damage. The study patients were followed till the time of delivery. Only those patients were further selected for the study in whom mode of delivery by C-section either emergency or elective. At the same time of C-section umbilical artery by surgeon using heparinized syringe within 5 minutes of taking sample blood gas parameters pH, PO2, PCO2 and base excess were measured. Sample was sent to hospital lab and reported. Collected blood samples were obtained in heparin treated syringes, sealed, and stored in ice. Radiometer ABL 300 analyzers were used to determine levels of respiratory gases within 5 to 10 minutes after sampling. The outcome variable noted at delivery was state birth weight and APGAR score at one and five minutes after delivery and results were documented on proforma find further analysis.

RESULTS

80 patients were included in this research and result indicated asymmetric fetal growth restriction on ultrasound criteria. 40 patients had normal Doppler parameters and 40 had abnormal Doppler parameters. The age ranged from 20 to 39 years with a mean age of 27.57± 4.6 years. The mean age of the patients with normal Doppler was 26.3±2.89 and those with abnormal Doppler was 28.8±5.61 years ; the two groups were mean age of the patients with normal ABGs was
27.7±4.29 and those with abnormal ABGs was 27.44±4.92 years; both groups were not significantly diverse to their age distribution; p=0.783. The gestational age ranged from 235 to 283 days with a mean gestational age of 258.7±10.82 days; the two groups were not significantly different with respect to their gestational age distribution; p=0.294. The mean gestational age of the patients with normal ABGs was 258.7±10.57 and those with abnormal ABGs was 260.83±11.04 days; both groups were not significantly different with respect to their age distribution; p=0.783. 40 patients had an abnormal and remaining 40 patients had a normal Doppler flow in umbilical artery. The pulsatility index ranged from 0.647 to 2.95. The mean pulsatility index was 1.457±0.617. The mean pulsatility index of Group A (normal Doppler) was 0.622±0.148 and that of group B (abnormal Doppler) was 0.862±0.120. The SD ratio ranged from 1.02 to 4.4. The mean SD ratio was 2.61±1.00. The mean SD ratio of Group A (Normal Doppler) was 1.84±0.100 and that of group B (Abnormal Doppler) was 3.38±0.649. The mean pulsatility index of normal ABGs group was 1.34±0.633 and that of abnormal ABGs was 1.55±0.594. This difference was statistically non-significant; p=0.121. The mean resistivity index of normal ABGs group was 0.699±0.183 and that of abnormal APGs was 0.778±0.171. This difference was statistically significant p=0.005. The mean SD ratio of normal ABGs group was 2.2±0.955 and that of abnormal ABGs was 2.96±0.917. This difference was statistically significant p=0.001 (46.25%) had normal ABGs and 43 (53.75) had abnormal ABGs out of 40 patients with normal doppler 27 (67.5%) had normal ABGs and 13 (32.5%) had abnormal ABGs. Out of 40 patients with abnormal Doppler 10 (25%) had normal ABGs and 30 (75%) had abnormal ABGs. Therefore, patients with abnormal Doppler had significantly more frequent abnormal acid base status. The OR for having abnormal ABGs in patients with abnormal Doppler was 6.231 (95% CI 2.351=16.513) the mean pH of the patients in the normal Doppler group ranged 7.14±0.098 and that in the abnormal Doppler group was 7.03±0.14. This difference in pH was statistically significant, the abnormal Doppler group having significantly more acidosis. The mean PCO2 of the patients in the normal Doppler group was 44.35±7.07 and that in the abnormal Doppler group was 52.07±8.66. This difference in the CO2 was statistically significant; the abnormal Doppler group having significantly more hypercapnia. The mean PO2 of the patients in the normal Doppler group was 16.90±1.81 and that in the abnormal Doppler group was 14.17±2.64. This difference in the PO2 was statistically significant; the abnormal Doppler group having significantly more hypoxia. The mean base deficit of the patients in the normal Doppler group was 4.25±8.43 and that in the abnormal Doppler group was -2.71±7.63. This difference in the base deficit was statistically significant; the abnormal Doppler group having significantly more acidosis.

**DISCUSSION**

Failure to achieve normal growth index in the fetus is characterized as fatal growth restriction. Fetus with growth restriction is designed as small for gestational age (SGA). Intrauterine growth restriction is major cause related perinatal mortality and morbidity. These infants have increased risk of handicap in later part of the life. There is no intrauterine therapy at present to treat such affected fetus. Doppler ultrasound is a known invasive method to investigate uteroplacental circulation. On serial Doppler ultrasound, changes in velocimetry values is helpful for the progress in circulation with therapy or to tell the need for the delivery. Few studies show the significance of umbilical artery Doppler velocimetry. The aim of this research work was to compare umbilical artery doppler velocimetry with biochemical measurements gained from fetal blood sampling in group of fetuses with growth hindrance. This study also helped to clarify the role of above investigation in the management of pregnancy having growth retardation fetuses. In our study out of 40 patients with normal Doppler 27 (67.5%) had normal ABGs and 13 (32.5%) had abnormal ABGs. Out of 40 patients with abnormal Doppler 10 (25%) had normal ABGs and 30 (75%) had abnormal ABGs. Therefore, patients with abnormal Doppler had significantly more frequent abnormal blood gas status. All biochemical parameters including pH, PCO2, PO2 and base deficit were significantly different between the two groups: the normal Doppler group having significantly more acidosis, hypercapnia, hypoxia, and baser deficit. The mean birth weight was not different between normal and abnormal ABG groups. The APGER score at 01 minute significantly more babies were distressed (scores 0-6) in both abnormal Doppler and abnormal ABG groups; p< 0.05. However, the 5-minuteAPGAR scores were significantly shorter abnormal Doppler group, but this association was not present in the abnormal ABG group. We therefore concluded that babies with abnormal umbilical artery Doppler had considerably more frequent chances of having abnormal blood gas status on cord umbilical artery blood gas analysis. Therefore, umbilical artery Doppler helps to predict acid-base status and improve fetal condition at the time of birth. Although, acid-base assessment from cord helps to measure neonatal condition at the time of birth but contrary there are lack of improvement of neonatal condition with other measures (APGAR scores, resuscitation, neonatal morbidity). Additionally, acidosis is defined according to the values of pH ranging from 7.20 down to 7.00. However, few attempts have been done to distinguish respiratory and metabolic causes of acidosis. Cord blood gases and pH
should be mentioned in all neonates with low APGAR scores. It helps to differentiate metabolic acidosis from hypoxemia, or any other causes related to APGAR scores. Although, metabolic acidosis confirm on cord blood is not a good indicator to predict long-term neurological injuries, however, it helps to exclude intrapartum or birth events causing acidosis. It is recommended that umbilical cord blood sampling soon after delivery should immediately be transported in heparin-containing syringe in plastic pack with cursed ice. The results of ABGs remain a questionable. Fetal hypoxia-acidosis is a part of pathway that may lead to intrauterine fetal demise. Antepartum surveillance is important for timely identification and delivery of the fetus having hypoxia or acidosis, so to prevent intrauterine fetus demise and long-term neurological damages. There is no optimal method to identify fetal hypoxia-acidosis to be determined. Umbilical artery Doppler velocimetry was best option for these outcomes. Arterial and venous specimens are used to check insights to ethology acidosis of newborn and umbilical cord blood provide a picture based on acid-base balance of the infant movement at the time of birth when umbilical circulation is caused to stop by the clamping of the cord. If the umbilical cord blood continues to flow along the umbilical cord, it continues to flow along the umbilical cord, indicating progressive changes in the acidity of the umbilical cord due to changes in gas exchange and metabolism. Minor changes have been noted in umbilical pH values occurring within 60 min of delivery and for 60 min cord arterial or venous pH have been dropped over than 0.2pH units. Similarly, placental surface vessels have been occurred in the blood samples. Additionally, changes have not been observed in the samples if the cord was doubly clamped at the time of birth, isolate a portion of blood from the both the placenta and environment. pH was remained comparatively constant at room temperature for an hour. Local data on the subject is sparse. More studies on a larger scale are required to document the role of umbilical artery blood gas analysis in the management of growth delimited fetuses. Babies containing abnormal umbilical artery Doppler had significantly more frequent chances of having abnormal blood gas status on cord umbilical artery blood analysis. Therefore, the umbilical artery Doppler can predict acid-base at birth time to improve fetal surveillance

CONCLUSION

Babies with abnormal umbilical artery Doppler had significantly more frequent chances of having abnormal blood gas status on cord umbilical artery bloodanalysis. Therefore, acid-base at the time of birth help to improve fetal surveillance.

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Author’s Contribution:
Concept & Design of Study: Isma Rauf
Drafting: Isma Rauf, Talat Nelofer
Data Analysis: Isma Rauf, Talat Nelofer, Yasir Arafat
Revisiting Critically: Isma Rauf, Talat Nelofer, Yasir Arafat, Adnan Rauf
Final Approval of version: Isma Rauf, Talat Nelofer, Yasir Arafat, Adnan Rauf

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

REFERENCES


Perinatal Outcome in Term Pregnancies with Isolated Oligohydramnios

Fatima Chaudhry Inayat¹, Nargis Shabana¹, Sana Iqbal¹, Jaweria Faisal², Aqsa Ikram ul Haq³, Sadia Kanwal²

ABSTRACT

Objective: To compare the perinatal outcome in pregnancies with isolated oligohydramnios induced at 37 weeks to those with isolated oligohydramnios observed till 40 weeks.

Study Design: Randomized Control Trial (RCT) study.

Place and Duration of Study: This study was conducted at the Gynae/Obs Unit II, Holy Family Hospital, Rawalpindi from February 2015 to July 2015.

Materials and Methods: A total of 144 patients were enrolled (72 patients in each group). GROUP A included pregnant ladies with oligohydramnios for whom induction of labour was done. GROUP B included pregnant ladies with oligohydramnios for whom expectant management was done.

Results: Meconium staining of liquor was positive in 23.61% of group A and 18.05% of group B babies with a P value of 0.835. Excellent APGAR score in group A and B were seen in 83.33% and 77.77% of babies respectively with a P value of 0.400.

Conclusion: Perinatal outcome in isolated oligohydramnios induced at 37 weeks is same as with expectant management of isolated oligohydramnios at term.

Key Words: Isolated oligohydramnios, AFI, meconium staining, APGAR score.

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INTRODUCTION

Amniotic fluid volume estimation is a part of fetal surveillance tool.¹ Oligohydramnios is defined as amniotic fluid volume less than expected for gestational age.² Diagnosis is by ultrasound examination and is described quantitatively either by amniotic fluid index (AFI)<5 or deepest vertical pool DVP <2.³ Certain maternal and fetal conditions such as congenital anomalies, hypertension, diabetes, preterm premature rupture of the fetal membranes (PROM) and fetal growth restriction (FGR) may present with oligohydramnios.¹ Each of this condition can predispose fetuses to adverse outcomes. Placental dysfunction leading to oligohydramnios puts the woman at an increased risk of fetal distress resulting in caesarean section, low Apgar score, meconium aspiration syndrome and perinatal mortality and morbidity.⁴ Isolated oligohydramnios is the low amniotic fluid volume in an otherwise low risk pregnancy.⁵ Isolated oligohydramnios complicates 1 to 5% of pregnancies at term.⁶ Good fetal outcome is generally expected in pregnancies with isolated mild or moderate oligohydramnios. Oligohydramnios diagnosed in third trimester is not as sinister as oligohydramnios found in the second trimester.²⁸ Oligohydramnios has been linked to compromised fetal status contributing to increased incidence of adverse perinatal morbidity and mortality.⁹ As a result, out of fear delivery is routinely advocated in these otherwise low risk pregnancies.⁸ Recent studies have also narrated isolated oligohydramnios an indication of labour induction and consequent increased risk of operative delivery.¹⁰ Though there are studies showing good perinatal outcome in term pregnancies with isolated oligohydramnios comparable to those of normal AFI consensus is lacking regarding management of isolated oligohydramnios.¹¹ Most of the obstetricians lean toward intervention for isolated oligohydramnios at term.¹² Induction of labour solely for oligohydramnios specially with unfavorable bishop score contributes to high caesarean section rate because of failed induction.¹³ Literature on comparison of active vs expectant management of isolated oligohydramnios is lacking. This study was planned to compare perinatal outcome in pregnancies with isolated oligohydramnios induced at 37 weeks to those observed till 40 wks. Good

¹ Department of Gynae and Obs, Fazaia Medical College, Islamabad.
² Department of Gynae and Obs, Al Nafees Medical College, Islamabad.
³ Department of Gynae and Obs, Holy Family Hospital, Rawalpindi.

Correspondence: Fatima Chaudhry Inayat, Assistant Professor of Gynae/Obs, Fazaia Medical College, Islamabad.
Contact No: 03335585407
Email: fatima.inayat85@gmail.com

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perinatal outcomes without intervention in these low risk pregnancies would support a policy of watchful waiting thus not only reducing the anxiety and cost associated with intervention, but also improving bishop score and eventually success of induction in those who do not go in to spontaneous labour thus contributing towards lower cesarean section rate over all.

**Operational Definitions:**

a. Oligohydramnios… Amniotic fluid index less than or equivalent to 5
b. Fetal outcome  
   1. Meconium staining (Yes / No)  
   2. APGAR score at 5 min after birth

APGAR Score: Excellent (8-10), Good (6-7), low (<6)

**MATERIALS AND METHODS**

This RCT study was conducted at the Gynae/Obs Unit II, Holy Family Hospital, Rawalpindi from February 2015 to July 2015.

A total of 144 patients were enrolled (72 patients in each group). GROUP A included pregnant ladies with oligohydramnios for whom induction of labour was done. GROUP B included pregnant ladies with oligohydramnios for whom expectant management was done.

**SAMPLE TECHNIQUE:** Consecutive non probability sampling

**SAMPLE SELECTION:**

**Inclusion Criteria:**

1. Singleton pregnancies at 37-40 weeks gestation  
2. Both Primigravida and multigravida  
3. Cephalic presentation

**Exclusion Criteria:**

1. PIH  
2. IUGR  
3. PROM  
4. Congenital anomalies

**Data Collection Procedure:** Patients were enrolled after informed consent from OPD after hospital ethical committee approval, and exclusion criteria were applied. Evaluation was done by history examination and ultrasound findings.

Induction of labour in patients of group A was done using intracervical Foley and tablet prostaglandin E2 vaginally.

During expectant management of group B patients they were followed up in OPD for weekly antenatal checkup to ensure fetomaternal surveillance. Some patients of group B went into spontaneous labour. Some patients of group B needed to be delivered by induction or LSCS due to any other indication at any stage before reaching 40wks of gestation. Some patients who did not go into spontaneous labour were induced at 40 week.

Fetal outcome in both groups was assessed through meconium staining and APGAR score.

Data was duly noted in a preformed proforma.

**PROFORMA**

<table>
<thead>
<tr>
<th>Serial Number:</th>
<th>Registration number:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years:</td>
<td>Address: ____________</td>
</tr>
<tr>
<td>Gestational age at the time of delivery (weeks):</td>
<td>Parity: ____________</td>
</tr>
</tbody>
</table>

**Group A** Induce  
**Group B** observe

**Neonatal Outcome:**

a) Meconium Staining (Yes/No)  
b) APGAR scoring at 5 minutes:
   (a) Excellent (8-10)  
   (b) Good (6-7)  
   (c) Bad (<6)

**Data Analysis:** Data was entered and analyzed by using SPSS version-10. Mean and standard deviation were calculated for quantitative variables such as age, gestational age, parity. Frequency and percentages were calculated for meconium staining and APGAR score at 5 minute of birth.

Chi-square test was used to compare the meconium staining and APGAR score at 5 minutes in both groups. P-value less than 0.05 was considered significant.

**RESULTS**

Mean maternal age in group A was 26.10. In group B mean maternal age was 26.31.

In group A 45.83 % of the patients were primigravidas while 54.17% of the patients were multiparas.

In group B 39.43 % of the patients were primigravida while 60.57 % of the patients were multiparas.

In group A n=55 (76.38%) had no meconium staining while n=17 (23.62%) had meconium staining while In group B n=59 (81.94%) had no meconium staining and n=13 (18.05%) had meconium staining as shown in Table 1.

In group A n=60 (83.33%) had excellent APGAR score while n =12 (16.66%) had good APGAR score at 5 minute of birth while in group B n=56 (77.77%) had excellent APGAR score while n =16 (22.22%) had good APGAR score at 5 minute of birth as shown in Table 2.

In both groups no baby was delivered with poor APGAR score.

**Table No.1: Meconium stained amniotic fluid**

<table>
<thead>
<tr>
<th>Meconium stained amniotic fluid</th>
<th>Group A</th>
<th>Group B</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>17</td>
<td>13</td>
<td>0.835</td>
</tr>
<tr>
<td>Negative</td>
<td>55</td>
<td>59</td>
<td></td>
</tr>
</tbody>
</table>
Isolated oligohydramnios in healthy pregnancy at term was thought to be associated with poor outcomes so much so that labour induction was recommended in most of the cases fearing poor perinatal outcomes. Reason for these fears were studies attributing poor perinatal outcomes to oligohydramnios, though these studies were biased owing to inclusion of pregnancies with congenital defects, pre-eclampsia or intrauterine growth restriction (IUGR), and post-term gestation in their samples. The poor outcomes might just be reflected because of these complications rather than oligohydramnios per se.

There is no evidence that isolated oligohydramnios per se at term is a risk factor for poor outcomes. However, induction for isolated oligohydramnios leads to higher cesarean section rates.

In 2003 Locatelli studied 3,049 healthy pregnant women between 40 and 41.6 weeks of pregnancy. Babies born to women with low amniotic fluid were more likely to have birth weights beneath the 10th percentile (13% vs. 6%) but there were no differences between groups as regards meconium staining, meconium aspiration, umbilical artery pH <7, or APGAR scores. There was only one stillbirth (in the normal fluid group) for a true knot in the umbilical cord. These results are comparable to favorable perinatal outcome in my study measured in terms of meconium staining and APGAR score at 5 min of birth. My study results are also comparable to a study by Manzaneres who found that inducing labor for isolated oligohydramnios at term increased cesarean and operative vaginal delivery rates without any improvement in newborn outcomes. Another study by Rainford found oligohydramnios to be associated with increased risk of labour induction but not to adverse pregnancy outcomes like NICU admission, 5 min APGAR score less than 7. Instead he narrated higher rate of meconium staining in pregnancies with normal AFI as compared to those with oligohydramnios. His study concluded that operative delivery rate was not higher in oligohydramnios group. Similarly, a study by Ashwal also compared adverse pregnancy outcome like Caesarean section /operative delivery due to non-reassuring heart rate (NRFHR), low Apgar score, umbilical artery pH <7.10, neonatal intensive care admission, meconium aspiration syndrome, intubation or hypoxic-ischemic encephalopathy in pregnancies complicated by oligohydramnios to pregnancies with normal AFI and found oligohydramnios not to be linked to these outcomes.

Results of my study cannot be generalized as it has a small sample size, including patients from one gynaec centre. However, looking at the favourable perinatal outcome of my study, a large scale study may be carried out including patients from different centres and such study may help us to reduce intervention policies merely for reduced amniotic fluid volume in otherwise low risk pregnancies at term. Considering recommended gestational age for induction of labour at 41 weeks for low risk pregnancies further studies may be planned where expectant management for isolated oligohydramnios may be extended till 41 weeks.

DISCUSSION


d| APGAR score at 5 min of birth | Group A | Group B | P-Value |
---|---|---|---|---|
**Excellent** | 60 | 56 | 0.400 |
**Good** | 12 | 16 | |
**Poor** | 0 | 0 | |

There is no evidence that isolated oligohydramnios per se at term is a risk factor for poor outcomes. However, induction for isolated oligohydramnios leads to higher cesarean section rates.

CONCLUSION

Conclusion of my study is that expectant management in term pregnancies with isolated oligohydramnios till 40 weeks is safe. Thus by avoiding induction done at poor bishop score solely for oligohydramnios, we can decrease overall cesarean section rate.

REFERENCES


Knowledge and Attitude of Pakistani Dentists Regarding Covid-19
Asma Munir Khan¹, Arham Riaz⁴, Shazia Nawabi², Muhammad Qasim Javed¹, Khurram Shahzad³ and Farzana Kulsoom⁵

ABSTRACT

Objective: The objective of the study was to examine the knowledge, and attitude of Pakistani dentists, regarding novel COVID-19 disease.

Study Design: Descriptive, Cross sectional study.

Place and Duration of Study: This study was conducted at the Department of Conservative Dental Sciences and Endodontics, College of Dentistry, Qassim University, Al-Qassim, Saudi Arabia and Department of Oral Pathology, Frontier Medical and Dental College Abbottabad from 15th to 31st March, 2020 in Pakistan.

Materials and Methods: A self-designed e-questionnaire was administered through e-mail to 500 dentists. SPSS version 23 was used to analysis data. Descriptive statistics were presented as frequency and percentages. The association between the dependent and independent variables was determined by utilizing Chi-square test and the level of significance was set at p value <0.05. Moreover, the inferential statistics (Mann Whitney U and Kruskal Wallis tests, p-value<0.05) were used for determining the significance among study variables. The correlation between the attitude and knowledge scores was assessed by utilizing Spearman’s rank correlation coefficient.

Results: A total of 306 dentists responded. Participants’ mean knowledge score was 10.69± 2.14, with 91.5 % participants having sufficient knowledge. 242 (79.1%) respondents showed positive attitude (≥4) towards COVID-19. The mean attitude score was 4.28±0.61. The results of current study showed a significant correlation of knowledge with both designation (p-value=0.002) and gender (p-value=0.04).

Conclusion: Pakistani dentists have exhibited adequate awareness about general symptoms, transmission mode, cross-infection control and dental practice management in perspective of the COVID-19 outbreak. However, their understanding to protect dental professionals from this highly contagious disease during specialized dental procedures was unsatisfactory.

Key Words: COVID-19, Attitude, practice management, cross-infection control.

INTRODUCTION

Human coronaviruses are highly communicable pathogens that have lately received attention at a global level following pandemic outbreak of a COVID-19 disease caused by novel coronavirus strain¹. This specific strain was isolated from a marketplace at Wuhan city, China in end of December, 2019 ².

¹ Department of Conservative Dental Sciences and Endodontics, College of Dentistry / Prosthetic Dental Sciences² / Deanship of Education³, Qassim University, Al-Qassim, Saudi Arabia.
² Academy of Continuing Health Education and Research, Islamabad.
³ Department of Oral Pathology, Frontier Medical and Dental College Abbottabad.

Later, it spread rapidly to other parts of the world. On 8th January 2020, it was formally declared as a causative means of COVID-19 by the Chinese Centre for Disease Control and Prevention ⁴. Subsequently, because of its rapid progression it was confirmed as a public health emergency of international concern (PHEIC)⁵ by World Health Organization (WHO). Later, in March, 2020 WHO officially proclaimed this outbreak as a pandemic owing to its persistent spread at an alarming rate. To date (April 10th, 2020) this deadly virus has reached over 209 countries worldwide with 1,470,441 confirmed cases and claimed 86,327 deaths ⁶. COVID-19 is an extremely infectious viral disease that is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)⁷. It is single stranded RNA virus that belongs to a large family of coronaviruses named as “Coronaviridae”. Its size ranges from 65-125nm in diameter. SARS-CoV-2 comprises of crown shaped spikes which are present on its outer surface that facilitates its entry into host cells⁸. Moreover, it possesses great binding affinity to the human angiotensin converting enzyme 2 receptors (ACE2) that facilitates its entry into host cells ⁹. It is further categorized into four subgroups: alpha (α), beta

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¹ Dr. Asma Munir Khan, Assistant Professor, Department of Conservative Dental Sciences and Endodontics Qassim University College of Dentistry, Saudi Arabia.
Contact No: 00966597472235
Email: dr.asma.munir@qudent.org

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(β), gamma (γ) and delta (δ) type coronavirus. Alpha and beta types primarily infect human beings and mammals targeting their gastrointestinal tract, central nervous system and respiratory system.

SARS-CoV-2 is regarded as the seventh identified human coronavirus that phylogenetically resembles other two highly communicable respiratory coronaviruses i.e Middle East respiratory syndrome coronavirus (MERS -CoV) and severe acute respiratory syndrome coronavirus (SARS-CoV). The routes of spread in humans involve direct contact with respiratory droplets and indirect transmission through fomite.

The outbreak of COVID19 has undoubtedly placed healthcare workers at increased risk of acquiring nosocomial infection. Bio-aerosols produced during dental procedures contain bacteria, fungi and viruses that have the potential to float in the air for considerable period of time. Bio-aerosols can be inhaled by dentists and patients. Hence, excessive mutation, increased pathogenicity and various routes of transmission of SARS-CoV-2 may add to nosocomial spread in the dental offices.

Due to the distinctive features of dental treatment procedures that involve aerosol generation, close contact with patient’s oropharyngeal region, and direct contact of contaminated hands with mucous membrane, the routine infection control measures in dental practice are not adequate to prevent the COVID-19 spread. Therefore, dental health care professionals (DCP) are at increased risk of acquiring infection and becoming potential carriers. In this context American Dental Association issued an update on 16th March 2020, where it was stated that all elective dental treatments should be postponed and only patients with actual dental emergencies should be accommodated.

The current coronavirus pandemic hit Pakistan in February 2020. As of 5th June 2020, the number of confirmed cases in the country is over 89249, with 31198 recoveries and 1838 deaths. Owing to limited resources and fragile health care system, Pakistan is facing a major COVID-19 challenge. WHO has expressed concerns that if prompt and effective measures are not taken Pakistan might emerge as the next epicentre of this pandemic. Health care workers being the frontline warriors are at an increased risk of acquiring nosocomial infections. Being a low-income country, limited data is available on infection prevention and control strategies but generally it is believed that basic infection control protocols are insufficient in health care settings in Pakistan. One of the recent study concluded that Pakistani health care workers are not fully prepared to face threat of a COVID 19 epidemic as they are not aware of dynamics of disease transmission via a vis strategy for its prevention and control. Effective implementation of infection control programs should be practiced which depends largely on awareness, training and cooperation of health care workers.

Therefore, the main aim of current study was to explore the level of knowledge and attitude of dentists towards the COVID19 disease. The results of this preliminary study will help in formulating future policies, training methods and robust infection control strategies that can be employed in dental settings for safeguarding dentist’s wellbeing.

MATERIALS AND METHODS

The present descriptive cross-sectional study was carried out on the dentists from 15th to 31st March, 2020 in Pakistan. A non-probability convenience sampling technique was employed. Self-administered e-questionnaire was sent through an electronic mail to 500 dentists in private and public sector, health and educational institutes across Pakistan. All the potential participants were informed about purpose of study. 306 dentists including Professors/Associate Professors, assistant professors, lecturers and general dental practitioners responded.

The study questionnaire was developed by authors after detailed literature review. Subsequently, the questionnaire was reviewed by the senior dental assistants and was simplified. The questionnaire had three sections. The first section embodied questions related to designation and gender of the participants. The second section of the e-questionnaire was comprised of thirteen questions with yes and no options in order to explore knowledge of the respondents in relation to COVID-19 disease. The last section of the e-survey had nine questions to evaluate the dentists’ attitude towards novel COVID-19 disease. The questions were developed on a five point Likert scale with a neutral midpoint and balanced responses.

The participants’ knowledge was scored from zero to thirteen. The cut-off point equal to or more than nine (≥9) was set for sufficient knowledge and less than nine (<9) for insufficient knowledge. Assessment for attitude was made and responses were documented on five point likert scale. Scores of 5,4,3,2 and 1 were assigned to strongly agree, agree, undecided, disagree and strongly disagree, respectively. The mean score of more than or equal to 4 (≥4) was considered as positive attitude and mean score of less than 4 (<4) was taken as negative attitude.

Data was analysed by utilizing SPSS version 23. Descriptive statistics were recorded as percentages and frequencies. The association between the dependent and independent variables was determined by utilizing Chi-square test and the level of significance was set at p-value <0.05. Moreover, the inferential statistics
RESULTS

A total number of 306 Dentists responded with an overall response rate of 61.2% with male to female ratio of 1:1.55. Majority of the participants were general dental practitioners (GDP) (35.3%) followed by lecturers (32.7%). The demographic details of the participants are shown in Table 3.

The average knowledge score of the respondents was 10.69±2.14. Adequate knowledge was displayed by 91.5% of participants (>9), whereas, 8.5% showed inadequate knowledge (<9). The respondents were most knowledgeable about the items related to the routes of transmission, urgent dental care techniques and personal protective equipment (>95%). On the other hand, minimum knowledge was noted in two questions, one concerning the use of ultrasonic devices while handling Covid-19 suspected cases (51.6%) and the other was associated with effectiveness of 1% of hydrogen peroxide mouthwash use as a pre-rinse (59.6 %). Table-1 is depicting the knowledge of respondents.

Attitude score of the participants is shown in Table 2. Out of 306 participants, 242 (79.1%) displayed positive attitude (>4) while 64 participants (20.9 %) showed negative attitude (<4) towards COVID19. The mean attitude score was 4.28 ±0.61. The highest mean attitude score was observed for the item regarding the treatment of emergency cases (4.68±0.76). Conversely, the lowest mean attitude score was noted for the item inquiring about the utilization of the chemo mechanical caries removal methods (3.83±1.04). Significant correlation was noted between the participants’ attitude and gender for the item exploring the fear of contracting COVID19 (p-value=0.003).

The association of gender and designation with mean knowledge and attitude among the dentist is displayed in Table 3. Results of the current study highlighted significant association of gender and designation with knowledge score. Spearman correlation showed significant correlation between the attitude and the knowledge score of the dentists (r=0.655, p value =0.01).

<table>
<thead>
<tr>
<th>Knowledge of COVID19</th>
<th>Correct Answer N (%)</th>
<th>Incorrect Answer N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mode of transmission of COVID 19 is Fomite transmission and by respiratory droplets. (True)</td>
<td>302(98.7)</td>
<td>4(1.3)</td>
</tr>
<tr>
<td>WHO suggests that washing hands with water and soap for minimum 20 secs can help in the prevention of disease transmission (True)</td>
<td>262(85.6)</td>
<td>44(14.4)</td>
</tr>
<tr>
<td>Tele-screening via phone is recommended as first line of action to identify patients with possible COVID 19 (True)</td>
<td>222(72.5)</td>
<td>84(27.5)</td>
</tr>
<tr>
<td>Urgent dental care includes severe toothache, cellulitis, Ludwig’s angina, uncontrolled bleeding and Oro-facial trauma (True)</td>
<td>298(97.4)</td>
<td>8(2.6)</td>
</tr>
<tr>
<td>Most effective mouth wash as a pre-rinse to protect against COVID 19 infection is 1% hydrogen peroxide (True)</td>
<td>182(59.6)</td>
<td>124(40.5)</td>
</tr>
<tr>
<td>Four handed dentistry is highly recommended for controlling the spread of disease (True)</td>
<td>264(86.3)</td>
<td>42(13.7)</td>
</tr>
<tr>
<td>Face shields and eye wear are essential while examining the patients (True)</td>
<td>298(97.4)</td>
<td>8(2.6)</td>
</tr>
<tr>
<td>Ultrasonic devices can be safely used in dental office for patients (False)</td>
<td>158(51.6)</td>
<td>148(48.4)</td>
</tr>
<tr>
<td>After extraction resorbable sutures should be used in patients (True)</td>
<td>254(83)</td>
<td>52(17)</td>
</tr>
<tr>
<td>N -95 mask is essential while examining the patients (True)</td>
<td>274(89.5)</td>
<td>32(10.5)</td>
</tr>
<tr>
<td>Rubber dam isolation is a prerequisite for every patient (True)</td>
<td>258(84.3)</td>
<td>48(15.7)</td>
</tr>
<tr>
<td>High volume suction is mandatory in dental practice (True)</td>
<td>262(85.6)</td>
<td>44(144)</td>
</tr>
<tr>
<td>Antibiotics are the first line of treatment (True)</td>
<td>238(77.8)</td>
<td>68(22.2)</td>
</tr>
</tbody>
</table>

Note: Assessment of knowledge was done by awarding 0 for incorrect answer and 1 for correct answer. The range of knowledge score was from 0 to 13. Cumulative score of less than 9 was considered as insufficient score whereas greater than 9 was considered as sufficient knowledge score. Mean value of knowledge score=10.69 ± 2.14
<table>
<thead>
<tr>
<th>Items</th>
<th>Faculty's Responses** N (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are you scared of getting infected with Covid -19 from a patient or a co-worker?</td>
<td>114(37.3)</td>
<td>122(39.9)</td>
</tr>
<tr>
<td>Are you anxious of providing treatment to a patient who is suspected of being infected with Covid 19?</td>
<td>122(39.9)</td>
<td>112(36.6)</td>
</tr>
<tr>
<td>Currently every patient's travel history and body temperature should be taken before performing any dental procedure?</td>
<td>206(67.3)</td>
<td>90(29.4)</td>
</tr>
<tr>
<td>Relevant medical history i.e respiratory illness like cough, sputum, fever, difficulty in breathing should be sought for every patient</td>
<td>204(66.7)</td>
<td>90(29.4)</td>
</tr>
<tr>
<td>Only emergency dental procedures should be carried out in current circumstances</td>
<td>238(77.8)</td>
<td>56(18.3)</td>
</tr>
<tr>
<td>Aerosol generating procedure such as use of triple syringe should be minimized as much as possible</td>
<td>204(66.7)</td>
<td>88(28.8)</td>
</tr>
<tr>
<td>Chemo mechanical methods should be used for caries removal in patients with Irreversible pulpitis</td>
<td>92(30.1)</td>
<td>110(35.9)</td>
</tr>
<tr>
<td>Would you like to attend any training sessions to handle any untoward Covid 19 situation?</td>
<td>142(46.4)</td>
<td>128(41.8)</td>
</tr>
<tr>
<td>Would you like to volunteer for working in support of medical teams in case of emergency?</td>
<td>130(42.5)</td>
<td>98(32)</td>
</tr>
</tbody>
</table>

Derived from 'Chi-square test and 'Kruskal Wallis test
**Strongly disagree=SD; Disagree=D; Undecided=U; Agree=A; Strongly agree=SA
Note: Mean attitude score=4.28±0.61
Mean Attitude Score ± Standard Deviation (SD): a3.98 ± 1.11, b3.97 ± 1.88, c4.59 ± 0.76, d4.58 ± 0.77, e4.68± 0.76, f4.58 ± 0.73, g3.83 ± 1.04, h4.25±0.95, i4.05±1.08
Furthermore, encouraging results came regarding personal protection and hand biotic use. The knowledge score of more than 85% was also noted in the study. This might be attributed to the connection with aerosol generating procedures, practicing rubber dam isolation and volume suction, urgent dental care appointments, for identifying the patients with possible or suspected COVID-19 disease18. Contrary to our findings, Khan and colleagues reported insufficient knowledge of participants regarding antibiotic use18, 19. The participants in current survey exhibited insufficient knowledge regarding the procedures utilizing ultrasonic apparatus for treating suspected Covid-19 patients. This may be due to their lack of understanding about this new disease and its connection with aerosol generating procedures20.

Current study suggested that the mean attitude score of Pakistani dentists regarding COVID-19 was in positive range (4.28 ±0.61), particularly when inquired about recording patient’s appropriate medical and recent travel history, checking body temperature and treating only emergency cases. These findings are in accordance with other researches that have reported mean positive attitude for physicians21. Likewise, the findings are also in line with the studies on Jordanian dentists, and on healthcare workers18, 22. On the other hand, relatively lower mean attitude scores (<4) were noted when respondents were questioned about fear of contracting COVID-19, anxiousness to treat suspected patients and caries removal methods. The fearless attitude of the Pakistani dentists might be attributed to the fact that COVID-19 disease didn’t hit the region that bad as compared to west and majority of the European countries. This outcome resulted in common perception that disease is moderately dangerous especially for younger individuals. The results are again in accordance with the recent study done in Jordan, where 71.7 % of dentists identified COVID-19 as moderately hazardous and not a major community health issue18. Furthermore, encouraging results came out regarding questions related to training workshops to deal with any unfortunate COVID-19 situation and volunteering their assistance as part of medical teams in case of potential emergencies. The findings were in line with results of Khader et al, where Jordanian dentists exhibited knowledge score of more than 85% for items related to PPE, mode of transmission and attitudes regarding personal protection and hand hygiene18.

The knowledge score of the respondents in present study ranged between 80 to 98% for the items that have investigated routes of transmission, hand hygiene, use of PPE and high-volume suction, urgent dental care procedures, practicing rubber dam isolation and employing four handed dentistry. These finding are in line with results of Khader et al, where Jordanian dentists exhibited knowledge score of more than 85% for items related to PPE, mode of transmission and hand hygiene18. The results were also in accordance with the outcome of other studies on SARS-CoV and MERS-CoV where the participants depicted sufficient knowledge regarding personal protection and hand hygiene18, 20.

Participants also displayed good knowledge for questions regarding tele screening and antibiotics use (score range 70% to 80%). This might be attributed to some recently published studies that recommended the initial screening through telephone, while scheduling appointments, for identifying the patients with possible or suspected COVID-19 disease18. The results were also in accordance with other researches that have reported mean positive attitude scores (<4) were noted when respondents were questioned about fear of contracting COVID-19, anxiousness to treat suspected patients and caries removal methods. The fearless attitude of the Pakistani dentists might be attributed to the fact that COVID-19 disease didn’t hit the region that bad as compared to west and majority of the European countries. This outcome resulted in common perception that disease is moderately dangerous especially for younger individuals. The results are again in accordance with the recent study done in Jordan, where 71.7 % of dentists identified COVID-19 as moderately hazardous and not a major community health issue18. Furthermore, encouraging results came out regarding questions related to training workshops to deal with any unfortunate COVID-19 situation and volunteering their assistance as part of medical teams in case of potential emergencies. The findings were in line with results of Khader et al, where Jordanian dentists exhibited knowledge score of more than 85% for items related to PPE, mode of transmission and attitudes regarding personal protection and hand hygiene18.
with the fact that was documented in the paper by United Nations where Pakistan was ranked 10th among the world with the total volunteer work force standing at 56 million. To the best of our knowledge the is no related data to evaluate the dentists’ attitude for their participation in the COVID 19 crisis support teams. Nevertheless, in recent study researchers has put forward dental outreach program model for managing the crisis situation during current pandemic.

Significant correlation was noted between the participants’ attitude and gender for the item exploring the fear of contracting COVID19 (p-value=0.003). The significantly higher percentage (44%) of female dentists strongly agreed that they are scared of contracting the disease as compared to 30% of the male dentists. This finding is in line with the research finding where females reported greater anxiety and fear than male counterparts.

Mann-Whitney U and Kruskal Wallis tests were used to analyse the correlation of designation and gender with mean knowledge and mean attitude score. The results showed the mean knowledge score of female dentists were significantly lower than the male dentists (P-value=0.04). Likewise, significant correlation was noted between mean knowledge score and designation (0.002). Senior faculty members were found to have high mean knowledge score. This can be credited to the wisdom of senior faculty members gained through the years of experience as compared to the lecturers and GDPs. The application of Tukey’s posthoc test suggested a statistically significant difference between the mean knowledge scores of GDP and Assistant professors (P-value=0.02). The difference may be due to the fact that more than 80% of the female dentists belonged to the GDP and lecturer groups.

Positive knowledge and attitude correlation of dental health care workers noted in the present research reaffirms their association. Considering this, it can be concluded that dentists with positive attitude regarding COVID-19 are motivated to acquire more information. The strength of this study is that it has highlighted the area of highest concern. The findings of this study would be critical for designing effective training sessions and cross infection control measures in the current circumstances.

The limitations of the study are the moderate response rate, because the pandemic has caused many to be upset and taking care of personal affairs, that resulted in a smaller than expected sample size, which diminishes the generalizability of our results. Further investigations are warranted in this perspective.

CONCLUSION

Pakistani dentists have exhibited adequate awareness about general symptoms, transmission mode, cross-infection control and dental practice management in perspective of the COVID-19 outbreak. However, their understanding to protect dental professionals from this highly contagious disease during specialized dental procedures was unsatisfactory. Effective implementation of infection control programs depends on adequate knowledge, awareness and teamwork of individuals. Absence of proper knowledge and training will adversely affect the attitude of the dentist and results in the inadequate infection control measures and delay of emergency dental treatment required for the COVID 19 patients. Furthermore, it is imperative that guidelines formulated on the basis of recommendations released by international reputable institutions should be relayed and implemented by the regional dental associations.

Author’s Contribution:
Concept & Design of Study: Asma Munir Khan
Drafting: Arham Riaz, Shazia Nawabi
Data Analysis: Muhammad Qasim Javed, Khurram Shahzad, Farzana Kulsoom
Revisiting Critically: Asma Munir Khan, Arham Riaz
Final Approval of version: Asma Munir Khan

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

REFERENCES


Role of Bone Marrow Clot Biopsy in Workup of Haematological and Non-Haematological Diseases

Jamila Farid¹, Muhammad Idris¹, Mumtaz Ahmad Khan², Nasreen Javed¹ and Shazia Moeen¹

ABSTRACT

Objective: To study the role of bone marrow clot biopsy in the diagnosis of haematological and non haematological disorders.

Study Design: Descriptive cross sectional

Place and Duration of Study: This study was conducted at the Department of Pathology, Ayub Medical College from January 2018 to December 2019 over two years.

Materials and Methods: 335 patients of both sex and age > two years were enrolled by non-probability convenience sampling after an informed written consent. Children <two years old were excluded. Venous blood sample taken for complete blood counts and blood film, bone marrow obtained from posterior iliac spine, smears made from the marrow aspirate and venous blood immediately and fixed in alcohol after drying. The remaining part of bone marrow sample was allowed to clot and fixed in 10 percent buffered formol saline and processed further like soft tissue biopsy. Trephine biopsy obtained from the same site, fixed in 10 percent formol saline, before processing further. Slides prepared from blood were stained by May Grunewald Giemsa (MGG). Slides of bone marrow trephine biopsy and clot biopsy were stained by haematoxylin & eosin stain after processing. These slides were examined independently by an experienced pathologist taking care of biasness and double blinding. Results of bone marrow clot biopsy were compared with trephine biopsy.

Results: Total of 335 patients (176 males and 159 females, Male to female ratio 1:1.1). Trephine biopsy made conclusive diagnosis in 326 and marrow clot biopsy in 121 patients.

Conclusion: There is statistically no significant difference in diagnostic role of trephine and clot biopsy.

Key Words: Bone marrow, trephine biopsy, marrow clot biopsy.

INTRODUCTION

Bone marrow examination plays a pivotal role in the diagnosis of a number of haematological conditions like anaemia, leukaemia, thrombocytopenia, myeloproliferative neoplasms as well as non haematological conditions like metastatic cancers, tuberculosis, pyrexia of unknown origin and osteopetrosis.¹⁻⁶ Patients coming to physicians, who are advised bone marrow examination, may benefit more if they are referred first to a haematologist to evaluate the need for this test. It may not be beneficial many a times.¹⁻²

¹ Department of Pathology, Ayub Medical College, Abbottabad.
² Department of Pathology, Abbas Institute of Medical Sciences Muzaffarabad.

Correspondence: Muhammad Idris, Associate Professor of Pathology, Ayub Medical College, Abbottabad.
Contact No: 0333-5037762
Email: midris63@yahoo.com

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Investigational procedures including bone marrow may be made more useful if primary focus is on treatable underlying pathology.³ The knowledge of normal histology of bone marrow, reactive changes, age related changes and use of newer techniques in addition to the basic clinical and haematological information may be more fruitful than simply focusing upon bone marrow findings only.⁴⁻⁶.³⁻⁹ Marrow in young children with visceral leishmaniasis may show dyserythropoiesis and prominent plasma cells, which may be confused with pathology of haemopoiesis if care is not observed.¹¹ Bone marrow examination has two parts, a fluid part known as bone marrow aspirate and a solid part which is called trephine biopsy. It comprises examination of marrow aspirate (fluid in nature) and trephine biopsy (solid cylinder of marrow). Samples for both the parts are obtained in one sitting. Bone marrow aspirate may not be enough to reach a conclusive diagnosis in conditions like multiple myeloma, lymphoma, metastatic bone disease and aplastic anaemia. A good-length trephine biopsy is necessarily taken if any of these conditions is suspected. Studies have revealed improved diagnostic yield if both the aspirate and trephine biopsy are taken simultaneously.¹²
marrow aspirate is smeared on slides, fixed and examined by the haematologist, while trephine biopsy is processed like a histopathology sample and also examined by histopathologist. The aspirated material left behind after making adequate number of slides is usually discarded. For the last few years, it has been observed that if is allowed to clot and processed like a soft tissue biopsy specimen for histopathology (also called bone marrow clot biopsy), it may provide valuable information regarding final diagnosis. It has also been learnt in the past years that examination of bone marrow clot biopsy specimen may also obviate the need of performing trephine biopsy in some cases. The studies have shown that if the left over aspirate is preserved and processed further, it can be used for further work up of the underlying condition i.e. Immunohistochemistry and cytogenetic studies. Utilization of bone marrow clot biopsy prepared by cell block technique is a valuable technique to avoid the wastage of precious bone marrow substance aspirated from the patient. The role of bone marrow clot biopsy as an adjuvant procedure in the diagnosis of diseases involving bone marrow has also been documented. The present study has been planned with a view to evaluate the utility of bone marrow clot biopsy in the diagnosis of haematological and non-haematological disorders.

MATERIALS AND METHODS

The present study focused upon processing and examination of bone marrow clot biopsy in different haematological disorders like anaemia, leukaemia, lymphoma, thrombocytopenia multiple myeloma, lymphoproliferative disorders, metastatic bone disease, tuberculosis and Visceral Leishmaniasis. The study was conducted over a period of 2 years from January 2018 to December 2019 at the department of Pathology Ayub Medical College Abbottabad Pakistan. A total of 335 consecutive patients referred for bone marrow examination were enrolled in the study. Children less than 3 years of age were excluded from the study because the facility for their trephine biopsy was not available in our department. After an informed written consent venous blood sample was taken for complete blood counts and blood film. Then, bone marrow sample was obtained from posterior iliac spine under local anaesthesia (2% lignocain). Smears were made from the marrow aspirate and venous blood immediately and fixed in alcohol after drying. The remaining part of bone marrow sample was allowed to clot and fixed in 10 percent buffered formol saline and processed further like soft tissue biopsy. At the same time, trephine biopsy was also obtained from the same site and fixed in 10 percent formol saline, before processing further. Slides prepared from peripheral blood were stained by May Grunewald Giemsa (MGG) and new methylene blue (for reticulocyte). Slides of bone marrow aspirate and trephine imprints were also stained by MGG stain. Pearl’s staining was done on bone marrow slides for iron content. Slides of bone marrow trephine biopsy and clot biopsy were stained by haematoxylin & eosin stain after processing. Slides of peripheral blood, bone marrow aspirate and trephine imprints were examined the next day and report was prepared. These slides were kept in a rack labeled “blood and bone marrow”. The slides of bone marrow clot and trephine biopsy were available for examination on day 7 and 15 respectively. They were examined independently without looking at the result of each other and that of the bone marrow aspirate. These slides were kept in separate racks labeled “bone marrow clot” and “trephine biopsy” respectively. Reports and slides of peripheral blood film, bone marrow aspirate, clot biopsy and trephine biopsy were then examined sequentially in separate sessions by double blind technique by the same pathologist to avoid bias. Final conclusive diagnosis was made on the basis of clinical information, examination of blood film, bone marrow and trephine biopsy slides. In those cases, where conclusive diagnosis could not be reached at, further tests were suggested on the study samples, in the light of microscopic findings. Results of bone marrow clot biopsy were compared with trephine biopsy to evaluate its diagnostic role. The results were expressed in tables 1 to 4 and fig 1.

Hypothesis: “There is no statistically significant difference between the results of trephine biopsy and bone marrow clot biopsy”.

RESULTS

Total number of participants was 335, 169 male and 159 female with male to female ratio 1.1:1. Iron deficiency anaemia, immune thrombocytopenia and acute leukemia were among the most common diagnosis (Table 1). The most common age group affected was 20 to 60 years. Trephine biopsy was positive in 326, while bone marrow clot biopsy was positive in 321 patients. Megaloblastic anaemia, normal marrow and visceral leishmaniasis were the three conditions in which clear disagreement was seen between trephine biopsy and marrow clot biopsy (Table 2). There was statistically no significant difference between the results of trephine biopsy and marrow clot biopsy, (p value >0.05, hypothesis not proved, table 3). Sensitivity, specificity and positive predictive value were high and negative predictive value was low (Table 4).
Table No.1: Demographic data and frequency distribution of disorders

<table>
<thead>
<tr>
<th>S.N</th>
<th>Disorder</th>
<th>No</th>
<th>Age in years</th>
<th>Mean age, range 2-65</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No %</td>
<td>No %</td>
<td>No %</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2-20 21-40 41-60 60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Iron deficiency anaemia</td>
<td>65</td>
<td>2</td>
<td>10 20 24 9</td>
<td>20 30.8</td>
<td>45 69.2</td>
</tr>
<tr>
<td>2</td>
<td>Immune thrombocytopenia</td>
<td>60</td>
<td>10</td>
<td>25 15 6 4</td>
<td>36 60</td>
<td>24 40</td>
</tr>
<tr>
<td>3</td>
<td>Acute Leukaemia</td>
<td>40</td>
<td>7</td>
<td>15 13 3</td>
<td>24 60</td>
<td>16 40</td>
</tr>
<tr>
<td>4</td>
<td>Reactive Change</td>
<td>30</td>
<td>2</td>
<td>18 6 2</td>
<td>18 60</td>
<td>12 40</td>
</tr>
<tr>
<td>5</td>
<td>Megaloblastic anaemia</td>
<td>25</td>
<td>3</td>
<td>8 6 4</td>
<td>15 60</td>
<td>10 40</td>
</tr>
<tr>
<td>6</td>
<td>Myeloproliferative neoplasm</td>
<td>25</td>
<td>0</td>
<td>8 10 2</td>
<td>10 40</td>
<td>15 60</td>
</tr>
<tr>
<td>7</td>
<td>Aplastic anaemia</td>
<td>20</td>
<td>2</td>
<td>3 10 2</td>
<td>12 60</td>
<td>8 40</td>
</tr>
<tr>
<td>8</td>
<td>Normal Marrow</td>
<td>20</td>
<td>1</td>
<td>4 10 5</td>
<td>12 60</td>
<td>8 45</td>
</tr>
<tr>
<td>9</td>
<td>Chronic Lymphocytic leukemia</td>
<td>14</td>
<td>0</td>
<td>0 0 6</td>
<td>8 57</td>
<td>6 43</td>
</tr>
<tr>
<td>10</td>
<td>Lymphoma</td>
<td>10</td>
<td>0</td>
<td>4 2 2</td>
<td>6 60</td>
<td>4 40</td>
</tr>
<tr>
<td>11</td>
<td>Multiple myeloma</td>
<td>5</td>
<td>0</td>
<td>0 0 0</td>
<td>3 60</td>
<td>2 40</td>
</tr>
<tr>
<td>12</td>
<td>Hypersplenism</td>
<td>5</td>
<td>0</td>
<td>0 0 2</td>
<td>3 60</td>
<td>2 40</td>
</tr>
<tr>
<td>13</td>
<td>Myelodysplastic syndrome</td>
<td>5</td>
<td>0</td>
<td>0 0 2</td>
<td>2 40</td>
<td>3 60</td>
</tr>
<tr>
<td>14</td>
<td>Metastatic solid malignancy</td>
<td>4</td>
<td>0</td>
<td>0 0 2</td>
<td>2 50</td>
<td>2 50</td>
</tr>
<tr>
<td>15</td>
<td>Granulomatous inflammation</td>
<td>4</td>
<td>0</td>
<td>1 3 0</td>
<td>3 66.7</td>
<td>1 33.3</td>
</tr>
<tr>
<td>16</td>
<td>Visceral Leishmaniasis</td>
<td>3</td>
<td>0</td>
<td>3 0 0</td>
<td>2 66.7</td>
<td>1 33.3</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>335</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table No.2: Results of Bone Marrow Trephine biopsy versus Bone Marrow Clot biopsy

<table>
<thead>
<tr>
<th>S.No</th>
<th>Name</th>
<th>No</th>
<th>Trephine biopsy</th>
<th>Bone Marrow Clot</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Positive %</td>
<td>Negative %</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>No %</td>
<td>No %</td>
</tr>
<tr>
<td>1</td>
<td>Iron deficiency anaemia</td>
<td>65</td>
<td>65 100</td>
<td>0 0</td>
</tr>
<tr>
<td>2</td>
<td>Immune thrombocytopenia</td>
<td>60</td>
<td>60 100</td>
<td>0 0</td>
</tr>
<tr>
<td>3</td>
<td>Acute Leukaemia</td>
<td>40</td>
<td>40 100</td>
<td>0 0</td>
</tr>
<tr>
<td>4</td>
<td>Reactive Change</td>
<td>30</td>
<td>30 100</td>
<td>0 0</td>
</tr>
<tr>
<td>5</td>
<td>Megaloblastic anaemia</td>
<td>25</td>
<td>22 88</td>
<td>3 12</td>
</tr>
<tr>
<td>6</td>
<td>Myeloproliferative neoplasm</td>
<td>25</td>
<td>25 100</td>
<td>0 0</td>
</tr>
<tr>
<td>7</td>
<td>Aplastic anaemia</td>
<td>20</td>
<td>20 100</td>
<td>0 0</td>
</tr>
<tr>
<td>8</td>
<td>Normal Marrow</td>
<td>20</td>
<td>16 80</td>
<td>4 20</td>
</tr>
<tr>
<td>9</td>
<td>Chronic Lymphocytic leukemia</td>
<td>14</td>
<td>14 100</td>
<td>0 0</td>
</tr>
<tr>
<td>10</td>
<td>Lymphoma</td>
<td>10</td>
<td>10 100</td>
<td>0 0</td>
</tr>
<tr>
<td>11</td>
<td>Multiple myeloma</td>
<td>5</td>
<td>5 100</td>
<td>0 0</td>
</tr>
<tr>
<td>12</td>
<td>Hypersplenism</td>
<td>5</td>
<td>5 100</td>
<td>0 0</td>
</tr>
<tr>
<td>13</td>
<td>Myelodysplastic syndrome</td>
<td>5</td>
<td>5 100</td>
<td>0 0</td>
</tr>
<tr>
<td>14</td>
<td>Metastatic solid malignancy</td>
<td>4</td>
<td>4 100</td>
<td>0 0</td>
</tr>
<tr>
<td>15</td>
<td>Granulomatous inflammation</td>
<td>4</td>
<td>4 100</td>
<td>0 0</td>
</tr>
<tr>
<td>16</td>
<td>Visceral Leishmaniasis</td>
<td>3</td>
<td>3 33.3</td>
<td>2 66.7</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>335</td>
<td>32 6 97.3</td>
<td>9 2.7</td>
</tr>
</tbody>
</table>

Table No.3: Chi square statistics of results of Bone marrow Trephine biopsy versus Clot biopsy

<table>
<thead>
<tr>
<th>Test</th>
<th>Diagnosed</th>
<th>Not diagnosed</th>
<th>Total</th>
<th>P- Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trephine biopsy</td>
<td>326</td>
<td>9</td>
<td>335</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Clot biopsy</td>
<td>321</td>
<td>14</td>
<td>335</td>
<td></td>
</tr>
</tbody>
</table>

(Chi-square- 1.13, df=1, p value= 0.289, > 0.05 not significant)

Table No.4: Statistical probability of Bone Marrow Trephine and Clot biopsy (N=335)

<table>
<thead>
<tr>
<th>Test</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>True Positive (TP)</td>
<td>326</td>
</tr>
<tr>
<td>True Negative (TN)</td>
<td>9</td>
</tr>
<tr>
<td>False Positive (FP)</td>
<td>14</td>
</tr>
<tr>
<td>False Negative (FN)</td>
<td>1</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>326/326+14</td>
</tr>
<tr>
<td>Specificity</td>
<td>9/14+9</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>326/326+1</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>9/14+9</td>
</tr>
</tbody>
</table>
DISCUSSION

Bone marrow aspirate and trephine biopsy are established diagnostic techniques since long. Role of these techniques is not fixed and varies from case to case. The important thing is that they are never interpreted separately. A conclusive opinion is made after thorough examination of the marrow aspirate and trephine biopsy and trephine imprints. Previously the usual practice was to make slides from bone marrow aspirate and discard the remaining part (also called marrow clot) of it. In the recent past, case reports and studies revealed that marrow clot may provide important clues in confirming or excluding the diagnosis, if it is processed like a soft tissue. An interesting observation was that marrow clot biopsy revealed better antigen retrieval for molecular and immunodiagnostic techniques. It can play role as adjuvant to the already established techniques of bone marrow and trephine biopsy. The present study was based upon the same hypothesis.

The present study also revealed that the diagnostic role of marrow clot biopsy is not fixed and varies from case to case, when compared with that of marrow aspirate and trephine biopsy e.g. in megaloblastic anaemia, myeloproliferative neoplasm, visceral leishmaniasis and normal marrow. A number of cases are missed which has statistical significance when looked as collective performance, despite the fact that this may not be true for individual cases like iron deficiency anaemia, immune thrombocytopenia and acute leukaemia. This is in accordance with the findings of an earlier studies. In a case series Cantadori and colleagues concluded that bone marrow clot biopsy had results almost equivalent to trephine biopsy with the advantage that no decalcification was required and the result was also available earlier than that of trephine biopsy. This is different from our findings. One of the reasons for this difference may be special fixation procedure adopted by the researcher which required special equipment, not available to us. Another study conducted by Ong MG and coworkers found excellent results on bone marrow clot biopsy compared with trephine biopsy and recommended it as a reliable alternative to trephine biopsy. Here again the major limitation is requirement of sophisticated processing method which is not available in every laboratory.

Jasim MA Al-Diab reported that as much as 81% of the bone marrow clot section replaced the need for doing trephine biopsy. The researcher however recommended that despite good yield of bone marrow clot sections, trephine biopsy should be conducted as a recognized standard procedure. Our findings are in accordance to this study.

A study conducted by Toi and colleagues revealed positive correlation between bone marrow aspirate and trephine biopsy, thus confirming that two procedures are complementary. The present study revealed positive correlation and complimentarity between trephine biopsy and marrow clot biopsy. Complementary nature of bone marrow aspirate, imprints of trephine biopsy and the trephine biopsy itself was also confirmed by another study. It was recommended that imprint cytology smears should be standard practice for evaluating any marrow. We also suggest that in addition to bone marrow cytology, trephine biopsy and imprints, due attention should be given to marrow clot biopsy as a complementary procedure.

CONCLUSION

Clot biopsy of bone marrow plays important role in the diagnosis of many haematological and non haematological diseases. At present, it is in experimental phase and cannot replace the trephine biopsy which is a time tested diagnostic test.

Recommendations: Bone marrow clot biopsy should always be performed as a complementary test, whenever possible.

Author’s Contribution:
Concept & Design of Study: Jamila Farid
Drafting: Muhammad Idris, Mumtaz Ahmad Khan
Data Analysis: Nasreen Javed, Shazia Moeen
Revisiting Critically: Jamila Farid, Muhammad Idris
Final Approval of version: Jamila Farid

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

REFERENCES
2. Gandapur ASK, Nadeem S, Riaz M, Mannan M. Diagnostic importance of bone marrow

Figure No.1: Gender wise distribution of patients


Objective: The objective of this study was to evaluate the morphology and associated pathologies of maxillary first molar using Cone beam computed tomography.

Study Design: Descriptive cross sectional study.

Place and Duration of Study: This study was conducted at the Department of Oral Biology, Rehman college of dentistry, Peshawar from 1st March 2016 till 30th April 2020.

Materials and Methods: A descriptive cross-sectional study was conducted using 128 Cone beam computed tomography scans at Rehman college of dentistry, Peshawar. The Cone beam computed tomography scans were evaluated for number of root canals, presence of caries, agenesis, anatomic abnormalities and ectopic eruption using 2D reconstruction of the images. Data collected was analysed by SPSS version 20

Results: In this study, 56.25% of the scans showed four root canals while 43.75% had 3 canals. Mesiobuccal canal-2 was more common in males (74.13%) compared to females. First molar teeth had a 47.65% prevalence of dental caries.

Conclusion: Within the limitations of this study, we conclude that mesiobuccal canal-2 is a common finding in the maxillary first molar with higher prevalence in males compared to females. Due to higher susceptibility of first maxillary molar to dental caries, there is a higher probability of missing the mesiobuccal canal-2 during endodontic treatment. Therefore, careful exploration of pulp chamber should be done to avoid treatment failure.

Key Words: cone beam computed tomography, maxillary first molar, mesiobuccal canal-2, dental caries.

INTRODUCTION

Maxillary first molar is key to the occlusion and erupt at 6-7 years of age. Maxillary first molar is the largest tooth in the maxillary arch, although its occluso-gingival dimensions are smaller compared to other molars. Usually maxillary first molar has 5 cusps and three roots. Several pathologies are associated with maxillary first molars including caries, agenesis, anatomical abnormalities and ectopic eruption.

Maxillary first molar is highly susceptible to dental caries because it is the first permanent tooth to erupt in the oral cavity, it has complex tooth surface morphology and post-eruptive enamel maturation time. Untreated caries can lead to pulpitis which may require endodontic treatment. For successful endodontic treatment, knowledge of the external and internal anatomy of tooth and related structures is very important. Maxillary first molars have considerable variations in root canal morphology and missing the extra canal can lead to endodontic treatment failure. Periapical radiographs at different angulations are the mainstay for assessing the length and number of root canals. However, periapical radiographs are affected by image distortion, magnification and superimposition of adjacent anatomical structures over the root which can result in inaccurate measurements and treatment failure. Cone beam computed tomography (CBCT) was initially used to evaluate hard tissues for surgical procedures and implant planning. CBCT is a useful tool in assessing complex root anatomy, extra canals, curved canals and associated pathologies which can greatly improve treatment outcomes. Intraoral radiography results in radiation exposure typically in the range of
1–8 microsieverts (μSv), whereas for CBCT the typical value is 50 μSv for small and 100 μSv for large scanning volumes. The higher doses of CBCT have health and ethical concerns but are considered safe for use in oral and maxillofacial region. Maxillary first molars normally have 3 canals i.e. mesiobuccal, distobuccal and palatal but a second mesiobuccal canal (mb-2) has been reported in some studies. There is even evidence of teeth having 4, 5 and even 6 canals in literature. It is very difficult to accurately assess the internal and external anatomy of teeth with conventional intraoral radiography. CBCT provides undistorted 3-dimensional images of teeth and surrounding tissues which help in clearly visualizing root canal anatomy and relationship with other anatomical structures such as maxillary sinus and root apices. This information is vital for successful endodontic treatment.

The objective of this study was to evaluate the morphology and associated pathologies of maxillary first molar analyzed using CBCT.

MATERIALS AND METHODS

This retrospective descriptive cross-sectional study was conducted at Rehman College of Dentistry, Rehman Medical Institute, Peshawar, from 1st March 2016 till 30th April 2020, after getting approval from the institutional ethical committee. Sample size was calculated using G*Power software version 3.1.9.7. CBCT scans of 128 patients, aged between 21 to 40 years of both genders having maxillary first molars with fully developed apices were included in this study. Teeth showing root canal treatment, resorption, posts or crowns were excluded. The images were taken by “carestream (CS) Germany, model no. 90003D” with 74 kv (male patients), 70 kv (female patients), 10mA. All CBCT scans consisted of standard resolution of 0.3mm voxel and 10.8 s. Images were analyzed by using CS Imaging Browser 7.0.20 software. Number of roots, root canals and associated pathologies i.e. caries, ectopic eruption, anatomical abnormalities and agenesis were recorded by analyzing coronal, sagittal and axial images. Prevalence of mb-2 and its relationship with sex was also determined. Results were analyzed using the SPSS (version 20). Chi square was applied for comparison of male and female groups.

RESULTS

128 CBCT scans of maxillary first molars (n = 128) were analysed. There were 70 women (54.68 %) and 58 men (45.32%) in our study having mean age of 28.77 years ranging from 22 years to 41 years (table I).

<table>
<thead>
<tr>
<th>Canals</th>
<th>Maxillary First Molar</th>
</tr>
</thead>
<tbody>
<tr>
<td>C shaped canal</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>56 (43.75%)</td>
</tr>
<tr>
<td>4</td>
<td>72 (56.25%)</td>
</tr>
<tr>
<td>Total</td>
<td>128</td>
</tr>
</tbody>
</table>

Table No. 2: Root canals in Maxillary First Molar

Table No. 1: Age and Gender distribution

<table>
<thead>
<tr>
<th>Age</th>
<th>Gender</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range: 22-41 years</td>
<td>Male: 58 (45.32%)</td>
</tr>
<tr>
<td>Mean (+ SD): 28.7 (+ 5.25)</td>
<td>Female: 70 (54.68 %)</td>
</tr>
</tbody>
</table>

Table No. 3: Presence of mesiobuccal-2 canal according to patients’ gender

<table>
<thead>
<tr>
<th>Mesiobuccal-2 canal</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>43 (74.13%)</td>
<td>29 (41.42%)</td>
<td>72</td>
</tr>
<tr>
<td>Absent</td>
<td>15 (25.86%)</td>
<td>41 (58.57%)</td>
<td>56</td>
</tr>
<tr>
<td>Total</td>
<td>58</td>
<td>70</td>
<td>128</td>
</tr>
</tbody>
</table>

Out of 128 patients, 60 had caries in their first maxillary molars. Only 1 tooth had ectopic eruption and all the maxillary first molars were fully formed. None of the teeth had any anatomical abnormalities (table 4).

Table No. 2: Pathologies associated with maxillary first molar

<table>
<thead>
<tr>
<th>Caries</th>
<th>Ectopic eruption</th>
<th>Agenesis</th>
<th>Anatomical abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>61 (47.65%)</td>
<td>1 (0.00078%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Absent</td>
<td>67 (52.34%)</td>
<td>127 (99.21%)</td>
<td>128 (100%)</td>
</tr>
<tr>
<td>Total</td>
<td>128</td>
<td>128</td>
<td>128</td>
</tr>
</tbody>
</table>

DISCUSSION

Several techniques have been described in the literature for evaluation of maxillary first molars. These include...
use of periapical radiographs, Orthpantomograms, tooth sectioning and canal staining\textsuperscript{11}. Tooth sectioning and canal staining are excellent methods for evaluation of morphology of maxillary first molars, but they are in vitro techniques.

Advances in technology has made it possible for computerized tomographic scans to be used in the diagnosis and evaluation of head and neck anatomy. CBCT offers significant advantages over conventional radiographs. They produce undistorted 3-dimensional images of dental structures whereas radiographs can only form two-dimensional images. CBCT is an accurate analysis of the 3-dimensional reconstructed images of dental structures\textsuperscript{12}. With every imaging modality there is inherent risk of ionizing radiation damage, but risk should always be weighed against benefit. Radiation produced by CBCT is considered safe in the oral and maxillofacial region and it can greatly improve treatment outcomes.

In the current study CBCT was used to evaluate maxillary first molar. Results demonstrate that all the maxillary first molars had 3 roots. These findings correlate with other studies\textsuperscript{13}. For successful endodontic treatment, location, number and length of root canals is vital for the clinician. In the present study most maxillary first molars had four root canals (56.25%). The second canal was always found in the mesiobuccal root and therefore called mesiobuccal-2. Although this prevalence is consistent with other studies, Betancourt P et al. found it to be 69.82% in their studied population\textsuperscript{14}. Mb-2 was more common in males (74.13%) compared to females (41.42%). Alrahabi M et al. also found mb-2 to be more prevalent in males\textsuperscript{15}. Treatment of MB-2 canal is vital in the success of endodontic therapy. Mb-2 can often remain undetected which can be a persistent source of infection in the periapical area. Shetty et al. reported the prevalence of the MB-2 canal in 80% of maxillary first molars\textsuperscript{16}. Most of maxillary first molars (77.19%) had an untreated MB-2 canal. Periapical lesions were found in unfilled MesioBuccal-2 canals in 72.7% of maxillary first molars\textsuperscript{16}. Since maxillary first molars are the first permanent teeth to erupt and have complex morphology, they are more susceptible to dental caries\textsuperscript{17}. Prevalence of dental caries in our studied population was found to be 47.65%. Different authors have also found similar prevalence in their studies\textsuperscript{18}. Agenesis and anatomical abnormalities of maxillary first molars such as 4 roots, change in shape of cusp of carabelli are extensively reported in literature\textsuperscript{19}, although, we did not find any tooth with these pathologies. Teeth which erupt in abnormal postion in the arch are termed ectopically erupted teeth. Our study only found one tooth which had ectopically erupted. Keneddy DB et al. have reported 3-4% of ectopically erupted teeth in their studied population\textsuperscript{20}. These differences in the results could be due to sample size and demographic variations.

Our study was based on data from a single region and therefore careful interpretation of results should be made. Larger multicentered studies should be made in the future focusing on relationship of external morphology of maxillary first molar with the number of root canals.

**CONCLUSION**

Within the limitations of this study, we conclude that mesiobuccal canal-2 is a common finding in the maxillary first molar with higher prevalence in males compared to females. Due to higher susceptibility of first maxillary molar to dental caries, there is a higher probability of missing the mesiobuccal canal-2 during endodontic treatment. Therefore, careful exploration of pulp chamber should be done to avoid treatment failure.

**Author’s Contribution:**

Concept & Design of Study: Arbab Zia ur Rehman Khan

Drafting: Muhammad Sheraz Alam, Muhammad Irshad

Data Analysis: Sobia Salam, Yusra Jamil, Sana Naeem

Revisiting Critically: Arbab Zia ur Rehman Khan, Muhammad Shazam Alam

Final Approval of version: Arbab Zia ur Rehman Khan

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

**REFERENCES**


Protective Role of Stem-Bark Ethanolic Extract of Sumbloo (Berberis Lycium Royale) against Rifampicin Induced Liver Damage in BALB/C Mice

Saima Rafique¹, Aysha Afzal¹, Sabeen Shakir³, Khalida Ajmal¹, Lubna Ghazal² and Lubna Ehtizaz²

ABSTRACT

Objective: To explore protective impact of stem-bark ethanolic extract of Sumbloo (Berberis Lycium Royale) against Rifampicin induced hepatotoxicity in BALB/c Mice.

Study Design: Exploratory randomized control study

Place and Duration of Study: This study was conducted at Animal Chamber of National Institute of Health (NIH), Islamabad in collaboration with Islamic International Medical College (IMC), Army Medical College (AMC) & Riphah Institute of Pharmaceutical Sciences (RIPS) from April 2014 to May 2014.

Materials and Methods: This experimental study was performed on 56 male BALB/c mice. They were arbitrary split up into 4 groups (n=14). Control Group A was kept on rodent pellet diet and water only. Drug treated group Group B was loaded with Rifampin 50mg/kg BW whereas Less dose group C & High dose ethanolic extract Group D were given Rifampicin low dose (150mg/kg BW) and high dose (200mg/kg BW) of Ethanolic extract of stem bark of the Sumbloo via gavage tube respectively. Baseline blood samples collected at day 0 and normal values of serum Alanine aminotransferase (ALT) were estimated. Mid-cycle blood sampling taken at day 15 to evaluate the progress of experimental study. Final blood sampling performed on day 30 by intra-cardiac puncture. Serum was stored in sterile tubes at 4°C for analysis of serum Alanine aminotransferase(ALT). Data analysis performed on SPSS version 20 and p-value (<0.05) regarded as statistically significant.

Results: Ethanolic extract of stem bark of Sumbloo depicted marked improvement of serum Alanine aminotransferase (ALT) values in group C & D. Serum ALT value of (17-77 U/L) was labeled as normal. Group A depicted normal value of (54 U/L). Group B manifested severe hepatotoxicity as shown by very high value of (186.1 U/L). Serum value of ALT measured in Group C was (96.6 UL) & (56 UL) in Group D.

Conclusion: Ethanolic extract of stem-bark of Sumbloo (Berberis lycium Royale) possesses remarkable protective potential for liver toxicity in high doses as compared to less dose.

Key Words: Berberis lycium Royale, Alanine Aminotransferase (ALT), Hepatoprotective, Rifampicin.


INTRODUCTION

Tuberculosis (TB) has remained among top leading causes of morbidity & mortality due to infecting one-third of population worldwide.¹

Mycobacterium tuberculosis is known as the culprit of this devastating disease and has proven to be one of the most notorious microorganism since ancient times.² Rifampicin firstly discovered in 1965 and now it is one of the first line treatment for tuberculosis. It has a remarkable potential of sterilizing activity and shortening the treatment span.³ Rifampicin binds with DNA dependent RNA polymerase of Mycobacterium tuberculosis and inhibits it. It blocks RNA synthesis of the mycobacterium leading to its death. Its MIC is 1 g/ml.⁴ Alongwith its useful anti-bacterial activity, it also causes side effect of hepatotoxicity due to being a strong inducer of various metabolic enzyme pathways of the body particularly of cytochrome P450 (CYP3A4) system.⁵ PPARy signaling mechanisms and oxidative stress were also found to be greatly linked to Rifampicin-induced toxicity to liver tissue.⁶ Liver injury

¹. Department of Pharmacology / Pathology,². Wah Medical College, Wah Cantt.
³. Department of Pharmacology, Rawal Institute of Health Sciences, Islamabad.

Correspondence: Samia Rafique, Assistant Professor of Pharmacology, Wah Medical College, Wah Cantt.
Contact No: 0300-8546013
Email: samiarafigu34@gmail.com

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Printed: September, 2020
caused by drugs is clinically manifested by raised serum liver function tests (LFT’s).\textsuperscript{7}

Berberis lycium Royle is well known for its hepatoprotective activity.\textsuperscript{8} It is known by its various regional names like ziarlargay, sumbloo & Barbery.\textsuperscript{9} Major constituent of the stem bark is found to be Berberine (4.2\%) which has significant hepatoprotective potential.\textsuperscript{10,11} It has been used for diabetes due to its hypoglycemic activity.\textsuperscript{12} It has found to be very useful for different ailments like headache, rheumatism, jaundice, whooping cough and eye infections.\textsuperscript{13}

Rationale of this experimental randomized trial was to investigate the protective activity of the Ethanolic extract of stem-bark of Sumbloo (Berberis lycium Royle) in dose dependent manner on rifampicin induced hepatotoxicity in male BABL B/c mice.

**MATERIALS AND METHODS**

The experimental randomized control trial has been conducted in research institute, National Institute of Health (NIH), Islamabad following ethical acceptance by RARE (Riphah Academy of Research & Education) from 10\textsuperscript{th} April 2014 till 10\textsuperscript{th} May 2014. Male BALB/c Mice, weighing 30-50 grams, age 7-8 weeks with normal serum Alanine aminotransferase (ALT) levels were housed in NIH under standardized conditions in wire topped cages at temperature (21-22°C) and acclimatized for a period of one week.

Grouping of Animals:

A total of fifty-six healthy BALB/c mice were arbitrary put into 4 groups. Control Group A: (n=14) was kept on normal diet & fresh water per mouth only. Drug treated Group B: (n=14) was given Rifampicin 50mg/kg BW.\textsuperscript{14} Low dose Group C: (n=14) was given Rifampicin 50mg/kg BW\textsuperscript{14} and 150 mg/Kg BW of Ethanolic extract whereas High dose Group D: (n=14) given Rifampicin 50mg/kg BW\textsuperscript{14} & 200 mg/Kg BW of Ethanolic extract of stem-bark of Sumbloo (Berberis lycium Royle). The drugs & herb were given through gavage tube once daily orally for 1 month.

Ethanolic extract preparation:

Stem bark of Sumbloo (Berberis lycium Royle) procured from a village of Charsadda and authenticated by renowned botanist from Peshawar University. It was then dried and crushed into fine powder form. For ethanolic extract preparation, 1kg of dried crushed fine powder was firstly soaked in ethanol at temperature (24°C) for 72 hours. Coarse filtration of ethanol soaked powder was done with the help of muslin cloth whereas fine filtration was performed by using Whatman filter paper no.1. Filtered filtrate initially kept in open air for evaporation and later it was evaporated by using rotary evaporator at temperature (41°C) under reduced pressure. After evaporation in rotary evaporator, a dark chocolate brown color extract with semi-solid and sticky consistency was obtained. Finally, ethanolic extract put in transparent air tight small glass jars in refrigerator with (2-8°C) temperature for future research use. Ethanolic extract yield was around 20\% (20g was obtained from 100g).\textsuperscript{15}

Blood Sample Collection:

Baseline blood samples of two mice from every cluster were taken at day zero. Mid-study cycle sample of two mice from each cluster were taken at day 15\textsuperscript{th} in order to evaluate progress of research and final blood samples were collected at 30\textsuperscript{th} day of experimental study for measurement of serum Alanine Aminotransferase (ALT). Blood samples were collected through cardiac puncture and poured in sterile serum tubes. Blood samples were kept at room temperature, separation of serum was done after doing centrifugation (3000 rpm) using bench top centrifuge machine and stored in serum cups.\textsuperscript{16} Serum Alanine Aminotransferase (ALT) was measured by using ALT kit (Merck) with Lot No. 505 on Micro lab 200 (Merck) as per IFCC principles.

Statistical analysis:

Analysis of data was done by using SPSS version 20. Final results of the serum analysis were expressed as Means & Standard Error of Means. Post-hoc tukey test was used for doing comparison b/w different groups. P <0.05 was taken as statistically significant.

**RESULTS**

**Table No.1: Mean ± SEM Values of ALT**

<table>
<thead>
<tr>
<th>Animal group no. (n=10)</th>
<th>ALT(17-77 U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>54±5.99</td>
</tr>
<tr>
<td>Group B</td>
<td>186.1±66.32</td>
</tr>
<tr>
<td>Group C</td>
<td>96.6±15.34</td>
</tr>
<tr>
<td>Group D</td>
<td>56±4.89</td>
</tr>
</tbody>
</table>

\textsuperscript{p}-value <0.001*  

\textsuperscript{*} = p - value Significant  

(ALT= Alanine aminotransferase)

**Table No.2: Post-Hoc Comparison of ALT**

<table>
<thead>
<tr>
<th>Group Comparisons</th>
<th>ALT(17-77 U/L)</th>
<th>Mean Difference</th>
<th>p - value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A vs. Group B</td>
<td>-132.1</td>
<td>&lt;0.001*</td>
<td></td>
</tr>
<tr>
<td>Group A vs. Group C</td>
<td>-42.6</td>
<td>0.079</td>
<td></td>
</tr>
<tr>
<td>Group A vs. Group D</td>
<td>4</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Group B vs. Group C</td>
<td>89.5</td>
<td>&lt;0.001*</td>
<td></td>
</tr>
<tr>
<td>Group B vs. Group D</td>
<td>134.1</td>
<td>&lt;0.001*</td>
<td></td>
</tr>
<tr>
<td>Group C vs. Group D</td>
<td>45.6</td>
<td>0.048*</td>
<td></td>
</tr>
</tbody>
</table>

Serum Alanine Aminotransferase (ALT) levels were significant raised in drug treated group (B) (p<0.001) as compared to the control group (A) owing to Rifampicin induced hepatotoxicity. Serum ALT levels remarkably restored in group D given high dose of ethanolic extract of the Sumbloo as compared to group C which received low dose of ethanolic extract of the herb. Results are summarized in the given table.
Berberis is highly efficacious in boosting up the major alkaloid compound known as berberine. Since ancient times, herbal medicine is very well known for its hepatoprotective and immune system of the body. Our research designed to explore the protective potential of low and high doses of ethanolic extract of stem bark of Sumbloo. This research study results have shown that ethanolic extract of stem bark of Sumbloo possesses remarkable hepatoprotective potential (p <0.001) in dose-dependent manner. Higher dose of ethanolic extract (200mg/kg BW.) reduced serum Alanine Aminotransferase (ALT) level significantly as compared to low dose of ethanolic extract (150mg/kg BW.). A greater upsurge was observed in serum Alanine Aminotransferase (ALT) level in drug treated group B given Rifampicin as compared to Control group A mice which was given no drug. Raised serum alanine aminotransferase (ALT) is a specific diagnostic marker of hepatotoxicity. Combined administration of Rifampicin along with low and high dose of ethanolic extract of stem-bark of Sumbloo in group C and D restored serum Alanine Aminotransferase (ALT) level to normal mainly due to its anti-oxidant activity. Our experimental results were found in correlation with the work done by Ahmed and his fellows in 2008 on crude powder & methanolic extract of Berberis lycium Royle by inducing paracetamol hepatotoxicity in rabbits. Our experimental results were also found in similarity with comparative study done by Ahmed in 2009 while performing research on Biochemical studies of Berberis lycium Royale and Analysis of its Extracts for their Bioactivity showing greater antimicrobial & wound healing activities of ethanolic & methanolic extract of root bark than its aqueous extract.  

CONCLUSION

Ethanolic extract of stem-bark of Sumbloo (Berberis lycium Royle) has significant protective potential for liver toxicity in high doses than low doses in Rifampicin induced hepatotoxicity in male BALB/c mice.  

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Effect of Cigarette Smoking on Lipid Profile and Throat in Male Population Smoker of Mirpur AJK

Muhammad Shoaib¹, Faisal Bashir², Abdul Waheed Khan⁴ and Asnad³

ABSTRACT

Objective: The objective of this study to evaluate the effect of cigarette smoking on lipid profile and throat in male population smoker of Mirpur AJK.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Community Medicine, Biochemistry and ENT of Mohtarma Benazir Bhutto Shaheed Medical College Mirpur AJK from January 2018 to September 2019.

Materials and Methods: Only adult male smokers and non-smokers were selected for the study. Those smokers who were reported in other disease such as hepatic diseases, diabetes and hypertension were excluded. We take study 200 chronic smoker and 100 non-smoker. This study was conducted in the department community medicine, Biochemistry Department and ENT of Mohtarma Benazir Bhutto Shaheed Medical College Mirpur AJK. We take blood samples from both groups chronic smoker and non-smoker and analyzed the samples on Micro lab 300 for serum lipid profile. (Cholesterol, HDL, LDL, VLDL and Triglyceride). For the study we use kits made of Merck Pvt. We also done other biochemistry test and hematological test and throat were clinically investigated and observation was recorded. Smoking history and medical history are obtained from both groups such as smoker and non-smoker.

Results: The result indicate that all the lipid profile (LDL, Triglyceride) is higher except HDL in smoker with as compare to non-smoker. Total cholesterol (253.5 ± 11.8) mg/dl, LDL (126.9 ± 22.5) mg/dl, and Triglyceride (198.2 ± 31.5) mg/dl, in smoker are higher as compare to non-smoker. While HDL (39.77 ± 8.5) mg/dl, is decreased in smoker as compare to non-smoker.

Conclusion: It is concluding that tobacco smoking alter the lipid profile and throat flora of the chronic smoker. Quitting of smoking is essential for the reduction, the risk of CHD and atherosclerosis among the Mirpur, AJK smoker.

Key Words: smoking, lipid profile, throat


INTRODUCTION

Cigarette smoking is caused atherosclerosis and Chronic Heart Diseases (CHD),¹⁴,¹⁵ Tobacco smoke produce dangerous and toxic effect on throat, lipid profile and health .³ Many scientist reported that smoking effect biochemical process in the body such as changes in the lipid profile , decreased nitric oxide and increased LDL-C.⁶,⁸

⁻¹ Department of Community Medicine / ENT² / Biochemistry³, Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur, AJK.
⁻² Department of Community Medicine, Poonch Medical College, Rawalakot, AJK.
⁻³ Correspondence: Dr. Asnad, Associate Professor of Biochemistry, Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur, AJK.

Smoking produce the endothelial dysfunction which effect the body function.⁷ Smoking also developed insulin resistance in the body which effect the body glucose level.¹⁰ Fibrinolysis process is effect in body with time being smoking .¹¹ Hematology of the body is also change with smoking such as platelet dysfunction.¹²,¹³

The viscosity of the blood is high with smoking and chances of inflammation is increased in smoker.¹⁴,¹⁵ athero-thrombotic diseases is developed in chronic smoker.¹⁶–¹⁸ The lipolysis process is increased in daily smoker which increase the free fatty acid .¹⁹ Arterial wall inflammation disorder is produced in chronic smoker.²⁰,²¹ Atherogenic factors are enhanced in chronic smoking such as Density Lipoprotein-Cholesterol (VLDL-C) and Very Low Density Lipoprotein-Cholesterol (VLDL-C).²² Previous scientist data showed that Tabaco smoking increased the level of VLDL, cholesterol, LDL-C and triglyceride.²³–²⁵ Some studies showed conflict to each other with lipid profile.²⁶,²⁷ cigarettes smoked is directly related to CVD development.²²,²³
The present study objective to evaluate the effects of smoking on lipid profile and throat among Mirpur AJK smokers.

MATERIALS AND METHODS

Only adult male smokers and non-smokers were selected for the study. Those smokers who were reported in other disease such as hepatic diseases, diabetes and hypertension were excluded. We take for study 200 chronic smoker and 100 non-smoker. This study was conducted in the department community medicine, Biochemistry Department and ENT of Mohtarma Benazir Bhutto Shaheed Medical College Mirpur AJK. We take blood samples from both groups chronic smoker and non-smoker and analyzed the samples on Micro lab 300 for serum lipid profile. (Cholestol, HDL, LDL, VLDL and Triglyceride). For the study we use kits made of Merck Pvt. We also done other biochemistry test and hematological test and throat were clinically investigated and observation was recorded.

Smoking history and medical history are obtained from both groups such as smoker and non-smoker. For data analysis, the results were analyzed using the SPSS, version 20. Mean and standard deviation between groups were determined. For comparison, T-test was used for both group’s smoker and non-smoker.

RESULTS

The result indicates that all the lipid profile (LDL, Triglyceride) is higher except HDL in smoker with as compare to non-smoker.

Table No.1: Participant characteristics

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Smoker (n=200)</th>
<th>Non-Smoker (n=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>35.54 ± 5.58</td>
<td>35.55 ± 4.58</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Education</th>
<th>Smoker (n=200)</th>
<th>Non-Smoker (n=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic</td>
<td>B-51%, S-29%, U-20%</td>
<td>B-50%, S-32%, U-18%</td>
</tr>
<tr>
<td>Secondary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>University</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body weight (Kg)</td>
<td>Smoker (n=200)</td>
<td>Non-Smoker (n=100)</td>
</tr>
<tr>
<td>75.1 ± 11.4</td>
<td>75.4 ± 11.5</td>
<td></td>
</tr>
</tbody>
</table>

B: Basic, S: Secondary, U:University

Table 2: Lipid profile of Chronic Smoker and non-smoker

<table>
<thead>
<tr>
<th>Chronic Smoker (n=200)</th>
<th>non-smoker (n=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Blood Glucose(mg/dl)</td>
<td>97.8 ± 4.3</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dl)</td>
<td>253.5 ± 11.8</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>126.9 ± 22.5</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>39.77 ± 8.5</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>198.2 ± 31.5</td>
</tr>
</tbody>
</table>

Total cholesterol (253.5 ± 11.8) mg/dl, LDL (126.9 ± 22.5) mg/dl, and Triglyceride (198.2 ± 31.5) mg/dl, in smoker are higher as compare to non-smoker. While HDL (39.77 ± 8.5) mg/dl, is decreased in smoker as compare to non-smoker. Minor irritation is caused by smoking on throat was observed in chronic smoker.

Table No.3: The risk of morbidity level among smokers and non-smokers

<table>
<thead>
<tr>
<th>Lipid profile</th>
<th>Non-smokers N (%)</th>
<th>Smokers N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol mmol/l</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal value</td>
<td>73.3%</td>
<td>58.9%</td>
</tr>
<tr>
<td>Moderate morbidity risk</td>
<td>26.0%</td>
<td>20.9%</td>
</tr>
<tr>
<td>High morbidity risk</td>
<td>2.9%</td>
<td>20.9%</td>
</tr>
</tbody>
</table>

Table No.4: Percentage irritations in throat among smokers and non-smokers

<table>
<thead>
<tr>
<th>Irritation %</th>
<th>Non-smokers</th>
<th>Smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-15%</td>
<td>80-85%</td>
<td></td>
</tr>
</tbody>
</table>

DISCUSSION

Critical enzymes of lipid transport is changed with smoking, hepatic lipase activity is changed, and cholesterol ester transfer protein activity is changed. In smokers compared to non smokers, level of HDL-C in serum is decreased. In the another study, VLDL, triglyceride and LDL-C are increased in chronic smoker. Only adult male smoker and non-smoker was selected for the study. those smoker who are reported in other disease such as hepatic diseases, diabetes and hypertension were excluded. We take for study 200 chronic smoker and 100 non-smoker. This study was conducted in the department community medicine, Biochemistry Department and ENT of Mohtarma Benazir Bhutto Shaheed Medical College Mirpur AJK. We take blood samples from both groups chronic smoker and non-smoker and analyzed the samples on Micro lab 300 for serum lipid profile. (Cholestol, HDL, LDL, VLDL and Triglyceride). For the study we use kits made of Merck Pvt. We also done other biochemistry test and hematological test and throat was clinically investigated and observation was recorded.

Smoking history and medical history are obtained from both groups such as smoker and non-smoker. Smoking history and medical history are obtained from both groups such as smoker and non-smoker. Smoking history and medical history are obtained from both groups such as smoker and non-smoker. Smoking history and medical history are obtained from both groups such as smoker and non-smoker. Smoking history and medical history are obtained from both groups such as smoker and non-smoker.
Levels of oxidized LDL-C is increased in smoker which is the risk of atherosclerosis and CHD.^{44}

The viscosity of the blood is high with smoking and chances of inflammation are increased in smoker. Athero-thrombotic diseases is developed in chronic smoker. The lipolysis process is increased in daily smoker which increase the free fatty acid. Arterial wall inflammation disorder is produced in chronic smoker. Atherogenic factors are enhanced in chronic smoking such as Density Lipoprotein-Cholesterol (VLDL-C) and Very Low Density Lipoprotein-Cholesterol (VLDL-C). Previous scientist data showed that Tabaco smoking increased the level of VLDL, cholesterol, LDL-C and triglyceride. Some studies showed conflict to each other with lipid profile cigarettes smoked is directly related to CVD development In one of study in rabbit, cigarette smoke extract when inject, it caused oxidative modification of LDL which atherosclerosis.^{45}

So it is conclude that tobacco smoking alter the lipid profile and throat flora of the chronic smoker.

**CONCLUSION**

So it is conclude that tobacco smoking alter the lipid profile and throat flora of the chronic smoker. Quitting of smoking is essential for the reduction, the risk of CHD and atherosclerosis among the Mirpur, AJK smoker.

**Author’s Contribution:**

Concept & Design of Study: Muhammad Shoai
Drafting: Faisal Bashir
Data Analysis: Abdul Waheed Khan, Asmad
Revisiting Critically: Muhammad Shoai, Faisal Bashir
Final Approval of version: Muhammad Shoai

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

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Histopathological Pattern of Gestational Trophoblastic Disease in Pakistani Patients

Saleha Masood¹, Bhawani Shanker² and Rafia Siddique³

ABSTRACT


Study Design: retrospective study

Place and Duration of Study: This study was conducted at the Department of Pathology, Jinnah Medical and Dental College, Karachi during the period from Jan 2014 to Dec 2019.

Materials and Methods: This study is based on the analysis of placental biopsies. All clinically diagnosed cases suspected as gestational trophoblastic disease on the basis of clinical presentation and serum/urine HCG levels.

Results: A total of 830 placental biopsies received were included in this study. Out of the above mentioned 830 biopsies, 151 were hydropic abortion and gestational trophoblastic disease and 679 were of simple abortion. Amongst 151 cases, 67 were complete hydatidiform mole, 52 were partial hydatidiform mole, 2 were chorionicarctomas and 30 were hydropic abortion.

Conclusion: From this study, it is evident that benign lesions are more common with 42.9% of the cases of partial hydatidiform mole and 55.3% of the cases of complete hydatidiform mole 86.6%, while malignant were found to be 1.65%. Trophoblastic tumour screening and treatment units should be available in all hospitals and patients with recurrent molar pregnancies should be registered. Post molar follow-up should be done including determination of B HCG levels every 1-2 wks after evacuation until HCG level is normal.

Key Words: Hydropic abortion, gestational trophoblastic disease.


INTRODUCTION

Gestational trophoblastic diseases (GTD) is a spectrum of cellular proliferations arising from placental villous trophoblasts¹. It arises from placental trophoblastic tissue after normal or abnormal fertilization. The W.H.O classification of GTD includes hydatidiform mole, invasive mole, choriocarcinomas, placental site trophoblastic tumour and miscellaneous and unclassified trophoblastic lesions². With increasing understanding of the biological evolution of GTD the terms “benign” and “malignant” for hydatidiform mole and persistent GTD is usually avoided³. Gestational trophoblastic neoplasia (GTN) is a term applied to invasive mole, choriocarcinoma and placental site trophoblastic tumours. These conditions can progress, invade, metastasize and lead to death, if left untreated. GTD was historically associated with significant morbidity and mortality. The countess of Henneberg who delivered a hydatidiform mole on Easter 1276 is the first identifiable individual with this disease entity⁴. The prognosis of GTN was very poor, 50 years back, before introduction of chemotherapy into its management. Nowadays, gestational trophoblastic neoplasms are most curable of all solid tumours, with cure rates > 90% even in the presence of widespread metastatic disease⁵.⁶. Although there is no accurate report for prevalence and incidence of GTD in Pakistan but according to one study in Nawabshah, the frequency of GTD is 28 per 1000 live births, which is quite significant⁷. The incidence of molar pregnancy demonstrates marked geographical and ethnic differences for example in Japan (2/1000), in Malaysia (2.8/1000), in North America (2.5/1000) and in Turkey (12.1/1000) deliveries⁸. Hydatidiform mole is a disorder of genomic imprinting. It is characterized by abnormal development of both fetus and trophoblasts⁹. The exact cause of HM is not known. Potential causes include defects in the egg, problems within the uterus or a diet low in protein, animal fat and vitamin A. Several risk factors contribute to the development of CHM but the two

¹. Department of Histopathology, Jinnah Medical & Dental College, Karachi.
². Department of Histopathology, MMC, Mirpurkhas.

Correspondence: Dr. Saleha Masood, Associate Professor of Histopathology, Jinnah Medical & Dental College, Karachi.
Contact No: 03330318781
Email: salehamasood@hotmail.com

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Printed: September, 2020
most known risk factors are extremes of maternal age and prior molar pregnancy. Advanced or very young maternal ages are usually correlated with high rates of CHM. Other risk factors include previous history of spontaneous abortions, deficiency of beta carotene and animal fat. Ovulation induction for fertility may also be associated with an increase in pregnancies consisting of a normal fetus or fetuses and molar gestation. Patients are more likely to have diets deficient in vitamin A precursor. The risk is reduced by increased consumption of carotene.

Hydatidiform moles are subclassified on the basis of histopathology, clinical features and ploidy as partial and complete. Partial moles develop from the fertilization of a normal egg by two spermatozoa or occasionally a diploid spermatozoan, resulting in a triploid gestation with one maternal and two paternal sets of chromosomes.

Mostly complete moles are entirely androgenetic lacking nuclear DNA of maternal origin. Androgenetic complete hydatidiform mole may originate by dispermny (XX or XY) or more frequently monospermy (always XX) resulting from fertilization of a functionally anucleate egg by a single sperm whose pronucleus replicate before the first cleavage division. Rarely, CHM are biparental rather than androgenetic in origin. BiCHM, mostly occur in patients who have a history of multiple CHM arising in different conceptions and mostly in women of families in which two or more individuals have molar pregnancies. BiCHM and AnCHM are histologically indistinguishable and requires DNA analysis to discriminate between them.

MATERIALS AND METHODS

This study was conducted at the department of pathology Jinnah Medical and Dental College, Karachi during the period from Jan 2014 to Dec 2019.

Inclusion Criteria: All clinically diagnosed cases suspected as gestational trophoblastic disease on the basis of clinical presentation and serum/urine HCG levels.

Exclusion criteria:
1. Foreign nationals.
2. Pakistanis living in foreign countries for more than 10 years.
3. Inadequate material

RESULTS

A total of 830 placental biopsies cases were included in this study. All of the specimens were obtained by dilatation and evacuation method. The results and observations thus obtained from the study are hereby presented and explained with the help of tables and figures.

Out of the above mentioned 830 biopsies, 151 were hydropic abortion and gestational trophoblastic disease and 679 were of simple abortion. Amongst 151 cases, 67 were complete hydatidiform mole, 52 were partial hydatidiform mole, 2 were choriocarcinomas and 30 were hydropic abortion as shown in figure 1.

The mean age of 830 patients was 32.0±9.3 years ranging from 19-42 years. The age range in non-molar pregnancy group and molar pregnancy group was between 10 – 50 years as shown in Table 1. The non-molar pregnancy group was common (63.3%) between 21-30 years and the molar pregnancy group was common (46.2%) between 41-50 years. No case of invasive mole and placental site trophoblastic tumour found in our study.

Table 2 shows the correlation of age with PHM and CHM. Majority of the patients (67.2%) of partial mole were found in the second and third decade and in case of complete mole most of the patients (82.6%) were found in third and fourth decade.

![Figure No.1: total number of specimens and distribution according to type of placental lesions (n=830)](image)

<table>
<thead>
<tr>
<th>Age Groups (Years)</th>
<th>Simple/Hydropic Abortions</th>
<th>Hydatidiform Mole (CHM &amp; PHM)</th>
<th>Invasive Mole</th>
<th>Choriocarcinoma</th>
<th>Placental Site Trophoblastic Tumours</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 – 20</td>
<td>86 (12.1%)</td>
<td>15 (12.6%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>21 – 30</td>
<td>451 (63.6%)</td>
<td>33 (27.3%)</td>
<td>-</td>
<td>2 (100%)</td>
<td>-</td>
</tr>
<tr>
<td>31 – 40</td>
<td>154 (21.7%)</td>
<td>16 (13.4%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>41 – 50</td>
<td>18 (2.5%)</td>
<td>55 (46.2%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>709 (100%)</td>
<td>119 (100%)</td>
<td>-</td>
<td>2 (100%)</td>
<td>-</td>
</tr>
</tbody>
</table>

Mean age: 32.04±9.3 years Ranging from 19-48 years

<table>
<thead>
<tr>
<th>Age groups (Years)</th>
<th>Partial Mole</th>
<th>Complete Mole</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 – 20</td>
<td>7 (13.4%)</td>
<td>8 (11.9%)</td>
</tr>
<tr>
<td>21 – 30</td>
<td>28 (53.8%)</td>
<td>4 (5.9%)</td>
</tr>
<tr>
<td>31 – 40</td>
<td>7 (13.4%)</td>
<td>10 (14.9%)</td>
</tr>
<tr>
<td>41 – 50</td>
<td>10 (19.2%)</td>
<td>45 (67.7%)</td>
</tr>
<tr>
<td>Total</td>
<td>52 (100%)</td>
<td>67 (100%)</td>
</tr>
</tbody>
</table>

Chi square=39.61 P < 0.001
In the present study, 830 placental biopsies were analyzed over a period of five years. Out of the 830 placental biopsies, 121 (14.5%) showed gestational trophoblastic diseases. Out of 121, complete hydatidiform mole were 55.3%, partial hydatidiform mole were 42.9%, choriocarcinomas were 1.65%. Out of the remaining 709 cases, 30 were hydropic abortions and the rest were simple abortions.

In the present study, simple and hydropic abortions make up 85% of the total number of cases. Most of our patients of simple and hydropic abortions were found between the ages 21 – 30 years. This is in close proximity with the study conducted in Iran which proved that the mean age of patients in nonmolar pregnancy was 26.2±5.08 years 15.

In the present study, 42.9% of the cases were partial hydatidiform mole. Most of the cases of partial hydatidiform mole were found between the ages 21 – 30 years. This is in concordance with the study conducted by Sadiq and Panjwani 16. They also found the commonest age group to be between 21 – 30 years. Osterheld and associates17 also proved that in partial hydatidiform mole the maternal age is usually between 21 - 30 years.

Present study shows that, 55.3% of the cases were complete hydatidiform mole which is closed to 60.7% reported by Mayun and associates 18. In the present study, the age ranges from 16 – 45 years. Peak incidence was seen between 21 – 50 years. The youngest was 16 years and oldest was 45 years. This is in accordance with the study conducted by Sadiq 16, who had also found the maximum number of cases in the fifth decade. Khanum and Shamsheer 19 reported the maximum number of cases to be between 21 – 39 years. However, they did not categorize hydatidiform mole into complete and partial. Most studies reported a significant increase, in women above 35 years of age and a further 10-26 fold increase beyond age of 40 20.

Incidence is also noted high at the beginning of reproductive life. The available evidence suggests that hydatidiform mole arises as a consequence of defective ova 21. It is premature in young and post mature in old ages. It is also stated that advanced maternal age may result in a weaker immune response against complete hydatidiform mole, therefore increasing the risk of gestational trophoblastic neoplasia due to ineffective elimination of trophoblastic cells after evacuation 22.

It is observed that majority of our patients in this study had low socioeconomic and poor educational status. This fact has been proved by a Korean study by decreasing the rate of incidence from 4.4 (1960s) to 1.6 (1990s) with improvement in medical care, socioeconomic and educational standards 23,24.

In our series, choriocarcinoma were found to be 1.65%. They were found in the third decade. This is in accordance with the study conducted by Sadiq 16 who found the percentage of choriocarcinomas to be 1.95%. They also found most of the cases in the third decade.

Beta HCG correlation could not be done uniformly as most of the cases did not revealed detailed clinical history of the patients including the HCG levels.

CONCLUSION

From this study, it is evident that benign lesions are more common with 42.9% of the cases of partial hydatidiform mole and 55.3% of the cases of complete hydatidiform mole 86.6%, while malignant were found to be 1.65%. Trophoblastic tumour screening and treatment units should be available in all hospitals and patients with recurrent molar pregnancies should be registered. Post molar followup should be done including determination of BHCG levels every 1-2 wks after evacuation until HCG level is normal.

REFERENCES

Bacterial Etiology of Chronic Suppurative Otitis Media of Patients Attending a Tertiary Care Teaching Hospital

Rabiya Jamil¹, Ayesha Sajjad¹, Faiqa Arshad², Aneela Khawaja³, Ghulam Muhtaba Siddiqui⁴ and Rizwan Ullah⁴

ABSTRACT

Objective: Chronic suppurative otitis media is a common infectious disease of worldwide prevalence. This study was conducted to identify the commonest microorganisms involved and their antibiotic sensitivity pattern in patients of CSOM.

Study Design: Descriptive study

Place and Duration of Study: This study was conducted at the Microbiology and ENT Department of Amna Inayat Medical college /Kishwar Fazal Teaching Hospital Sheikhupura from August 2015 to July 2016.

Materials and Methods: A total of 85 patients with unilateral or bilateral ear discharge attending the ENT OPD clinically diagnosed as CSOM were selected for the study. Pus samples were taken and sent to microbiology lab for culture and sensitivity. All data was analyzed using SPSS version 21.0.

Results: Pseudomonas aeruginosa (36.47%) was the most common organism isolated followed by Staphylococcus aureus (20%), Coagulase negative Staphylococci (9.42%), Methicillin resistant Staphylococcus aureus (8.23%), Escherichia coli (7.05%), Klebsiella pneumoniae (7.05%), Proteus spp. (4.71%), Enterobacter cloacae (3.53%), Aspergillus niger (2.35%), and candida species (1.17%). Drug sensitivity pattern of Pseudomonas aeruginosa showed that Imipenem was active against major (95%) cases followed by Tazobactam and Levofloxacin (88%), Ceftazidime (85%), Ciprofloxacin (80%) and Gentamicin (75%). Pseudomonas showed complete resistance to augmentin. Among Gram positive organisms Staphylococcus aureus was the most common pathogen and drug sensitivity pattern showed that Vancomycin has 100% susceptibility to all the gram-positive pathogens.

Conclusion: Pseudomonas aeruginosa is the most common gram-negative organism isolated from the patients of CSOM and it is highly sensitive to Imipenem. Staphylococcus aureus is the commonest among gram positive organisms and Vancomycin is the most effective drug against gram positive pathogens of CSOM.

Key Words: Chronic suppurative otitis media, bacterial pathogens, antibiotic sensitivity.


INTRODUCTION

Chronic suppurative otitis media (CSOM) is a socially embarrassing disease of almost all age groups. Globally its pervasiveness is high in people with low socioeconomic status, having potentially serious long-term effects.¹

1. Department of Pathology, Amna Inayat Medical College, Sheikhupura.
2. Department of Pathology, Gujranwala Medical College, Gu/wala.
3. Department of Pathology / Community Medicine, Rahbar Medical & Dental College, Lahore.

Correspondence: Dr. Rabiya Jamil, Associate Professor Pathology, Amna Inayat Medical College, Sheikhupura.
Contact No: 034740525617
Email: rabiyaghaffar@gmail.com

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World Health Organization (WHO) has defined chronic suppurative otitis media as a disease stage in which there is chronic infection of the middle ear cleft i.e., Eustachian tube, middle ear and mastoid and in which a non-intact tympanic membrane (e.g., perforation or tympanostomy tube) and discharge (otorrhea) are present for at least 2 weeks or more.¹,² The main clinical features of CSOM are aural discharge and variable degree of hearing loss. In long standing cases it can also result in a number of otogenic complications like facial nerve palsy, intracranial abscess, and meningitis.³

Etiology and pathogenesis of otitis media are multifactorial including genetic predisposition, infections, allergy, environmental, social and racial factors and Eustachian tube dysfunction.³ CSOM is associated with a number of bacterial pathogens. The study of bacterial pathogens and their antimicrobial sensitivity is very important for a clinician to start the initial antibiotic therapy.³ The present study was carried out to determine the common microorganisms involved and their antimicrobial susceptibility patterns in patients.
with CSOM in our tertiary care setting, so that an antibiotic policy is established for better management of these patients.

MATERIALS AND METHODS

This descriptive study was conducted in the Microbiology Department of Kishwar Fazal Teaching Hospital/ Amna Inayat Medical College Sheikhupura from August 1, 2015 to July 31, 2016. A total of 85 patients between 5 and 62 years of age, comprising of 46 males and 35 females who were clinically diagnosed as CSOM were selected for the study. Inclusion criteria was patients having tympanic perforation and ear(s) discharge for more than 3 months. Patients with H/O using antibiotics (oral & systemic) for the last 5 days were excluded from the study. All of our patients were from rural background with low socio-economic status. Informed consent from the patients was obtained at the time of enrolment.

Pus swabs were taken aseptically in the Microbiology Department with commercially prepared sterile cotton swabs after cleaning the external auditory canal. Two sterile swabs were used to collect the discharge in each patient. One swab was used for Gram's stain (direct smear examination) and the other swab was used for isolation of causative organism by inoculating on different culture media. The pus swabs were inoculated on Blood, MacConkey & Chocolate agar, incubated aerobically at 37°C for 24-48 hours. Incubation onto two slopes of Sabouraud's dextrose agar was done and incubated at 25°C & 37°C for 14 days for isolation of fungus. The isolates were identified based on colony appearance, Gram stain, culture characteristics and biochemical tests as described by Cheesbrough. Antibiotic susceptibility testing was performed on Mueller-Hinton agar plates using Kirby Bauer disc diffusion method and the results were interpreted as per Clinical Laboratory and Standards Institute (CLSI) guidelines (2018). The antibiotics tested were Amoxycillin (20/10 µg), Co-trimoxazole (25 µg), Gentamicin (10 µg), Amikacin (30 µg), Cephalexin (30 µg), Cefuroxime (30 µg), Ceftazidime (30 µg), Ciprofloxacine (5 µg), Levofloxacine (5 µg), Linezolid (10 µg), Vancomycin (5 µg), Imipenem (10 µg), Piperacillin/Tazobactam (100/10µg), Sulbactam/ Cefoperazone (75/30µg) and Cefoxitin (30µg) for Methicillin resistant Staphylococcus aureus (MRSA). Susceptibility for fungal isolates was not done.

RESULTS

Of the 85 patients, 4 showed bilateral ear discharge. Single growth was obtained from 81 samples. Pseudomonas aeruginosa (36.47%) was the most common organism isolated followed by Staphylococcus aureus (20%), Coagulase negative Staphylococci (9.42%), Methicillin resistant Staphylococcus aureus (8.23%), Escherichia coli (7.05%), Klebsiella pneumoniae (7.05%), Proteus spp. (4.71%), Enterobacter cloacae (3.53%), Aspergillus niger (2.35%), and Candida species (1.17%).

Table No.1: Frequency of bacterial pathogens isolated from patients of CSOM

<table>
<thead>
<tr>
<th>Type of Organism</th>
<th>Number=85</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>31</td>
<td>36.47%</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>17</td>
<td>20%</td>
</tr>
<tr>
<td>CoNS</td>
<td>8</td>
<td>9.42%</td>
</tr>
<tr>
<td>MRSA</td>
<td>7</td>
<td>8.23%</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>6</td>
<td>7.05%</td>
</tr>
<tr>
<td>Klebsiella pneumonia</td>
<td>6</td>
<td>7.05%</td>
</tr>
<tr>
<td>Proteus spp.</td>
<td>4</td>
<td>4.71%</td>
</tr>
<tr>
<td>Enterobacter cloacae</td>
<td>3</td>
<td>3.53%</td>
</tr>
<tr>
<td>Aspergillus niger</td>
<td>2</td>
<td>2.35%</td>
</tr>
<tr>
<td>Candida</td>
<td>1</td>
<td>1.17%</td>
</tr>
</tbody>
</table>

CoNS= Coagulase negative Staphylococci, MRSA= Methicillin resistant Staphylococcus aureus.

Table No.2: Antibiogram Of Gram-Negative Isolates (N=50)

<table>
<thead>
<tr>
<th>Type of organism</th>
<th>Total No. (n=50)</th>
<th>AUG (%)</th>
<th>GM (%)</th>
<th>AK (%)</th>
<th>CAZ (%)</th>
<th>CP (%)</th>
<th>LEV (%)</th>
<th>IM (%)</th>
<th>TZ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P. aeruginosa</td>
<td>31 (36.47%)</td>
<td>0</td>
<td>75</td>
<td>70</td>
<td>85</td>
<td>80</td>
<td>88</td>
<td>90</td>
<td>88</td>
</tr>
<tr>
<td>E. coli</td>
<td>6 (7.05%)</td>
<td>28</td>
<td>55</td>
<td>80</td>
<td>71</td>
<td>22</td>
<td>80</td>
<td>90</td>
<td>72</td>
</tr>
<tr>
<td>Klebsiella</td>
<td>6 (7.05%)</td>
<td>80</td>
<td>88</td>
<td>100</td>
<td>50</td>
<td>70</td>
<td>100</td>
<td>60</td>
<td>75</td>
</tr>
<tr>
<td>Proteus</td>
<td>4 (4.71%)</td>
<td>65</td>
<td>60</td>
<td>72</td>
<td>68</td>
<td>80</td>
<td>70</td>
<td>50</td>
<td>50</td>
</tr>
</tbody>
</table>

AUG- Augmentin, GEN- gentamicin, AK- amikacin, CAZ- Ceftazidime, CP- Ciprofloxacine, LEV- Levofloxacine, IM- Imipenem, TZ- Tazobactum/Piperacillin.

Table No.3: Antibiogram of Gram-Positive Isolates (N=32)

<table>
<thead>
<tr>
<th>Type of organism</th>
<th>Total No. (n=32)</th>
<th>AMP (%)</th>
<th>AUG (%)</th>
<th>PR (%)</th>
<th>TE (%)</th>
<th>COT (%)</th>
<th>Gm (%)</th>
<th>AK (%)</th>
<th>CP (%)</th>
<th>LZ (%)</th>
<th>VM (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. aureus</td>
<td>17 (20%)</td>
<td>22</td>
<td>92</td>
<td>90</td>
<td>41</td>
<td>60</td>
<td>55</td>
<td>58</td>
<td>72</td>
<td>96</td>
<td>100</td>
</tr>
<tr>
<td>CoNS</td>
<td>8 (9.42%)</td>
<td>40</td>
<td>100</td>
<td>100</td>
<td>50</td>
<td>66</td>
<td>46</td>
<td>52</td>
<td>66</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>MRSA</td>
<td>7 (8.23%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>92</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

Antimicrobial sensitivity patterns of gram-negative organisms were tested and results are shown in Table 2. Antimicrobial sensitivity patterns of gram-positive organisms were tested and results are shown in Table 3

**DISCUSSION**

Chronic suppurative otitis media is a common condition in most of the developing countries. Most of the cases first present to a variety of healthcare personnel including general physicians. Though some cases surface to ENT specialists – a situation that is not a peculiarity in Pakistan but a norm in most of the developing world especially Southeast Asia. Culture and sensitivity of ear discharge is infrequently carried out. This trend means bacteriological characteristics of most of CSOM cases remains concealed. Chances of complications such as hearing impairment increases substantially if effective empirical and or sensitive antibiotics are not instituted in a timely fashion.

This situation that provided a perfect rationale to conduct current study at a newly opened tertiary health setting in outskirts of Lahore i.e. Kishwar Fazal Teaching Hospital/ Amna Inayat Medical College Sheikhupura. Our study yielded a positive culture in 96% of samples. Comparable studies from other tertiary health settings of Pakistan have yielded 84% to 97% positive cultures. In our study, frequency of microorganisms in descending order was Pseudomonas aeruginosa (36.47%), Staphylococcus aureus (20%), Coagulase negative Staphylococci (9.42%), Methicillin resistant Staphylococcus aureus (8.23%), Escherichia coli (7.05%), Klebsiella pneumoniae (7.05%), Proteus spp. (4.71%), Enterobacter cloacae (3.53%), Aspergillus niger (2.35%), and Candida species (1.17%). An agreement study by Tariq et al found that Pseudomonas aeruginosa (38%) was the most common bacterial isolate, followed by staphylococcus (28%), Proteus mirabilis (21%), E. coli, (3%), Klebsiella (3%) and Candida (2%). The results are in comparison to our study. Khan and coworkers demonstrated that Pseudomonas aeruginosa was found in 51 (42.5%) cases followed by Staphylococcus aureus in 28 (23.4 %) cases, MRSAs (Methicillin Resistant Staphylococcus aureus) in 7 (5.8%) cases, Proteus in 6 (9.2%) cases, Klebsiella in 8 (6.7%) cases and E-Coli in 6 (5%) case. Hydri et al. studied 140 patients of CSOM and found Pseudomonas aeruginosa was the most common organism isolated alone in 76 ears and in combination with other micro-organisms in 18 ears, followed by staphylococcus aureus in 23 and MRSA in four cases. Mixed organisms were found in 20 patients. Zakirullah and colleagues also concluded that the most common causal organisms isolated from CSOM cases were Pseudomonas aeruginosa in 35 (31.8%) and Staphylococcus aureus in 32 (29.1%) followed by Proteus species in 16 (14.55%) and Morganella in nine (8.25%) cases.

Fatima et al. isolated Pseudomonas aeruginosa in 141 (68.44%) cases of CSOM which was the most common microbe in their study and was followed by Staphylococcus aureus in 53 (25.72%). Study by Chaudhary and coworkers differs from our study, that from 47% of CSOM cases Staphylococcus aureus was isolated, followed by Pseudomonas aeruginosa (34%). Most of these recent publications from within Pakistan have shown invariably consistent bacteriology in CSOM with minor differences in overall frequency of microbes causing CSOM. Our study findings are therefore consistent with recent literature from within the country where socioeconomic and demographic characteristics of studied population were generally alike.

According to our study, drug sensitivity pattern of Pseudomonas aeruginosa showed that Imipenem was active against majority (95%) cases followed by Tazobactum and Levofloxacin (88%), Ceftazidime (85%), Ciprofloxacin (80%) and Gentamicin (75%). Pseudomonas showed complete resistance to Augmentin. Among Gram positive organisms Staphylococcus aureus was the most common pathogen and drug sensitivity pattern showed that Vancomycin has 100% susceptibility to all the gram-negative pathogens. Drug sensitivity patterns of Pseudomonas aeruginosa and Staphylococcus aureus varied from study to study but the differences were significant. In short, the microbial predominance and their antibiotic sensitivity pattern is not generalizable. Therefore, we strongly suggest that periodical monitoring of microbiological profile is essential for making effective empirical protocol for the cases in a particular geographical location.

**CONCLUSION**

Pseudomonas aeruginosa is the most common gram-negative organism isolated from the patients of CSOM and it is highly sensitive to Imipenem. Staphylococcus aureus is the commonest among gram positive organisms and Vancomycin is the most effective drug against gram positive pathogens of CSOM.

**Author’s Contribution:**
- Concept & Design of Study: Rabiya Jamil
- Drafting: Ayesha Sajjad, Faiqa Arshad
- Data Analysis: Aneela Khawaja, Ghulam Mujtaba, Siddiqui, Rizwan Ullah
- Revisiting Critically: Rabiya Jamil, Ayesha Sajjad
- Final Approval of version: Rabiya Jamil

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

**REFERENCES**

Antioxidant Effects of Walnuts on Superoxide Dismutase Levels Reduced by Lead Toxicity in Mice
Roomisa Anis¹, Ayesha Shafqat¹, Misbah Batool², Beenish Zafar¹, Naveeda Zaigham¹ and Shahzadi Ambreen³

ABSTRACT

Objective: To evaluate the antioxidant effects of walnuts on lead toxicity by estimating the superoxide dismutase levels.

Study Design: Quasi Experimental Study

Place and Duration of Study: Department of Biochemistry, ANMCH, Islamabad, Pakistan in collaboration with NIH, Islamabad from November, 2015 to April, 2016.

Materials and Methods: 60 BLAB/C mice were divided into three groups of 20 mice each. Group I was given normal standard diet. Group II was given lead acetate in drinking water along with normal diet without any supplementation. Group III was given lead acetate along with the diet supplemented with walnuts. Superoxide Dismutase (SOD) was estimated at the end of the study by xanthine oxidase method.

Results: Toxicity of lead caused decrease in the SOD in group II. Supplementation of walnut along with lead showed increase in SOD levels in group III (p value ≤0.001) as compared to group II.

Conclusion: This study concludes that antioxidants present in walnuts decrease lead induced lipid peroxidation by increasing the levels of antioxidant enzyme SOD.

Key Words: Antioxidants, Lead Toxicity, Lipid peroxidation, Superoxide Dismutase, Walnuts

INTRODUCTION

The pollution caused by heavy metals is considered as a major problem worldwide.¹ Industries are the major cause of heavy metal pollution which include: refineries of metal processing, power plant which run on coal burning and petroleum products, nuclear power stations, high tension lines, plastics, textiles, microelectronics, wood preservation and paper processing plants.²

The unsupervised use of heavy metals like lead in Pakistan is a serious threat to the human health. Toxicity of lead interferes with variety of biochemical processes, rather than disrupting a single mechanism.³

Lead mine workers, plumbers, workers at the glass manufacturing industry, cosmetic workers and battery workers are at a greater risk of lead exposure as an occupational hazard. Around 2.5 million tons of lead is being produced per annum around the world. Chronic exposure of lead leads to its bio deposition in vital organs and it is measured as per gram weight of the tissue.⁴ The proposed underlying mechanism responsible for the lead toxicity is oxidative stress which is caused by two dissident mechanisms yet parallel to each other. The first mechanism implicates the production of reactive oxygen species (ROS) whereas the other mechanism exhausts the natural antioxidant pools of the cell. These two mechanisms are associated in such a way that high levels of reactive oxygen species on one hand and the consumption of antioxidant pools on the other result in the cellular injury.⁵ As lead is capable of inducing the production of ROS and also intrudes the natural antioxidant pool of humans, this property of lead results in its intense binding to thiol groups which leads to deterioration of function of antioxidant enzyme like superoxide dismutase, catalase or glutathione peroxidase.⁶

The intrinsic pool of antioxidants ascertains the vulnerability of a cell towards oxidative damage and defends the tissues against detrimental effects of reactive species at cellular level but not at plasma level.⁷ The fundamental antioxidant enzymes of the body include superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX). Superoxide dismutase is basically an antioxidant enzyme present in
the body which plays important role in the natural defence process majorly by blocking the induction of free radical chain reactions leading to synthesis of free radicals. SOD belongs to the group of metal containing enzymes which causes the disposal of superoxide anion by catalysing it to hydrogen peroxide. It is one of the endogenous antioxidant enzymes which protects against oxidative stress and has been used as an oxidative stress marker in lead poisoned individual in some recent studies. 

It has been observed that utilization of natural resources has increased in recent years. Among the natural antioxidants phenolic compounds are obtaining significant attention because of their advantages to human health. Walnut are abundant in phenolic compounds and have beneficial role in retrenchment of oxidative stress and termination of macromolecular oxidation. Walnuts vary from all other nuts by a high content of α-linolenic acid, a vegetable n-3 fatty acid, and they also exhibit a distinct combination of nutrients and many phytochemical species like phenolic acids, flavonoids, tannins. Walnut has been used in several studies as an antioxidant and its antioxidant properties are well known. It has been used as anti-neoplastic and anti-inflammatory agent in different studies. 

Lead as a biological toxin has been studied with several natural antioxidants. The rationale of this study was to assess the antioxidant role of walnut on SOD decreased by lead toxicity. This study was conducted to investigate the effect of lead on SOD as a marker of oxidative stress in the tissues of mice, along with the possible valuable role of walnut in reducing the lead toxicity in the mice kernels were obtained.

**MATERIALS AND METHODS**

After the approval of Institutional Review Board (IRB) Isra University Islamabad; a Quasi experimental study was conducted in Department of Biochemistry, Al Nafees Medical College & hospial, Islamabad, Pakistan in collaboration with National Institute of Health Islamabad. The laboratory tests were conducted at the Multi-disciplinary laboratory at Al Nafees medical college & hospital. Lead acetate was purchased from a local scientific shop manufactured by United Laboratory Chemical Works, Garden Town, Lahore. Walnuts (Jugland Regia) were purchased from local cultivator and seller in Mansehra District. The BALB/C mice were procured from animal house of National Institute of Health (NIH) Islamabad. These animals were bred at the NIH and were used in the experiment. Adult healthy mice 60 days old weighing 50gms±20gms of either gender were included in study. Whereas mice with disease or those mice who developed disease in the course of experimentation were excluded. Mice chow was supplemented with walnuts. Walnut shells were discarded, and walnut Whole walnut kernels were stored at -20°C until
grounded and added to the diet. Lead acetate was dissolved in drinking water and given by gauge. Mice were randomized into three groups Group I, Group II, Group III by convenience sampling technique. Each group contained 20 mice. Group I served as a control group and contained 20 mice. Group I was treated with normal mice chow for two months and was given plain tap water along with 0.5 ml plain water by gauge tube Group II was treated with normal mice chow and lead acetate 30mg/kg body weight in drinking water for two months. Group III was treated with standard mice chow, lead acetate 30mg/kg body weight in drinking water. Along with Lead acetate, group III was treated with whole walnut kernels. Group III was treated with standard mice chow, lead acetate 30mg/kg body weight in drinking water. Along with Lead acetate, group III was treated with whole walnut kernels 111 g/kg diet. All the samples were taken at the end of the study by intracardiac puncture. The antioxidant capacity of Super Oxide Dismutase was calculated by Super Oxide Dismutase assay kit purchased from Abcam. This kit utilizes water soluble tetrazolium-1 (WST-1) salt by xanthine oxidase and produces water soluble formazan dye (WST-1 formazan). In this assay superoxide dismutase reduces superoxide anion and has a linear relationship with the activity of xanthine oxidase. The SOD assay measures all three types of SOD (Cu/Zn, Mn, and Fe-SOD) and provides a simple, reproducible and fast tool for assaying SOD activity in serum, plasma, erythrocyte lysates, tissues etc.

![SOD Assay Diagram](image)

All the solutions were mixed and were incubate at 37°C for 20 minutes. Absorbance was calculated for each well at 450nm. SOD percent inhibition of each sample was measured with the help of formula:

\[
\text{Inhibition rate} \% = \frac{(A \text{ blank1 } - A \text{ blank3}) - (A \text{ sample } - A \text{ blank2}) \times 100}{A \text{ blank1 } - A \text{ blank3}}
\]

**Statistical Analysis:** The data obtained was analysed on SPSS version 20. Descriptive studies were done. One-way ANOVA was applied followed by Post Hoc Tukey’s test for multiple comparisons. Difference in mean among the control and treated groups was calculated by independent sample ‘t test’ for two group comparisons. The difference was considered significant if p value was found ≤ 0.05.
RESULTS

We exposed group II with Lead for two months; it resulted in the significant decrease in the activity of serum superoxide dismutase when it was compared with control group Table- I. This table shows that the Serum Superoxide dismutase activity in control group was 55.53±3.84 whereas in group II it was 25.96±3.56; it showed significant decline (p value < 0.01) revealing that lead has significantly compromised the antioxidant defence enzyme in the serum of mice. Supplementation of walnuts for two months along with lead in group III was able to protect against the lipid peroxidation. This was seen as significantly increasing activity of antioxidant enzyme superoxide dismutase. Table – 2. This table shows that the serum superoxide dismutase activity of group III was 71.24±4.30 whereas in group II it was 25.96±3.56 (p value < 0.01).

Table No.1: Effect of two-month supplementation of lead acetate on serum superoxide dismutase levels in mice.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I Control (n=20) Mean±SD</th>
<th>Group II Lead acetate (n=20) Mean±SD</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Superoxide dismutase</td>
<td>55.53±3.84</td>
<td>25.96±3.56</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>% inhibition</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*(p value of ≤ 0.05 is taken as statistically significant)

Table No.2: Effects of two-month supplementation of lead acetate and walnuts on serum superoxide dismutase activity in mice.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I Lead acetate (n=20) Mean±SD</th>
<th>Group II Walnut (n=20) Mean±SD</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum Superoxide dismutase</td>
<td>25.96±3.56</td>
<td>71.24±4.30</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>% inhibition</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*(p value of ≤ 0.05 is taken as statistically significant)

DISCUSSION

Lead is a heavy metal and one of the ubiquitous pollutants. It is being extensively used in different industries and it induces extensive damage to human population. Despite of being noxious metal it is still used in many industries.

The present study was designed to investigate the protective effect of walnut on lead acetate induced oxidative stress in a mice. Group I was given normal mice chow and distilled water for two months. Enzymatic antioxidant defence system contains SOD, a metal containing enzyme, which is one of the significant antioxidant enzyme causing dismutation of superoxide anion and halts the damage caused by this highly reactive molecule. Decrease in the levels of SOD is associated with oxidative stress. Our data of the control group generated the SOD levels in the range of 55.53±3.84. These results of the control group were in accordance with another study conducted on albino...
mice. Another study conducted on wistar rats also showed results similar to the results of control group of our study.

In our experimental design, we exposed group II with lead acetate in drinking water. In recent few years, research studies have suggested that lead poisoning is a major concern for human population and consequences into oxidative stress. Lead is a heavy metal which binds to the thiol groups of proteins and enzymes and inhibits their activity. To check the antioxidant status of this group SOD activity was measured in the serum. SOD is one of the major enzymatic antioxidants which removes toxic substances and achieves this role with the help of its antioxidant enzymatic function. One of the studies used wistar rats to study lead toxicity. In this study rats were exposed to different heavy metals including lead acetate. After 30 days the results showed significant decrease in SOD. A similar study conducted on male wistar rats where they were treated with another heavy metal, cadmium for 21 days also shown marked decrease in SOD.

Lead poisoning was also studied in Japanese Quails in 2017 by Abo Ismail et al. In this study birds were introduced with lead acetate in drinking water for one month. After one month of intake lead was able to attenuate all the antioxidants including SOD when compared with control group similar to the results of our study. A similar study conducted on male albino rats, showed marked decrease in SOD when they were exposed to lead for 4 weeks. Lead causes enhanced lipid peroxidation and it may cause deleterious effects to a living organism. To ensure the security of food and public health a study was conducted on cauliflower in which the seeds were germinated under lead acetate stress for 12 days and the results of this study were contrary to the results of our study. The results showed increase in the activity of SOD after lead exposure in the seedlings. This contradiction in the results could possibly be due to short duration of exposure in the study mentioned above.

In contrary to the results of our group II, another study was conducted on human subjects by Dobrakowski M. et al in 2017. 36 male were included subjects in this study who were occupationally exposed to lead for 12 hours daily for 36 to 44 days. His results showed no decrease in SOD after lead exposure and were contrary to our results which suggested that lead causes significant decrease in SOD.

To investigate the beneficial role of walnut against lead toxicity, at the end of the study SOD estimation was done. The results showed significant increase in the activity of SOD when compared to control group and lead acetate group which supported our hypothesis that walnuts have antioxidant properties. Walnuts are used as antioxidants in several studies; one such study was reported on pregnant rats. In this study pregnant diabetic rats were given walnut oil in different doses for 12 days and walnut oil was able to prevent hepatotoxicity and caused increase in SOD. The antioxidant role of walnut was studied in another study conducted on rats in which oxidative stress was induced by scopolamine. Administration of walnut for 28 days was able to increase the SOD levels in rats similar to our results.

Walnuts have phytochemicals which prevent oxidative stress and enhance the antioxidant status. In another study conducted on wistar albino female rats, studied the effects of walnut against oxidative stress produced by alcohol on lungs and muscle tissues. Supplementation of walnut for 50 days was able to combat oxidative stress and resulted rise in SOD.

CONCLUSION

This study concludes that antioxidants present in walnuts decrease lead induced lipid peroxidation by increasing the levels of antioxidant enzyme SOD.

Author’s Contribution:

Concept & Design of Study: Roomisa Anis

Drafting: Ayesha Shaqfat, Misbah Batool

Data Analysis: Beenish Zafar, Naveeda Zaigham, Shazad Ambreen

Revisiting Critically: Roomisa Anis, Ayesha Shaqfat

Final Approval of version: Roomisa Anis

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

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antioxidant effect of Walnut (Juglans regia L) on 
lung and muscle tissue. J Nat Appl Sci East 
Objective: To determine accuracy of age estimation by comparison of deciduous teeth eruption and ossification of carpal bones of hand.

Study Design: Randomized controlled trial study.

Place and Duration of Study: This study was conducted at the Department of Forensic Medicine, Govt. KMSMC Sialkot in collaboration of Radiology Department, THQ Hospital Pasrur, District Sialkot from 25th August 2019 to 25th August 2020.

Materials and Methods: One hundred and forty children of both genders with ages 5 to 15 years were enrolled in this study. All the patients were equally divided into two groups, each group consist of 70 patients. In group A dental age estimates were made using radioscopic (RVG) pictures of the left quadrant mandibular teeth by Demirjian method and the right hand wrist radiograph by Greulich and Pyle method was used for the estimation of the age of the skeleton in Group B. Statistical analysis on differences between chronological age and approximate skeletal and dental age was carried out.

Results: There were 40 (57.14%) male and 30 (42.86%) females in group A and in group B, 38 (54.29%) male and 32 (45.71%) females. The difference between chronological age and dental age in children with ages 5 to 10 years was 0.64±1.24 years and children with ages 11 to 15 years the difference was 0.67±0.18 years in group A and in group B difference between chronological age and skeletal age among children with age group 5 to 10 years was 0.72±1.18 years and among children with ages 11 to 15 years the difference was 0.66±1.18 years. No significant difference was observed between both groups with p-value >0.05.

Conclusion: Both procedures dental age estimation and skeletal age estimation are effective for forensic age estimation. No significant difference was observed between both methods, but the combination of both methods for age assessment in children provides us more accurate age with very narrow range.

Key Words: Age estimation, Forensic, Dental age (Demirjian’s), Bone age (Greulich and Pyle).

assessment techniques based upon dental ripening can be divided into atlas methods or scoring methods like Schour and Massler, Moorrees, Anderson and Demirjian. The methods of morphological and radiological age estimation in adults are Gustafson, Bang and Ramn, Solheim, Kvaal and Solheim and Kvaal. The Demirjian method of age assessment has been generally accepted among many proposed methods. Demirjian's classifications of stages are best suited for the forensic purpose because stages are characterized by shape and development changes of teeth, which are independent of potentially complicated measurements in length. Demirjian's advantages include the objective criteria defining stages of tooth growth instead of tooth eruption, which were clearly illustrated with line diagrams and radiographic images. We conducted present study to compare the accuracy of tooth eruption (Demirjian method) versus ossification of carpel bone of hand (Greulich and Pyle method) for forensic age estimation.

**MATERIALS AND METHODS**

This randomized controlled trial was conducted at Department of Forensic Medicine, Govt. KMSMC Sialkot in collaboration of Radiology Department, THQ Hospital Pasur District Sialkot from 25th August 2019 to 25th August 2020. A total of 140 children of both genders with ages 5 to 15 years were enrolled in this study. Individual’s detailed demographics were recorded after taking written consent from parents/guardians. Individuals who didn’t agree to the procedure, who were uncooperative, patients with psychiatric illness, patients with abnormal tooth and hand wrist radiographic morphology were excluded.

All the patients were equally divided into two groups, each group consist of 70 patients. In group A dental age estimates were made using radioscopic (RVG) pictures of the left quadrant mandibular teeth by Demirjian method and the right hand wrist radiograph by Greulich and Pyle method was used for the estimation of the age of the skeleton in Group B. Statistical analysis on differences between chronological age and approximate skeletal and dental age was carried out. All the data was analyzed by SPSS 24. Chi square test was applied to compare the accuracy between both procedures. P-value <0.05 was taken as significant.

**RESULTS**

There were 40 (57.14%) male and 30 (42.86%) females in group A and in group B, 38 (54.29%) male and 32 (45.71%) females. In group A 37 (52.86%) patients were ages 5 to 10 years and 33 (47.14%) were ages 11 to 15 years. In group B 36 (51.43%) patients had ages 5 to 10 years and 34 (48.57%) were ages 11 to 15 years (Table 1).

In group A, children with age group 5 to 10 years were mean chronological age 7.42±2.36 years, the dental age was 6.81±1.12 years the difference was 0.64±1.24 years the difference was not significant with p-value 0.063. Among children with ages 11 to 15 years the mean chronological age was 13.53±1.84 years and the dental age was 12.86±2.02 years, the difference was 0.67±0.18 years. The difference was not statistically significant with p-value >0.05. In group B children with age group 5 to 10 years were mean chronological age 7.75±2.33 years, the skeletal age was 7.03±1.15 years the difference was 0.72±1.18 years the difference was not significant with p-value 0.063. Among children with ages 11 to 15 years the mean chronological age was 12.65±1.82 years and the skeletal age was 11.99±0.64 years, the difference was 0.66±1.18 years. The difference was not statistically significant with p-value >0.05 (Table 2).

**DISCUSSION**

As it reduces the search for an unskilled individual to allow a more effective and long time saving approach, age estimation should be as accurate as possible. Whilst there are different age determination methods, due to the differing differences of different ethnic groups, no standardized framework has been established.

**Table No.2: Comparison of age estimation between both groups**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group A</th>
<th>Group B</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>40 (57.14%)</td>
<td>38 (54.29%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Female</td>
<td>30 (42.86%)</td>
<td>32 (45.71%)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 – 10</td>
<td>37 (52.86%)</td>
<td>36 (51.43%)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>11 – 15</td>
<td>33 (47.14%)</td>
<td>34 (48.57%)</td>
<td></td>
</tr>
</tbody>
</table>

Therefore, in various communities each solution must be checked. To ensure ethnic uniformity in the research sample, the research group was chosen. This study consisted of 140 subjects; 70 individuals were categorized into two groups each. Group A received dental age method while group B received skeletal age method. 40 (57.14%) male patients and 30 (42.86%) females patients in group A and in group B 38
(54.29%) patients were male and 32 (45.71%) were females. In group A 37 (52.86%) patients were ages 5 to 10 years and 33 (47.14%) were ages 11 to 15 years. In group B 36 (51.43%) patients had ages 5 to 10 years and 34 (48.57%) were ages 11 to 15 years. These results were comparable to the study by Schmeling et al and AlQahtani et al.

In present study we found that children with age group 5 to 10 years were mean chronological age 7.42±2.36 year, the dental age was 6.81±1.12 years the difference was 0.64±1.24 years the difference was not significant with p-value 0.663. Among children with ages 11 to 15 years the mean chronological age was 13.53±1.84 years and the dental age was 12.86±2.02 years, the difference was 0.67±0.18 years. The difference was not statistically significant with p-value >0.05. A study by Patel et al regarding dental and skeletal age estimation and they used Demirjian and Willem method for dental age and Greulich and Pyle method for skeletal age estimation, they reported no significant difference between both procedures however Willem's dental age estimation method proved to be the most accurate and consistent.

Azzawi et al reported that the increase of dental age was found to be statistically important of 400 both boys and girls in accordance with their chronological age. 0.208 years of age were boys and 0.294 years before the girls. They also suggested that Demirjian is not applicable to Egyptian children. For each sex and age it is important to create a new adapted dental score separately for Egyptian children.

In our study, among children who received skeletal age method, we found that children with age group 5 to 10 years, the mean chronological age was 7.75±2.33 year, the skeletal age was 7.03±1.15 years the difference was 0.72±1.18 years the difference was not significant with p-value 0.663. Among children with ages 11 to 15 years the mean chronological age was 12.65±1.82 years and the skeletal age was 11.99±0.64 years, the difference was 0.66±1.18 years. The difference was not statistically significant with p-value >0.05. A study by Mughal et al reported that on radiation-based hand & wrist visualization techniques including bone age estimation ultrasound were theorized, but not as precise as radiographic approaches. Bone age cannot be determined from hand & wrist X-rays when 18 years old, and thus, the medial end of the clavicle in individuals aged 18-22 years is used for the measurement of bones. Another study by Saadé et al showed similarity to our study findings and reported both the dental and skeletal method can be used for age estimation with dental method being more accurate than the skeletal method.

CONCLUSION

Both procedures, age of deciduous teeth eruption (dental age) and ossification of carpal bones of right wrist (skeletal age method) can be applied for estimation of forensic age. Both procedures are safe and easy to perform, but when we estimate age by combining both skeletal and dental data, the accuracy of age estimation increase to a lot. So instead of having single parameter for forensic age assessment, the two or even multiple parameters usage give us more precise and accurate age with very narrow gap and this narrow range is more helpful and authentic in deciding criminal proceedings.

Author’s Contribution:
Concept & Design of Study: Muhammad Faheem Ashraf
Drafting: Samina Kanwal, Mehak Khalid
Data Analysis: Mariam Malik, Shereen Rafiq
Revisiting Critically: Muhammad Faheem Ashraf, Samina Kanwal
Final Approval of version: Muhammad Faheem Ashraf

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

REFERENCES

Histopathological Findings in Malignant and Benign Parotid Glands Tumors

Sadia Yaseen¹, Ayesha Khalid², Rizwan Saghir Chatha³ and Burhan-ul-Haq⁴

ABSTRACT

Objective: To understand the pathology of benign and malignant salivary gland tumors in parotid glands and its relation with gender.

Study Design: Cross-sectional-analytical study.

Place and Duration of Study: This study was conducted at the Department of Pathology, Government Said Mitha Teaching Hospital Lahore from 11st August 2017 to 15th September 2019.

Materials and Methods: Sixty-two parotid glands neoplastic lesions were included. The specimens consisted of incisional biopsies, partial parotidectomy and complete parotidectomy. All the samples were fixed in 10 percent formalin, processed, sectioned and stained according to standard protocol. Slides were analyzed by the authors and categorized according to the historical tumor class of the World Health Organization and were reviewed for descriptions of cellular morphology, encapsulation, perineural and vascular structures and the surrounding environment.

Results: The age of patients was 13-74 years. Twenty-five (40.3%) patients were male and 37(59.57%) patients included were female. Forty-four (70.96%) cases were classified as benign tumors and 18 (29.03%) cases as malignant tumors. In benign lesions pleomorphic adenoma was most common found in 36 (81.82%) patients and among malignant lesions Mucoepidermoid Carcinoma was most frequent found in 11 (61.11%) patients. No significant difference was found for distribution of benign, malignant and their subtypes between males and females.

Conclusion: Parotid gland tumors are relatively less common and they exhibit a wide variety of microscopic appearances even within one particular lesion. Accurate diagnosis with histological correlation is essential as parotid gland neoplasms have diverse clinical and prognostic outcomes.

Key Words: Salivary gland tumor, Parotid glands tumor, Neoplastic lesion

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INTRODUCTION

Salivary organ tumors have made a lot of discussion due to the complexity and variability in structure and clinical presentation. A number of non-neoplastic and neoplastic lesions originate in parotid gland. They are a diagnostic challenge due to their relative recurrence.¹ The yearly incidence of salivary gland neoplasm spans from 0.5 to two per million in various countries of the world with highest occurrence in Croatia.²

Around 80 percent of the salivary neoplastic lesions occur in parotid gland and are mostly benign. Salivary neoplastic lesions are noticed in all age groups with highest occurrence in third or fourth decade for benign but 4th to 5th decades for cancers.³ Incidence of salivary gland neoplasm between male and female is equal.⁴ Rarity of salivary gland neoplasm is a challenge to expertise of pathologist. Most of the tumors occur in major salivary glands especially parotid and few of these occur in minor salivary glands that occur in palate,⁵ risk factors leading to the neoplasm comprise of processed meat, excessive alcohol consumption, obesity and radiation exposure.⁶ Workers exposed to chemicals in tannery and saw dust are also at risk of salivary gland tumors.⁷ Lymphomas of salivary glands are associated with Sjogern syndrome.⁸ Presenting complaints encompass simple palpable lesions with associated symptoms like rapid increase in lump size, pain, fix to surrounding deep tissue and over lying skin. Signs and symptoms of malignancy are nerve involvement and lymphadenopathy.⁹ This study entails the dire need to identify different microscopic histological pattern of salivary gland neoplasms and their age frequency and distribution.

¹. Department of Histopathology, Shaikh Zayed Hospital, Lahore.
². Department of Hematology, LGH, Lahore.
³. Department of Community Medicine, Azara Naheed Medical College, Lahore.
⁴. Govt. Said Mitha Teaching Hospital Lahore.

Correspondence: Dr. Muhammad Ali Raza, Head of ENT Department, Govt. Said Mitha Teaching Hospital Lahore. Contact No: 0300-4494379 Email: drraliraza321@gmail.com

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Accepted: July, 2020
Printed: September, 2020
MATERIALS AND METHODS

This cross-sectional study was conducted at Department of Histopathology, Government Said Mitha Teaching Hospital Lahore from 11th August 2017 to 15th September 2019. A total of 62 cases of parotid gland lesion were included. Sources of class, age and form of histopathology reported at histopathology lab have been studied. The research involves parotid gland neoplastic lesions. The specimens included incisional biopsies, partial parotidectomies and complete lymph node drainage or node parotidectomies. Following detailed history and clinical review in the initial application forms, samples were set in formalin and parts taken from the lesion, its edges, underlying tissue and, wherever possible, lymph nodes were extracted. Upon gross inspection, the blocks were processed in automatic tissue processor and inserted into paraffin. Sections were taken from paraffin block. Hematoxylin and eosin stain was done on slides and special stains like periodic acid Schiff were done in selected cases. This whole process was outsourced. Microscopic histological features were studied under microscope comprising of cellular architecture, encapsulation, perinural and vascular invasion patterns examined by histopathologist. The data gathered were analyzed and the findings obtained correlated with current literature studies. The tumors were identified by the histological form of salivary tumors of the World Health Organization (WHO). Patients who give informed consent, presenting with palpable lesion were included. Non consenting patients and diagnosed metastatic neoplasm cases were excluded.

RESULTS

The mean age of patients was 39.7±12.2 years. 25 (40.3%) were male patients others were female patients. Mean BMI of patients was 23.24±2.46 kg/m² (Table 1). Forty four (70.96%) cases were classified as benign tumors and 18 (29.03%) cases as malignant tumors (Fig. 1). Though malignant cases were higher in percentage among males as compared to females but the difference was insignificant with p-value 0.320 (Fig.2). The most common benign lesion was pleomorphic adenoma in 36 (81.82%) patients followed by Warthin’s tumor in 4 (9.09%) patients, lymphangiom in 2 (4.55%) patients and basal cell adenoma in 2 (4.55%) patients respectively. The distribution of classification was not significantly different between two genders (Table 2).

### Table 1: Descriptive statistics for the patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>39.7±12.2</td>
<td>-</td>
</tr>
<tr>
<td>Mean BMI</td>
<td>23.24±2.46</td>
<td>-</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gender</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>25</td>
<td>40.3</td>
</tr>
<tr>
<td>Female</td>
<td>37</td>
<td>59.7</td>
</tr>
</tbody>
</table>

![Figure 1](image1.png)  
**Figure No.1:** Incidence of benign and malignant parotid gland tumors

![Figure 2](image2.png)  
**Figure No.2:** Incidence of benign and malignant parotid gland tumors by gender

### Table 2: Histopathological classification of benign lesions according to gender

<table>
<thead>
<tr>
<th>Benign lesion</th>
<th>No.</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pleomorphic adenoma</td>
<td>36 (81.82%)</td>
<td>13</td>
<td>23</td>
</tr>
<tr>
<td>Warthin’s tumor</td>
<td>4 (9.09%)</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Basal cell adenoma</td>
<td>2 (4.55%)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Lymphangiom</td>
<td>2 (4.55%)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>44 (100%)</td>
<td>16(36.4%)</td>
<td>28 (63.6%)</td>
</tr>
</tbody>
</table>

Likelihood ratio = 0.55  
*p-value = 0.909*
Table No.3: Histopathological classification of malignant lesions according to gender

<table>
<thead>
<tr>
<th>Malignant lesion</th>
<th>No.</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucoepidermoid carcinoma</td>
<td>11</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Adenoid cystic carcinoma</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Acinic cell carcinoma</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Carcinoma expleomorphic adenoma</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Malignant lymphoma</td>
<td>5</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
<td>9</td>
<td>9</td>
</tr>
</tbody>
</table>

Likelihood ratio = 5.98 p-value = 0.201

DISCUSSION

Salivary gland tumors are typically unprecedented; their associated clinical presentation, however, differ in anatomy and somewhat capricious prognostic characteristics tend to be taken into consideration. Human and ethnic influences, as described in the prose, have an incredible influence on the spread of these neoplasms.

Five years of research between January 2011 and December 2015 for Mallepogu's Anil Kumar et al. The study was performed on 55 patients with salivary gland lesions from the Division of Patients in the ENT and Surgery Division, SVS Medical College, Mahabubnagar and Telangana Hospital. The findings of this study were published. Specimens of the salivary gland is directly fixed into 10% formalin and handled with paraffin incorporation. Hematoxylline and eosin stain is stained in sections. In end, a descriptive microscopy was done.

The most frequent location of a pleomorphic adenoma in the parotid glands was submandibular gland (18.18%) followed by submandibular gland and Bashir et al., close to studies performed on Amin et al. In the middle age group (21-50 years) there is peach occurrence of male preponderance (M:F ratio, 1.31:1) such as Laishram et al and Amin et al. Amin et al. also reported 124 cases of salivary tumors in their overall study, 81 (65.3%) as benign and 43 (34.6%) as malignant. Parotid gland (57.2 percent) appeared in most tumors. The most common tumor was pleomorphic adenoma (59.6%), followed by non-specified adenocarcinoma (8.8%). The tumors appeared more commonly in women (54.8%) than men (45.2%). In 31.4 percent of cases (p < 0.05), malignant tumors have been associated with discomfort. 35 papers from various countries became part of the literature analysis. Females with an average age of 41.7 years were most affected. Pleomorphic adenoma was the most prevalent benign tumor (48.2%) with Reinheimer et al. being the common malignant tumor (8.7%).

In the second-to-third decade of life, benign SGLs were more prominent and malignant tumors in the fourth-sixth decade of life more prominent. The ratio of men to women was 1.72:1. Benign tumors were more common in parotid gland 26(81.25%), non-neoplastic lesions 20(54.05%) and malignant tumors 11(29.72%) both were more common in minor salivary glands. Pleomorphic adenoma 27(34.17%) was most common SLG tumor amongst all. Malignant SLG tumors mucoepidermoid carcinoma and adenoid cystic carcinoma had equal incidence 5(6.33%). Immunohistochemistry markers were applied in 8(10%) cases.

CONCLUSION

Parotid gland tumors are relatively less common and they exhibit a wide variety of microscopic appearances even within one particular lesion. The malignancy Accurate diagnosis is essential as parotid gland neoplasms have diverse clinical and prognostic outcomes.

Author's Contribution:
Concept & Design of Study: Sadia Yaseen
Drafting: Ayesha Khalid, Rizwan Saghir Chatha
Data Analysis: Burhan-ul-Haq
Revisiting Critically: Sadia Yaseen, Ayesha Khalid
Final Approval of version: Sadia Yaseen

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

REFERENCES

INTRODUCTION

General anesthesia may expose patients to aspiration of gastroesophageal contents because of disappearance of pharyngeal reflexes and can result in morbidity and mortality attributable to aspiration pneumonitis. In addition, in spite of full abstinence and fasting prior to surgery, patient pain, delayed gastric emptying (DGE) and other factors often increase the risk of vomiting and aspiration. In this study used techniques, for preventing vomiting and aspiration during general anesthesia can be discussed as follows: cricoid pressure, the use of postural changes, pre-oxygenation without inflation of lung, and the placement of gastric tube preoperatively.

These techniques give us a relatively clear indication that the most effective way to reduce the occurrence of vomiting and aspiration is closely related to lowering gastric pressure during general anesthesia. During the apnoea phase between tracheal intubation and pre-oxygenation, it is resulted that some patients can become hypoxic. In this process RSII hypoxia can be as high as 35.9% (SpO 2 <95%). In this stage hypoxia is especially prevalent in those separately with lower apnoea tolerance which may include infants, obese patients, and pregnant women. The patient whose weight is over using oxygen desaturation during RSII was observed earlier to receive succinylcholine versus rocuronium. In this inspection, it was described by excessive metabolism secondary to succinylcholine fasciculations.

MATERIALS AND METHODS

This cross-sectional study was carried out in collaboration with Rashid Latif Hospital, Lahore and Lahore General Hospital Lahore from 1st October 2019 to 31st March 2020 and comprised 80 patients. The age including 25-60 years and BMI lower than 30kg/m² were included. We arranged to divide patients into two groups with equal numbers. In the patients, there was no any deformity or chronic lung disease. Ventilation was performed using the standard mask ventilation with

Objective: To determine the efficacy of ventilation using face mask induction of general anesthesia.

Study Design: Cross-sectional study.

Place and Duration of Study: This study was conducted at the in collaboration with Rashid Latif Hospital, Lahore and Lahore General Hospital Lahore from October 2019 to March 2020.

Materials and Methods: Eighty patients were enrolled. Average age of patients was 25 to 60 years, with a BMI lower than 30. Subsequently, the patients were arranged to divide into two groups Group A and Group B. In the group A, ventilation was performed using the standard mask ventilation with 100% oxygen for 4 minutes. And in other group B, ventilation was undertaken through an anatomical nasal mask. The mean expiratory volume, mean SpO2, mean end tidal CO2 (Et CO2) and mean airway pressure were measured, recorded and compared in both groups. Once placed on the operating table, 100% oxygen were provided to the patients using a face mask for 4 minutes, after which medication (anesthesia) were arranged.

Results: The ventilation parameters, maximum airway pressure after starting of mask ventilation in the face mask group is higher than the nasal mask group (15.1±1.8 and 11.8±1.4 during the 3rd minute respectively, p< 0.001) and the face mask group (94.5±2.1 and 96.1±4) is lower than the SpO2 at this time respectively (p< 0.001). There is no any significant difference related to other parameters.

Conclusion: The ventilation with a face mask is less effective than the nasal mask which is more efficient with a BMI less than 30 and is observed by a minimum amount of complications and risk.

Key Words: Mask, Ventilation, Induction, Anesthesia.

100% oxygen for 4 minutes in group A. While in the group B, ventilation was undertaken through an anatomical nasal mask. The mean SpO2, the mean expiratory volume, mean airway pressure and mean end tidal CO2 (Et CO2) were measured, documented and compared in both groups. Using the face mask detained near to the face for 4 minutes, 100% oxygen were provided and anesthesia induction medication were arranged for all patients once placed in the operating table. Patients were pre-oxygenated for 3 minutes on the surgical table during the day of surgery, mask detained closed to the face using 100% oxygen. Subsequently, anesthesia induction medication together, a bolus injection IV injection of sodium thiopental 5 mg/kg, fentanyl 2 mc/kg, midazolam 0.03 mg/kg were provided to all the patients. We arranged to divide patients into two groups, and used computer software to randomize them. In the group A, 100% oxygen were provided for 3 minutes and ventilation was undertaken using the standard anatomical face mask and in the group B, ventilation was performed using the examiner new method with a nasal mask. We used anesthesia machine with 8 cc/kg tidal volume and a rate of twelve breaths/minutes for ventilation of patients. The mean expiratory volume, mean SpO2, mean end tidal CO2 (Et CO2) and mean airway pressure in 3 successive breaths in the 3rd minute were observed after ventilation, recorded and differentiate in these groups. We used to secure the tube and arranged to connect patients with anesthesia machine; all the above mentioned parameters were observed in the 5th minute after endotracheal intubation. Hemodynamic changes occurred which includes heartbeat, diastolic and systolic blood pressure were also differentiate between these two types of groups. In distinct, the mean expiratory volume at this time was peculiarly differentiated to the mean volume of expiratory before intubation as the standard parameter. After this we extracted the data, categorized and added into the computer software. Statistical analysis was performed using SPSS version 22 software. This provided result, using T-test and analysis of variance by repeated differentiation, it was significantly considered p<0.05.

RESULTS

The mean age of 40.78±10.86 comprising of 21 males and 19 females were added in the face mask group and 40 patients including mean age of 38.42±12.32 years comprising of 22 males and 18 females in the nasal mask group (Table 1). There is no any demonstrate or significantly difference (p>0.05) between the participants including height, weight and BMI. The comparison between face mask and nasal mask groups. It is apparent, after ventilation during the 3rd minute the mean maximum airway pressure is significantly higher (p<0.001) in the face mask group (15.1±1.8) than the nasal mask group (11.8±1.4 respectively, p< 0.001) The level of SpO2 is higher in the nasal mask group (94.5±2.1 and 96.1±4, respectively in the 3rd minute p< 0.001) [Table 2].

Table No.1: Attributes of members in groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Face Mask</th>
<th>Nasal Mask</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) male/female</td>
<td>40.78±10.86</td>
<td>38.42±12.32</td>
<td>0.45</td>
</tr>
<tr>
<td></td>
<td>(21/19)</td>
<td>(22/18)</td>
<td></td>
</tr>
<tr>
<td>Body mass index kg/m²</td>
<td>33.24±6.89</td>
<td>32.01±5.34</td>
<td>0.30</td>
</tr>
<tr>
<td>Weights (kgs)</td>
<td>93.2±12.98</td>
<td>89.4±13.7</td>
<td>0.320</td>
</tr>
</tbody>
</table>

Table No. 2: Differentiation of variables related to feature of ventilation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Face Mask</th>
<th>Nasal Mask</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum airway pressure at 3 minutes</td>
<td>15.1±1.8</td>
<td>11.8±1.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SpO2 level at 3 minutes</td>
<td>94.5±2.1</td>
<td>96.1±4.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean end tidal CO2 at 3 minutes</td>
<td>632±80.52</td>
<td>620±76.52</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

DISCUSSION

Many methods are applied in clinical practice to assess gastric volume, including epigastric auscultation, magnetic resonance imaging and ultrasound. Several studies have previously shown that the incidence of gastric insufflations increased with inspiratory pressure during the induction of general anesthesia, with a threshold of 20 cmH2O in adults and 15 cmH2O in children by epigastric auscultation. These values are significantly higher than those of this study, which used ultrasonography. Research shows that when auscultation is used, a large amount of diagnostic gas with a mask ventilation pressure of 20 cmH2O enters the gastric cavity. This difference may be in part attributed to the fact that auscultation is far less sensitive than real-time ultrasound. Auscultation is easily disturbed by personal subjective factors, which can only be caught when the stomach intake accumulates quantitatively. In addition, one study described MRI examination of the stomach that was performed with a slice thickness of 6 mm without a gap, using an 8-channel and 8-element phased array coil that covered the entire stomach area.

This detection can fully display the rhythmic movement of the stomach and quantitatively calculate the stomach volume, and is thus more accurate than ultrasonography. However, Magnetic Resonance Imaging is suitable for comprehensive preoperative evaluation of gastric function and fasting conditions. It is not possible to quickly monitor gastric intake during induction of general anesthesia. In this experiment, ultrasound as a noninvasive instrument can judge the stomach inlet quickly and efficiently. This study shows that CSA of all patients increased a certain extent more after ventilation than it did before ventilation. Hence,
ultrasound as a portable tool can judge the volume of the stomach quickly and efficiently. With the use of ultrasound in clinical anesthesia, real-time ultrasound is adopted to accurately and reliably predict CSA. Studies have shown that CSA ≥340 mm² is a risk threshold for diagnosis of pulmonary aspiration. A tidal volume of 6 ml/kg is the minimum threshold for mechanical ventilation. Therefore, this study used a CSA < 340 mm² and tidal volume ≥6 ml/kg to assess the appropriate mask ventilation pressure. In this study, the first patient received 15 cmH2O initial pressure and two patients who underwent anesthesia with the same pressure turned out to have the appropriate pressure. However, the modified up-and-down method was used to conclude that the lower airway pressure was also suitable for lung ventilation. In the previous studies, the mask ventilation pressure was artificially divided into equal groups, and the conclusions obtained may be biased. This improved method can improve the accuracy of the final estimator and reduce the mean squared error under normal tolerance distribution. It has also been proven to be much better than the random grouping method. The initial pressure is a valid measurement and the next test results prove that CSA is within the normal range. The modified up-and-down method was used to determine that the ED50 and ED95 of pressure for facemask ventilation were 12.31 cmH2O and 13.12 cmH2O, respectively. It is worth noting that the area of the gastric antrum was significantly rising after facemask ventilation, which proved that the facemask ventilation does increase the risk of aspiration pneumonia. To prevent the patients’ increased airway resistance caused by the tongue after entrance of mask ventilation gas into the gastric cavity, this study’s mask ventilation was placed before the oropharyngeal airway by anesthesia doctors with more than 5 years of working experience. In this study, there were many limitations in our experiment. First, this research was conducted in a non-blind manner and the anesthesiologist knew about the group assignments, which may cause observer bias. Second, studies have shown that the correlation between CSA and gastric contents is stronger in the right lateral position. However, because the right lateral position of the patient is not convenient for clinical operation after general anesthesia, the CSA is measured in the horizontal position. Third, excessive obesity and pregnancy status affected CSA measurement and this study excluded patients with a BMI of more than 30 kg/m2, which reduced the difficulty of traditional operation.

CONCLUSION

The ventilation with a face mask is less effective than the nasal mask which is more efficient with a BMI less than 30 and is observed by a minimum amount of complications and risk.

Author’s Contribution:
Concept & Design of Study: Umer Iqbal
Drafting: Aqeel Moazzam, Ahsan Khan
Data Analysis: Sohail Nazir, Zahid Hanif, Muhammad Saqib
Revisiting Critically: Umer Iqbal, Aqeel Moazzam
Final Approval of version: Umer Iqbal

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

REFERENCES


Hyperglycemia in Acute Subarachnoid Hemorrhage
Muhammad Moosa¹, Farhan Fateh Jang², Amna Malik¹ and Rizwan Jamil³

ABSTRACT

Objective: To determine the frequency of hyperglycemia in patients presented with subarachnoid hemorrhage.

Study Design: Cross-sectional/observational study

Place and Duration of Study: This study was conducted at the Department of Neurology, Sharif Medical City Hospital, Lahore from 1st August 2017 to 31st March 2020.

Materials and Methods: One hundred and five patients of both genders with ages 20 to 75 years presented with subarachnoid hemorrhage were enrolled. Patient’s detailed demographics including age, sex, body mass index and Hunt Hess grade were recorded after taking informed consent. Serum glucose level was examined. Hyperglycemia was defined as serum glucose level >140mg/dl.

Results: Seventy-six (72.38%) were males while 29 (27.62%) were females. Thirty-two (30.48%) patients were ages ≤40 years, 56 (53.33%) were ages 41 to 60 years and 17 (16.19%) were ages above 60 years. Hyperglycemia was found in 67 (63.81%) patients while 38 (36.19%) patients were non-hyperglycemic.

Conclusion: The frequency of hyperglycemia in patients with subarachnoid hemorrhage was too high.

Key Words: Hyperglycemia, Acute subarachnoid hemorrhage, Frequency.

Citation of article: Moosa M, Jang FF, Malik A, Jamil R. Hyperglycemia in Acute Subarachnoid Hemorrhage. Med Forum 2020;31(9):84-86.

INTRODUCTION

A critical acute health emergency with an incidence of 9 per 100,000 person-years is subarachnoid hemorrhage. The cerebral aneurysm rupture accounts for 85% of cases of subarachnoid hemorrhage. Further circulation fatality of aneurysm is 10-15 percent higher in comparison to the previous circulation aneurysm (10-15% in all aneurysm).¹ Since the path to poor clinical outcome seems to involve hyperglycemia, insight into these mechanisms can reveals new treatment options. In order to give an overview of the potential cause and consequences of hyperglycemia in acute subarachnoid hemorrhage patients, and discuss pathophysiological mechanisms to link hyperglycemia to poor clinical result, we have undertaken a non-systematic literature search.²

Hyperglycemia is common in non-diabetic patients and associated with higher morbidity and mortality in both critically ill patients and surgical patients.³

Clinical traits of subarachnoid hemorrhage are severe and common, thunderclap, headache, pathologic disease, neck stiffness, loss of consciousness and decerebrate. Intensive therapy of insulin for medical and surgical intensive care units (ICU) has shown that sepsis incidence decreases, acute renal failure, blood transfusions, critical illness polyneuropathy, ICU stay long and mortality are reduced.⁴⁻⁶ The present study was conducted aimed to examine the frequency of hyperglycemia in patients with subarachnoid hemorrhage.

MATERIALS AND METHODS

This cross-sectional/observational study was conducted at Sharif Medical City Hospital, Lahore from 1st August 2017 to 31st March 2020. A total of 105 patients of both genders with ages 20 to 75 years presented with subarachnoid hemorrhage were enrolled. Patients detailed demographics including age, sex, body mass index (BMI) and Hunt Hess grade of subarachnoid hemorrhage were recorded after taking informed written consent. Patients with history of diabetes mellitus, patients with surgical intervention of stroke, patients who had lobar (frontal/parietal/temporal/occipital regions of brain) or central (brainstem/basal ganglia/thalamus) bleed on CT brain were excluded. The diagnostic criteria for SAH are defined on the basis of the CT scan brain, where one is in the CT brain: hyperdensity (blood) in the interhemispheric crack, sylvian fissure, or ventricular / parenchymal-extensed perimesencephalic cistern. Serum glucose level was examined by glucometer at admission. Hyperglycemia was defined as serum glucose level >140mg/dl.
glucose level >140mg/dl. All the data was analyzed by SPSS 24. Chi-square test was applied to examine the stratification hyperglycemia between male and female. P-value <0.05 was taken as significant.

RESULTS

There were 76 (72.38%) males while 29 (27.62%) were females. Thirty-two (30.48%) patients were ages ≤40 years, 56 (53.33%) were ages 41 to 60 years and 17 (16.19%) were ages above 60 years. Mean BMI was 24.51±2.38 kg/m². 26 (24.76%) patients were Hunt Hess grade 1-2, 33 (31.43%) had grade 3, 35 (33.33%) had grade 4 and 11 (10.48%) had grade 5 (Table 1). According to the random glucose level, hyperglycemia was found in 67 (63.81%) patients while 38 (36.19%) patients were non-hyperglycemic (Fig. 1). When we stratified, we found that frequency of hyperglycemia was high in females 22/29 (75.86%) as compared to males 45/76 (59.21%). A significant association was found between hyperglycemia and female gender with p-value <0.05 (Table 2).

Table 1: Demographic information of all the patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>76</td>
<td>72.38</td>
</tr>
<tr>
<td>Female</td>
<td>29</td>
<td>27.62</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;40</td>
<td>32</td>
<td>30.48</td>
</tr>
<tr>
<td>41 – 60</td>
<td>56</td>
<td>53.33</td>
</tr>
<tr>
<td>&gt; 60</td>
<td>17</td>
<td>16.19</td>
</tr>
<tr>
<td>H-H score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1-2</td>
<td>26</td>
<td>24.76</td>
</tr>
<tr>
<td>Grade 3</td>
<td>33</td>
<td>31.43</td>
</tr>
<tr>
<td>Grade 4</td>
<td>35</td>
<td>33.33</td>
</tr>
<tr>
<td>Grade 5</td>
<td>11</td>
<td>10.48</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>24.51±2.38</td>
<td></td>
</tr>
</tbody>
</table>

DISCUSSION

Hyperglycemia is one of the most commonly found complications in patients with severe neurological disorders and associated with higher morbidity and mortality. Majority of patients in our study were male 72.38%. 32 (30.48%) patients ages were ≤40 years, 56 (53.33%) were ages 41 to 60 years and 17 (16.19%) were ages above 60 years. These results were comparable to many of previous studies in which male patients were high in numbers and accounted 60% to 75% and majority of patients were ages above 50 years 70% [9-10]. We found that 26 (24.76%) patients were Hunt Hess grade 1-2, 33 (31.43%) had grade 3, 35 (33.33%) had grade 4 and 11 (10.48%) had grade 5. A study conducted by Frontera et al reported that majority of patients of subarachnoid hemorrhage had Hunt Hess grade 3 to 5 that was similar to our study. In present study, hyperglycemia was found in 67 (63.81%) patients while 38 (36.19%) patients were non-hyperglycemic. A study conducted by Malik et al reported in their study that out of 75 subarachnoid hemorrhage patients, hyperglycemia was found in 78.67% patients while 21.33% were non-hyperglycemic. Another study by Azar et al regarding metabolic complication in patients with subarachnoid hemorrhage, in their study they reported that hyperglycemia was observed in 23% patients among 483 subarachnoid hemorrhage patients.

Hyperglycemia patients are about three times more susceptible, with no association to the various cut-off levels used for the purposes of hyperglycemia. This is a risk for poor outcomes. The relationship between high blood glucose levels and poor clinical outcome is stronger than hyperglycemia at admission. The median highest glucose burden in the study population of 7.6 mmol / L, 3.2 to 40.5 mmol / L, and the median glucose burden of more than 5.8 mmol / L was 1.8 mmol / L (range of 0.1 to 12.9 mmol / L) reported by Frontera et al. Patients with hyperglycemia have also reported poor clinical outcomes compared to those with non-hyperglycemia. Hyperglycemia intensifies the injury caused by subarachnoid hemorrhage by increasing mitochondrial dynamic imbalance, apoptosis and inflammation, and thereafter. The level of glucose at entry depends on the severity of the initial bleeding. Previous studies have showed an autonomous predictor for the incidence of delayed brain ischemia and poor outcomes in subarachnoid hemorrhage patients in the initial hyperglycemia. In management protocols of subarachnoid hemorrhage patients, the prognostic potential of the plasma glucose level was proposed to be beneficial.

CONCLUSION

The frequency of hyperglycemia was high in patients with subarachnoid hemorrhage. Examination of serum
glucose level at admission is very essential for the management of hyperglycemia and it will help to reduce the morbidity and mortality in patients with subarachnoid hemorrhage.

Author’s Contribution:
Concept & Design of Study: Muhammad Moosa
Drafting: Farhan Fateh Jang, Amna Malik
Data Analysis: Rizwan Jamil
Revisiting Critically: Muhammad Moosa, Farhan Fateh Jang
Final Approval of version: Muhammad Moosa

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

REFERENCES
Determination of Stature from Correlation between Height and Hand Length and Hand Breadth in General Male Population of Khyber Pakhtunkhwa Pakistan

Sadia Syed, Sabika Hussain, Rubina Salma Yasmin, Younas Khan, Mehwish Zaib and Rizwan-ul-Haq

ABSTRACT

Objective: To determine stature of a person from the correlation between his height and length and breadth measurements of his hands.

Study Design: Cross sectional study.

Place and Duration of Study: This study was conducted at the Department of Forensic & Medicine, Peshawar Medical College Peshawar from March 2019 to June 2019.

Materials and Methods: The study was carried out among general population of KPK including 82 male participants aged between 21 to 60 years. The height was measured with a stature meter. Length of hands was measured using a measuring tape, while breadth of hands was measured by Vernier caliper.

Results: The linear regression equations were derived and the values of minimum, maximum and mean of anthropometric measurements were substituted in those equations in order to calculate the estimated stature.

Conclusion: Hand length is the most reliable parameter to estimate stature. We have derived linear regression models that could be used to determine stature of a male person, when only part of the body i.e. hand is available.

Key Words: Stature, Height, Hand length, Hand breadth.

INTRODUCTION

Stature estimation from the body parts and remnants has been one of the most widely used methods for identification of unknown corpses. Whenever the establishment of identity of an individual is concerned, the four basic criterion are age, gender, stature and race. It has always been of utmost importance for anthropologists and anatomists to determine the correlation between the whole body and the various body parts. There is a relationship between the whole body and the body parts that enabled the researchers to derive linear regression equations that help in determining stature when the dimensions of hands are known.

Department of Forensic Medicine and Toxicology, Peshawar Medical College, Peshawar.

Correspondence: Dr. Sadia Syed, Postgraduate Trainee, Department of Forensic Medicine & Toxicology, Peshawar Medical College, Peshawar.

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Accepted: July, 2020
Printed: September, 2020
were excluded. Height was measured with the help of stature meter. Anthropometric length measurements were recorded in millimeters with the help of a measuring tape and a vernier caliper to measure breadth of hands. Measurements were taken according to the anthropometric techniques described by Valois. The data was entered and analyzed through SPSS-20.

RESULTS

It has been observed that the values for hand length were greater than those for Hand breadth (Table 1). Table 2 depicts the correlation coefficients between stature and anthropometric measurements of hands. Correlation coefficients for length measurements were higher than those for breadth measurements. In males, the highest correlation was observed to be exhibited by right hand length ($r=0.6$) and the lowest by hand breadth ($r =0.31$). The standard error of estimate (SEE) explains the degree or amount of diversion of estimated stature from the actual stature of a person. In the current study, it ranges from ±0.7 to ±1.54 in male population. The reliability in the estimated stature is considered maximum when SEE is lesser in value. The hand length has been observed to have lesser values of SEE on right and left sides and hence it could serve as a reliable index to predict stature (Table 3).

### Table No.1: Descriptive statistics for stature and measurements (mm) of length and breadth of hands

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stature</td>
<td>1726.5±164.9</td>
</tr>
<tr>
<td>Right Hand Length</td>
<td>182.9±8.2</td>
</tr>
<tr>
<td>Left Hand Length</td>
<td>182.9±7.9</td>
</tr>
<tr>
<td>Right Hand Breadth</td>
<td>85.7±4.5</td>
</tr>
<tr>
<td>Left Hand Breadth</td>
<td>84.8±4.8</td>
</tr>
</tbody>
</table>

### Table No.2: Correlation between stature and anthropometric measurements of hand

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value of r</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right hand length</td>
<td>0.6</td>
<td>0.000</td>
</tr>
<tr>
<td>Left hand length</td>
<td>0.58</td>
<td>0.000</td>
</tr>
<tr>
<td>Right hand breadth</td>
<td>0.31</td>
<td>0.0042</td>
</tr>
<tr>
<td>Left hand breadth</td>
<td>0.31</td>
<td>0.0042</td>
</tr>
</tbody>
</table>

### Table No.3: Linear regression equations for estimation of stature (mm) from measurements of hand length and breadth

<table>
<thead>
<tr>
<th>Regression equation</th>
<th>± SEE</th>
</tr>
</thead>
<tbody>
<tr>
<td>S=847.4+4.4(RHL)</td>
<td>±0.7</td>
</tr>
<tr>
<td>S=866.7+4.7(LHL)</td>
<td>±0.74</td>
</tr>
<tr>
<td>S=1338.2+4.5(RHB)</td>
<td>±1.54</td>
</tr>
<tr>
<td>S=1373.8+4.15(LHB)</td>
<td>±1.43</td>
</tr>
</tbody>
</table>

Table 4 shows the comparison of actual and estimated stature from length and breadth measurements of hands. The linear regression equations were derived and the values of minimum, maximum and mean of anthropometric measurements were substituted in those equations in order to calculate the estimated stature. It was found that the mean values of estimated stature were much closer to the actual stature since regression equations have been derived from measures of central tendency. However, the minimum and maximum values of estimated stature showed variations with that of actual stature. In the current study, minimum and maximum values of stature estimated from hand length were found to be much closer to the minimum and maximum values of the actual stature.

### Table No.4: Comparison of actual stature and stature estimated (mm) from measurements of hand dimensions

<table>
<thead>
<tr>
<th>Estimated stature using regression equations for</th>
<th>Minimum estimated stature</th>
<th>Maximum estimated stature</th>
<th>Mean estimated stature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right hand length</td>
<td>1633.6</td>
<td>1821.8</td>
<td>1725.32</td>
</tr>
<tr>
<td>Left hand length</td>
<td>1614</td>
<td>1830.2</td>
<td>1726.3</td>
</tr>
<tr>
<td>Right hand breadth</td>
<td>1681.1</td>
<td>1797.5</td>
<td>1726.4</td>
</tr>
<tr>
<td>Left hand breadth</td>
<td>1680.4</td>
<td>1793.8</td>
<td>1725.7</td>
</tr>
<tr>
<td>Actual Stature</td>
<td>1584</td>
<td>1859</td>
<td>1726.5</td>
</tr>
</tbody>
</table>

DISCUSSION

Studies have shown that fusion of ossification centres in wrist and elbow joints by the age of 18 years and complete union in distal end of radius occurs in 20 years. This supports the age range we have selected for our study population. Since stature and anthropometric measurements show variations between both genders and among different populations, there is always a need to derive gender specific regression equations in order to estimate stature from isolated body parts in males and females seperately. In the current study statistically significant bilateral differences were observed in measurements in males except bilateral hand length measurements ($p=0.8$). The derived multiplication factors showed minimal differences bilaterally. Thus, in case only a hand of an individual is available for identification and the anatomical side cannot be justified, any multiplication factor either for right or left sides can be utilized to estimate stature.

In our study, the correlation coefficients for length measurements were greater than those for breadth measurements. The highest correlation between stature and anthropometric measurements in males was exhibited by right hand length. A study among Iranian adults as well as in Australian population also showed that strong correlation exists between hand length and
stature (r=0.78)\textsuperscript{20,21} In our study, the lowest correlation with stature was exhibited by hand breadth in male population.\textsuperscript{22}

The least standard error of estimate (SEE) in our study was observed for hand length so hand length can serve as a reliable index to estimate stature efficiently.\textsuperscript{23} Mean values of estimated stature were very closer to those of actual stature. Yet we compared our results with populations having similarity in terms of race and culture with our population like Iran and Kashmir and found much similar results as ours. In a study conducted in Iranian population, strong correlation was found between the stature and hand length similar to current study.\textsuperscript{24} Similar findings were reported by Khan et al in a study in Kashmir, that showed right hand length to be the most highly correlated parameter to estimate stature of a person.\textsuperscript{25}

CONCLUSION

We have determined linear regression models that could be used to determine stature of a person from his hand length or hand breadth, when only part of the body i-e hand is available. Among all the variables, hand length is the most reliable parameter to estimate stature in males.

Author’s Contribution:

Concept & Design of Study: Sadia Syed
Drafting: Sabika Hussain, Rubina Salma Yasmin
Data Analysis: Younas Khan, Mehwish Zaib, Rizwan-ul-Haq
Revisiting Critically: Sadia Syed, Sabika Hussain
Final Approval of version: Sadia Syed

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

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1. Kornieieva M, Elelemi AH. Estimation of Stature from Hand Measurements and Handprints in a Sample of Saudi Population= تجربة لرونده
LA mawa3a Luma3a 5ayyadat لـ معينة من المجتمع السعودي من خلال قياسات يد
Demographic and Haematological Features of Aplastic Anemia in Adult Population: A Single Centre Experience
Humera Rafiq¹, Arsala Rashid², Filza Saeed² and Samina Naeem²

ABSTRACT

Objective: To determine the frequency of different demographic and haematological features of patients diagnosed to have aplastic anemia,
Study Design: Purposive, case-series study.
Place and Duration of Study: This study was conducted at the Department of Pathology, King Edward Medical University Lahore from January 2007 to December 2014.
Materials and Methods: One hundred and forty-six consecutive aplastic anemia cases were included. The sociodemographic details, medical history, environmental, clinical and haematological features were included.
Results: The median age of patients was 28 years, 75 were female and 71 male. The disease was graded according to severity and results were as follows: 1) non-severe 50%, 2) severe 34% and 3) very severe aplastic anemia 16%. Majority of patients were from low socioeconomic 57.5% or middle class 32%.
Conclusion: Aplastic anemia shows almost equal sex distribution. Non-severe aplastic anemia is the most common type of aplastic anemia presenting in a diagnostic set up of a tertiary care hospital.

Key Words: Aplastic anemia, Pancytopenia, Features, Population.

INTRODUCTION

The definition of aplastic anemia; peripheral pancytopenia with a hypocellular bone marrow and absence of an abnormal infiltrate and little or no increase in reticulin.¹ Diagnosis of aplastic anemia (AA) requires standard criteria.² This criteria requires to have at least two out of three of the following: Haemoglobin concentration (Hb) <100 g/l, neutrophil count <1.5×10⁹/l and platelet count <50×10⁹/l. The precise cause of AA is not known. In adults, the environmental factors include radiations, drugs, viruses, toxins, and chemicals. This disease may follow conditions like pregnancy, different viral hepatitis and immunological disorders. Despite all this the majority i.e. 70-80% of cases are idiopathic.³ The remainder mainly consist of failure syndrome of bone marrow. Its incidence is 2-3 per million per year in Europe, but higher in East Asia.⁴

¹ Department of Pathology, PGMI/AMC/General Hospital Lahore.
² Department of Pathology, King Edward Medical University Lahore.

It generally shows a bimodal distribution, with peaks at 10-25years and over 60years. The modified Camitta criteria is used to assess disease severity⁵ Patients commonly present with anaemia, infections and thrombocytopenia, if left untreated, most of the patients die due to infections and bleeding. There is not much data from Pakistan showing incidence of the disease. Our purpose was to get an insight into demography and other features of Pakistani aplastic population.

MATERIALS AND METHODS

This purposive, case-series study was conducted at Department of Pathology, King Edward Medical University Lahore from 1st January 2007 to 31st December 2014. One hundred and forty-six adults male and female with aplastic anemia were included. Adult patients of 14years and above were included. Patients of aplastic anemia less than 14 yrs of age were excluded. The data was entered and analyzed through SPSS-20.

RESULTS

There were 71 (49%) males and 75 (51%) were females. Majority of the patient n=88 fell in the age group of 15-25years, followed by n=19 in age group of 26-35years, the n= 18 patients in 45-55 years age group and followed by age group 35-45 (n=13) and more than 55years(n=8) respectively. Mean age of patients was 28 years. Presenting complain was fever and pallor in majority of cases, bleeding manifestations were
relatively few (Table 1). Generally aplastic anemia patients have no organomegaly and this was true in our result as well but a few patients showed features of splenomegaly (Table 2). The modified Camitta criteria was used to assess disease severity. Majority of the patients belong to non-severe aplastic anemia (Table 3).

**DISCUSSION**

Aplastic anemia is a rare disease in west. Its incidence varies considerably worldwide. The incidence reported by Montané et al in Spain is 2.34/million which is similar to studies in Europe and Israel. Other international studies in France, the United Kingdom, Scandinavia and Brazil show about similar results. The incidence of aplastic anemia is higher in Asia than in the West. A large study from Thailand, found a rate of 3.9/million and 5/million in the northeast region of Khonkaen. In a Chinese Epidemiologic Study Group an incidence of 7.4/million was reported. Asian studies of similar incidence figures of about 5/million in Sabah in Malaysia. Uptil now there is not enough data that incidence of aplastic anaemia in Pakistan be determined. A Few studies showing frequency and demographic features are available. In our study the peak age was around 28years other studies done in Pakistan also show a peak age around 30. peak age of presentation of AA in India is still younger that is 20 which resembles our study.

However, a bimodal peak is seen in studies in Spain and other European countries. Male to female ratio was 1:1 in this study however other studies in Pakistan show male to female ratio 2.1:1,2.8:1 and 3:1, may be the limited number of patients in the study led to such different results, a longer study may show other results; some international studies collaborate with us.

Presenting features were pallor and fever but bleeding manifestations were in few patients. It seems that with mere pallor or weakness patient generally does not communicate for medical attention it is only when fever supervenes due to low white cell count that they come to hospital set up. Our findings are similar with Ahmed et al and Vincent and Gruchy published literature. Organomegaly is not a feature of aplastic anemia but we had 3 patients with splenomegaly. Case reports in literature have also shown similar features plus tropical spleen is also an explanation in our setup.

This study shows majority of pts belonged to non-severe aplastic anemia followed by severe aplastic anemia and least no of cases in very severe aplastic anemia. Other studies in India and Pakistan have one thing in common with us that they contained least number of patients in very severe aplastic anemia. Other studies in India and Pakistan have one thing in common with us that they contained least number of patients in very severe aplastic anemia group which matches our study. However, study of Ahmed et al is close to a study in Spain which have a significant number of patients belonging to very severe aplastic anemia group.

**CONCLUSION**

Aplastic anemia shows equal sex distribution and presents in younger age. Aplastic anemia registry set in Pakistan and its incidence recorded. Future directions refer to genetic studies due its presentation at early age.

**REFERENCES**

Examining the Outcomes of Surgical Procedures in Patients with Giant Cell Tumors

Muhammad Ishaq¹, Karim Bakhsh² and Attiq-ur-Rehman²

ABSTRACT

Objective: To examine the outcomes of different surgical procedures in patients with giant cell tumor also determine the frequency of involved bone required surgical treatment.

Study Design: Retrospective study.

Place and Duration of Study: This study was conducted at the Department of Orthopedic & Traumatology, Qazi Hussain Ahmad Medical Complex Nowshera from January 2018 to March 2020.

Materials and Methods: Sixteen patients of both genders presented with biopsy proven giant cell tumor were analyzed in this study. Patients detailed demographic including age, sex and residence were recorded after written consent. Types of bones and different surgical procedures for the treatment were examined. Outcomes of surgical treatment were examined by Musculo Skeletal Tumor Society score (MSTS). Follow-up was taken at 1 year after surgery.

Results: Ten (62.5%) patients were males and 6 (37.5%) were females. 3 (18.75%) patients were ages less than 20 years, 11 (68.75%) patients were ages 20 to 40 years and 2 (12.5%) patients had ages above 40 years. Pain and swelling was commonly found symptom in 8 (50%) patients. Distal femur was the commonest site in 5 (31.25%) patients followed by proximal tibia in 4 (25%) patients. Curettage and bone cementation was the commonly performed surgical procedure in 5 (31.25%), followed by wide excision of bone and cementation and implant in 4 (25%) patients, 3 (18.75%) patients received curettage and bone grafting, 2 (12.5%) had received disarticulation, 1 (6.25%) patient were received arthroplasty and amputation was done in 1 (6.25%) patient. Recurrence was found in 1 patient with curettage and bone grafting and 2 with curettage and bone cementation. The mean MSTS score was 26.2 out of 30.

Conclusion: Giant cell tumor is commonly found in patients with 3rd and 4th decade of life. Distal femur and proximal tibia were the most common site of bones involved and curettage and cementation was the commonly performed surgical procedure. Patients with giant cell tumor were on high risk of recurrence after surgical treatment.

Key Words: Giant cell tumor, Site of bones, Surgical techniques, Outcomes.

Citation of article: Ishaq M, Bakhsh K, Rehman A. Examine the Outcomes of Surgical Procedures in Patients with Giant Cell Tumors. Med Forum 2020;31(9):94-97.

INTRODUCTION

Cooper in 1818 first described Giant cell tumors (GCT) of the bone. Later Nelaton showed their local aggressiveness, and Virchow revealed their malignant potential.¹ The term “giant cell tumor” implies that the multinucleated giant cells are responsible for the proliferative capacity of this tumor, there is evidence that the stromal cells, the major components of the mononuclear cell population, represent the true neoplastic components of giant cell tumor of the bone (GCTB).² It accounts for 5% of primary skeletal tumors and 21% of all benign bone tumors.³ The disease is more common in China and India, where it constitutes approximately 20% of all primary bone tumours. Most lesions develop in the long bones (75-90%), with most cases (50-65%) occurring near the knee.⁴ Approximately 1% of cases present as multiple synchronous or metachronous lesions.⁵ It primarily occurs in young adults between the ages of 20 and 40 years and paediatric cases of GCT are even less frequent and are believed to comprise only 1.7% of all cases of GCTB. Although usually benign tumors, GCTB frequently recur locally after surgical resection.⁶ Muramatsu et al.⁷ reported a recurrence rate of 34% after intra-lesional excision, 7% after marginal excision, and none after wide excision. Secondary transformation, which follows radiation therapy or less commonly surgical intervention, accounts for approximately 70% of malignant GCT. Primary malignant GCT, which arise de novo alongside typical GCT, make up the remainder of malignant...

¹ Department of Orthopaedic & Traumatology, Qazi Hussain Ahmad Medical Complex Nowshera, KPK.
² Department of Orthopaedic, Bolan Medical College Hospital, Quetta.

Correspondence: Dr. Muhammad Ishaq, Head of Department, Orthopaedic & Traumatology, Qazi Hussain Ahmad Medical Complex Nowshera, KPK.
Contact No: 0300-9524169
Email: wamiqishaq@yahoo.com

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The incidence of metastases is estimated to be from 1-6%. The metastatic lesions are histologically identical to the primary lesions, showing no tendency to differentiate. The majority of metastatic lesions are to the lung. Solitary metastasis to regional lymph nodes, the mediastinum and the pelvis have been reported, as has involvement of the scalp, bone and para-aortic nodes. The mean interval between the onset of the tumor and the detection of lung metastases is about four to five years.

Treatment often involves curettage, with or without bone filler or adjuvants such as polymethylmethacrylate (PMMA) or phenol. Early treatment methods of GCT involved simple curettage with or without a bone graft and the consequent recurrence rate was approximately 40%. In 1969, Vidal et al. introduced reconstruction with bone cement after thorough intralesional curettage.

MATERIALS AND METHODS

This retrospective case series study was conducted at Department of Orthopaedic & Traumatology, Qazi Hussain Ahmad Medical Complex Nowshera from 1st January 2018 to 31st March 2020. A total of 16 patients of both genders presented with biopsy proven giant cell tumor were analyzed in this study. Patients detailed demographic including age, sex and symptoms were recorded. Patients with recurrence, patients with lost their follow-up and those with no consent were excluded. All the patients were received biopsy and the lesions were staged according to the grading system by Campanacci et al. Grade I, II and III. Different sites of involved bones and different surgical procedures for the treatment were examined. Functional outcomes of surgical treatment were examined by Musculo-Skeletal Tumor Society score (MSTS) including pain, function, walking ability, walking aids, emotional acceptance and gait. Recurrence rate was also examined. Follow-up was taken at 1 year after surgery. All the data was analyzed by SPSS 24.0. P-value <0.05 was considered as significant.

RESULTS

Out of 16 patients, 10 (62.5%) patients were males and 6 (37.5%) were females. 3 (18.75%) patients were ages less than 20 years, 11 (68.75%) patients were ages 20 to 40 years and 2 (12.5%) patients had ages above 40 years. Pain and swelling was commonly found symptom in 8 (50%) patients followed by only pain 4 (25%), only swelling in 2 (12.5%) patients and 2 patients were with fracture. 4 (25%) patients had Grade I tumor, 9 (56.25%) patients had Grade II and 3 (18.75%) patients had Grade III tumor (Table 1). Distal femur was the commonest site in 6 (37.5%) patients followed by proximal tibia in 5 (31.25%) patients, 2 (12.5%) had proximal humerus and 3 (18.75%) patients had other bones involved (Table 2).

Curettage and bone cementation was the commonly performed surgical procedure in 5 (31.25%), followed by wide excision of bone and cementation and implant in 4 (25%) patients, 3 (18.75%) patients received curettage and bone grafting, 2 (12.5%) had received disarticulation, 1 (6.25%) patient were received arthroplasty and amputation was done in 1 (6.25%) patient (Table 3). Recurrence was found in 1 patient with curettage and bone grafting and 2 with curettage and bone cementation. The mean MSTS score was 26.2 out of 30 (Table 4).

| Table No.1: Demographical details of all the patients |
| Variable | No. | %  |
| Gender   | No. | %  |
| Male     | 10  | 62.5 |
| Female   | 6   | 37.5 |
| Age (years) | No. | %  |
| < 20     | 3   | 18.75 |
| 20-40    | 11  | 68.75 |
| > 40     | 2   | 12.5 |
| Clinical presentation | No. | %  |
| Pain and Swelling | 8   | 50 |
| Pain     | 4   | 25 |
| Swelling | 2   | 12.5 |
| Fracture | 2   | 12.5 |
| Tumor grade | No. | %  |
| Grade I  | 4   | 25 |
| Grade II | 9   | 56.25 |
| Grade III| 3   | 18.75 |

| Table No.2: Site of bones involved |
| Site            | No. | %  |
| Distal femur    | 6   | 37.5 |
| Proximal tibia  | 5   | 31.25 |
| Proximal humerus| 2   | 12.5 |
| Other           | 3   | 18.75 |

| Table No.3: Different surgical procedure performed |
| Procedure                             | No. | %  |
| Curettage and bone cementation        | 5   | 31.5 |
| Wide excision of bone, cementation and implant | 4   | 25 |
| Curettage and bone grafting           | 3   | 18.75 |
| Disarticulation                       | 2   | 12.5 |
| Arthroplasty                          | 1   | 6.25 |
| Amputation                            | 1   | 6.25 |
Giant cell tumor is one of the common life’s threatening malignant disorder with high rate of morbidity. Patients received surgical treatment reported poor quality of life, it is due to delay in visiting hospital, inaccurate diagnoses, self-medication and unawareness of the disease.\(^{12-14}\) Many of studies have been conducted regarding surgical outcomes of giant cell tumor. Present study was also conducted to determine the surgical outcomes of different surgical procedures for the treatment of giant cell tumor of bones. In present study 10 (62.5%) patients were males and 6 (37.5%) were females. 3 (18.75%) patients were ages less than 20 years, 11 (68.75%) patients were ages 20 to 40 years and 2 (12.5%) patients had ages above 40 years. These results showed similarity to some previous studies in which male patients were high in number as compared to females.\(^{15,16}\) Some of other studies reported that female patients had high incidence rate of giant cell tumors 60 to 80\% \[^{9-15}\]. Several previous studies regarding giant cell tumor demonstrated that the incidence rate of giant cell tumor was high in patients with ages 3\textsuperscript{rd} or 4\textsuperscript{th} decades of their lives.\(^{18,19}\)

In this study we found that pain and swelling was commonly found symptom in 8 (50\%) patients followed by only pain 4 (25\%), only swelling in 2 (12.5\%) patients and 2 patients were with fracture. Distal femur was the commonest site in 6 (37.5\%) patients followed by proximal tibia in 5 (31.25\%) patients, 2 (12.5\%) had proximal humerus and 3 (18.75\%) patients had other bones involved. A study conducted by Ahmad et al\(^\text{20}\) regarding outcomes of different surgical procedures in patients with giant cell tumor, in which they reported pain and swelling combine was the most common presented symptom 42.6\% followed by only pain. But in contrast to our study Ahmad et al\(^\text{20}\) also reported proximal tibia was the commonest site of bone 29.63\% followed by distal femur 18.52\%.

In the present study, we found recurrence in 3 patients in which 1 patient was treated with curettage and bone grafting and 2 patients were received curettage and bone cementation. The mean MSTS score was 26.2 out of 30. These results showed similarity to some previous studies in which recurrence rate was high in patients treated with bone grafting and cementation.’’\(^{21,22}\)

### DISCUSSION

Giant cell tumor is one of the common life’s threatening malignant disorder. Early diagnosis and better treatment modality may help to reduce the mortality and morbidity rate. It is concluded that giant cell tumor is commonly found in patients with 3\textsuperscript{rd} and 4\textsuperscript{th} decade of life. Distal femur and proximal tibia were the most common site of bones involved and curettage and cementation was the commonly performed surgical procedure. Patients with giant cell tumor were on high risk of recurrence after surgical treatment.

### CONCLUSION

Giant cell tumor is one of the common life’s threatening malignant disorder. Early diagnosis and better treatment modality may help to reduce the mortality and morbidity rate. It is concluded that giant cell tumor is commonly found in patients with 3\textsuperscript{rd} and 4\textsuperscript{th} decade of life. Distal femur and proximal tibia were the most common site of bones involved and curettage and cementation was the commonly performed surgical procedure. Patients with giant cell tumor were on high risk of recurrence after surgical treatment.

### REFERENCES

Reliable Bone Source in Forensic Investigations to Determine the Age by X-Ray Radiography of Pakistani Population

Iqra Kanwal¹, Muhammad Faheem Ashraf², Samina Kanwal², Shahid Nazir Paracha¹ and Muhammad Farhan Khan¹

ABSTRACT

Objective: To know the reliable bone source in forensic investigations to determine the age by x-ray radiography of Pakistani population.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Forensic Medicine Department, Government Khawaja Muhammad Saifdar Medical College, Sialkot and UHS, Lahore from July 2019 to June 2020.

Materials and Methods: For age assessment at hand-wrist joint 60 subjects aged between 5-19 years and posteroanterior radiographs of chest were examined to determine age at sternal end of the clavicle of 62 subjects aged between 17 to 27 years were selected for this cross-section study. Chronological and skeletal age of each participant was observed.

Results: The age range from 5-19 years with mean chronological age for male was 9.96±3.04 while mean skeletal age for male subjects was found 9.30±3.21. Mean chronological age for female subjects was 9.13±2.68 while mean skeletal age for female subjects was 8.65±3.06. Results of G&P method were found to be statistically significant for both males and females. The mean with interquartile range for stages 2-5 by gender. Stage 2 was first found in both genders at the age of 17.

Conclusion: For age assessment at hand and wrist joint Greulich & Pyle method proved to be reliable for use is Pakistani population. When compared to other populations, Pakistani population followed a delayed and narrow time frame for development of medial epiphysis of clavicle. At stage 5 of ossification minimum age estimated was 25 years for both genders.

Key Words: Bone, Forensic, X-ray, Chronological, Skeletal, Age, Gender


INTRODUCTION

Forensic age evaluation of anonymous cadavers and their skeletons for recognition purposes has remained custom in legal science. In forensic research age evaluation of living individuals experiencing criminal lawsuits has created a generally new zone that is progressively becoming imperative. In case of living individuals such age evaluations are carried out to confirm whether the accused of doubtful age has achieved culpable age for crime and if universal criminal statute of adults can be practiced. Particularly in case of non-nationals, with no valid identification records, such difficulties are faced when it comes to differentiate between juvenile and adult offenders. For criminal responsibility various age limits of confinement are given by different laws. In numerous states, the age threshold of legal applicability ranges between 14-21 years of age. On government level and in many countries this age threshold is set at 18 years. In the year 2000, “Study Group on Forensic Age Diagnostics” (AGFAD) distributed its ground rules for the assessment of the historical age of alive persons forensically, for criminal proceedings. The rules elaborated the performance of the relevant tests to decide the age of majority or minority (18-years); a) Physical examination: anthropometrical estimations including, stature, weight, physique and assessment of signs of sexual development(clinical examination is first and foremost imperative to interpret any disease, syndrome or hindrance which could impact the assessment of skeletal and dental development); b) roentgenographic left hand’s examination is the second mainstay of criminological age diagnostics with the end
goal of criminal execution; c) teeth external examination and dental x-rays, d) Radiographic clavicular examination, to affirm if the authentic age is greater or lesser than 21.\(^6\)

Keeping in mind the end goal to figure bone age different approaches have been created utilizing diverse skeletal components and different visualization methods. The ossification pattern in the hand and wrist bone is in a quite certain manner with varying epiphysis shapes that are age particular till end of puberty. In crime scene investigations globally utilized method for age determination by hand and wrist radiographs is the atlas method of Greulich and Pyle. Along with its clinical applicability this method has forensic applications as well.\(^7\)

Purpose of the present study is to determine juvenile age at left wrist and adult age at medial end of clavicle to be used as a forensic tool in differentiating juvenile and adult delinquent, to support to the criminal justice system of Pakistan and NADRA in cases of falsifying age representatives.

**MATERIALS AND METHODS**

This cross sectional study was conducted at the Forensic Medicine Department, Government Khawaja Muhammad Safdar Medical College, Sialkot and UHS, Lahore from 1\(^{\text{st}}\) July 2019 to 30\(^{\text{th}}\) June 2020. For age assessment at hand-wrist joint 60 subjects (25 female, 35 male) aged between 5-19 years were selected for this cross-section study. The local citizen of Pakistan, mentally and physically sound, who have negative history of any chronic diseases, predominant right hand with no history of injury or damage to left hand and wrist were included. The cases were selected to rule out any hormonal, nutritional and developmental abnormality. On the basis of positive history of any chronic disease, any medication intake within previous six months, like vitamin and food supplements and calcium, participants were excluded. The completed information for each child to record their historical age was recorded. Age was confirmed from history, B-Form or birth certificate and by CNIC in case of adults. The left hand-wrist region was exposed in posteroanterior (PA) position without using Bucky.\(^3\)

Examinations were performed on computerized radiography (CR) system and images were processed digitally on green sensitive, 14x14 films (Kodak), with exposure factors selected between 65-70 KVP, 3-6 MAs depending on patient anatomy. The ossification status of medial end of clavicle was defined according to 5 staging system suggested by Schmeling.\(^10\) The radiographs were interpreted for staging by radiologist. While interpreting the stage of ossification we all were known with the age and sex of each candidate.

To perform statistical analysis of data collected SPSS 21.0 software was used. Skeletal age (SA) and chronological age (CA) of each participant was observed. The mean value and standard deviation of chronological and skeletal age were calculated for each gender. Paired t-test was performed and p-value was computed to determine the significance for each gender.

**RESULTS**

In the study population of 5-19 years, mean chronological age for male subjects was 9.96±3.04. While mean skeletal age for male subjects was found 9.30±3.21. Results of G&P method were found to be statistically significant for males (P=0.015). Mean chronological age for female subjects was 9.13±2.68 while mean skeletal age for female subjects was 8.65±3.06. Results of G&P method were found to be statistically significant for females (P=0.04) (Table-1). A positive correlation (r=0.89) was found between calculated and chronological age (Fig. 2). Majority of the male participants presented complete ossification of hand &wrist bones at 19 years of age while female participants presented closure of all epiphysis at 18 years of age.

Table 2 presents the mean±standard deviation (SD) with interquartile range for stages 2-5 by gender. In the age spectrum that was selected for sample analysis (17-27 years old) for both genders, stage 1 did not appear. So no calculations were made for stage 1. Stage 2 was first found in both genders at the age of 17. Differences produced in gender comparison at Stage 4 with female participants reaching at this stage one year prior to their male counterparts. Stage 4 was first noted in female subjects at the 22 years of age and in male participants earliest observation of stage 4 was at age 23. Whereas in each gender lowest age for stage 5 was observed at 25 years of age. Sexual differences were analyzed. On analysis, there were statistically significant differences between genders calculated for the stages 2 to 5, assessed P value was 0.399.
Figure No.1: Male children’s x-ray images of CA 5, 13 and 18 years (SA 5, 13, 18 years respectively) with examination points while evaluating skeletal age: (1) Size, appearance and shape of distal radial epiphysis (2) Presence of epiphyseal fusion line of distal radius (3) Size of epiphysis of distal ulna (4) Number of carpals, their size and shape (5) First metacarpal’s proximal end epiphysis size (6) Size of distal epiphysis (head) of 2nd to 5th metacarpal (7) Appearance, size, shape and union of epiphyseal plate of phalanges. 8) Metacarpal’s proximal end cupping.

Table No.1: Presenting mean skeletal and chronological age of participants according to gender

<table>
<thead>
<tr>
<th>Gender</th>
<th>Mean±SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronological age</td>
<td>9.96±3.04</td>
<td>0.015</td>
</tr>
<tr>
<td>Skeletal age</td>
<td>9.30±3.21</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronological age</td>
<td>9.13±2.68</td>
<td>0.04</td>
</tr>
<tr>
<td>Skeletal age</td>
<td>8.65±3.06</td>
<td></td>
</tr>
</tbody>
</table>

Figure No.2: Correlation between chronological age and calculated age

Table No.2: Comparison of mean age in different gender with respect to stages 2-5

<table>
<thead>
<tr>
<th>Stage</th>
<th>Gender</th>
<th>Mean±SD</th>
<th>IQ (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Male</td>
<td>17.50±0.70</td>
<td>10.50-11.50</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>17.00±0.73</td>
<td>10.42-11.47</td>
</tr>
<tr>
<td>3</td>
<td>Male</td>
<td>20.28±1.60</td>
<td>0.94-2.18</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>19.66±1.32</td>
<td>1.02-2.25</td>
</tr>
<tr>
<td>4</td>
<td>Male</td>
<td>23.61±1.64</td>
<td>0.47-2.19</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>22.75±1.16</td>
<td>0.32-2.04</td>
</tr>
<tr>
<td>5</td>
<td>Male</td>
<td>25.88±0.78</td>
<td>0.44-1.72</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>25.25±1.28</td>
<td>0.50-1.78</td>
</tr>
</tbody>
</table>

Figure No.3: (a) Stage 2: 17 years old male, right clavicle from PA chest radiograph, showing the non-ossified epiphyseal cartilage. (b) Stage 3: 19 years old female, presenting left clavicle, PA chest radiograph, indicating the partially ossified epiphyseal cartilage. (c) Stage 4: 23 years male, right clavicle PA chest radiograph, showing complete ossification with discernible scar. (d) 25 years male, depiction of clavicle from chest radiograph, indicating that epiphyseal scar has vanished.

DISCUSSION

The study was carried out to determine the age of Pakistani population by hand wrist radiographs. To assess age, radiographs were compared with G&P Atlas, a holistic method accepted worldwide to determine age. Similar study was carried out by Patil et al regarding applicability of the GP atlas in Indian population between age group 1 to 19 years. Study showed delay in skeletal growth of 0.5 years for the group who were in range of 4-15 years for males and between the age group 4-7 years and 9-10 years for the female group. Study found that GP atlas method is not definitive method, especially in middle and late childhood, for the Indian population for both genders. In our study, results were statistically significant for females (P=0.04) and males (0.015). Result of our study is strongly supported by a research conducted by van Rijn et al on Dutch Caucasian population by X-ray imaging of hand and wrist and the observed significance was (P<0.001) for both genders. A similar study conducted by Büken et al in Turkish population revealed statically significant results for females (P<0.001), but insignificant results for males (P>0.05). A study performed by Groell et al reported a difference of about 1 year between actual age and skeletal, and according to researchers, bone age estimation by G&P is reliable to use for Central European children. Based on data of our study, radiography of hand-wrist region is a reliable indicator to determine skeletal age and G&P method proved to be statistically significant for Pakistani population.

To study correlation between sequential age and ossification status of medial extremity of clavicle several studies have been conducted, to be used as a
forensic tool in several medico-legal cases as well as in the field of anthropology. In view of forensic practice, our concern is to determine the minimum chronological age of Pakistani individuals at which ossification of the medial clavicle epiphysis completed. Recent studies defined complete ossification as 4th stage proposed by Schmeling et al. with full ossification of medial clavicular epiphysis while epiphyseal scar still discernible. In our study stage 4 was observed in females at 22 years of age while in males at 23 years of age. These results are similar to a study conducted by Flecker in which 655 individuals were analyzed aged <30 years by X-ray examination and found a complete fusion of epiphysis at age of 22 in majority of individuals. Appearance of stage 4 has been reported at younger age by a number of researchers. As in our case stage 4 was seen at 22 years in females and 23 in males but it does not reveal conformity with radiographic study conducted on German population by Schmeling et al. in which he demonstrated minimum age of epiphyseal fusion at 20 years of age, likewise Schulz et al. observed 21.2 years by CT examination of German population and Schafer and Black noted minimum age of 21 years in population of Bosnia by osteological examination. In the same way Richel and Schultze et al. reported complete fusion of medial clavicular epiphysis at 18 years of age. Comparative to these reference studies, our study revealed delayed observation of stage 4 in Pakistani population. During study we also find out results for stage 5 proposed by Schmeling et al. and defined as complete ossification but scar of epiphysis no longer visible. According to results minimum age observed for stage 5 was 26. Contrary to this, our study reported an early appearance of stage 5 at 25 years of age for both genders. So in case of an individual who is undergoing criminal prosecution if an X-ray examination reveals stage 5 it means that individual has attained age of 23 years at least 2 years before this examination or has attained 20 years of age at least 6 years before X-ray examination. Now the question related to practical use of this study in forensics arises, whether the results of this study can be applied to different socioeconomic status populations. In case of criminal prosecutions, it is not justified to underestimate the age of individual who is in charge of a serious crime. This condition demands a reference data based on bone age of Pakistani population. As per criminal acts, an adult criminal and juvenile offender is tried and punished differently depending upon their age, which essentially requires age estimation to spare innocents from culprits. So this research study provides a reference data to be used as forensic tool in criminal justice system of Pakistan, to provide fair justice system to the juveniles and adults in this society. Immigration rules are very clear regarding age determination so this study is legally applicable to immigrants along with criminal justice system.

CONCLUSION

To conclude for age determination, the reference values established on Pakistani population can be applied in forensic practice to support to the justice system.

Author’s Contribution:
Concept & Design of Study: Iqra Kanwal
Drafting: Muhammad Faheem Ashraf, Samina Kanwal
Data Analysis: Shahid Nazir Paracha, Muhammad Farhan Khan
Revisiting Critically: Iqra Kanwal, Muhammad Faheem Ashraf
Final Approval of version: Iqra Kanwal

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

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15. Flecker H. Roentgenographic observations of the times of appearance of epiphyses and their fusion with the diaphyses. J Anat 1932;67:118.
Detection and Stratification of Antibodies in Autoimmune Haemolytic Anaemia in Chronic Lymphocytic Lukemia
Arsala Rashid, Humera Rafiq, Mukarrama Rashid, Sobia Ashraf and Ambreen Hamid

ABSTRACT

Objective: Chronic lymphocytic leukemia is characterized by proliferation, accumulation and sustained increase of morphologically mature but functionally incompetent lymphocytes. Autoimmune phenomena are well-known complications of lymphoproliferative diseases. Autoimmune Haemolytic Anaemia is the most frequent autoimmune disorder associated with chronic lymphocytic leukaemia.

Study Design: Detection of frequency of autoimmune haemolytic anaemia in chronic lymphocytic leukaemia.

Place and Duration of Study: This study was conducted at the Department of Pathology and Oncology, King Edward Medical University and Institute of Nuclear Medicine & Oncology Lahore from January 2013 to December 2016.

Materials and Methods: One hundred adult patients with chronic lymphocytic leukemia were enrolled. All patients age above 18 years to 85 years either gender and newly diagnosed cases and cold cases of chronic lymphocytic leukaemia included. Patients on treatment or having being treated with chronic lymphocytic leukaemia were excluded.

Results: 82% were males and 18 patients were female. Mean age was 65.8±1.33 years with the greatest number of patients falling in the group of 71-80 years. Out of total patients 27% had Coombs positive. Most of the patients having Coombs positive were in stage 4. The maximum number of patients had haemoglobin of 8.1 to 14 g/dl and 70% patients had TLC up to 100,000 ×10^3. The antibodies detected had the following percentages in terms of stratification. The antibody was of the IgG class in 85 of patients (85%) and C3d was present in 77 of them. IgM class in 15 patients (15%). Out of 15, only 8 showed presence of C3d.

Conclusion: The treatment modalities are different in different causes of anaemia and complications due to chronic lymphocytic leukaemia. Therefore, detection and stratification of antibody is significant and related with disease progression and overall survival in number of chronic lymphocytic leukaemia patients.

Key Words: Chronic lymphocytic leukaemia, Autoimmune haemolytic anaemia, Antibodies.


INTRODUCTION

Autoimmune induced hemolytic anaemia is the product of auto antibodies to patients with red cell antigens typically present in the plasma of their individual. Anaemia is the disorder that is inadequate in the amount of red blood cells (in turn the ability to carry oxygen) to satisfy body physiologic requirements.

The haemolytic autoimmune anaemia can be either idiopathic or secondary. Lymphoproliferative and autoimmune diseases are mostly affected. The most prevalent type of leukaemia in western countries is chronic lymphocytic leukaemia (CLL), but in Asia it is greatly reduced. In the USA, Europe and Australia the median age of diagnoses is approximately 70 years old, and in approximately a quarter of the patients under 65 years old. The most common form of Western leukaemia with 4.2/100 000 per year is chronic lymphocytic leukaemia. At >80 years of age, this trend is rising to > 30/100 000 / year. The average age is 72 years for diagnosis. CLL patients estimated to be 10% younger than 55 years. 30 percent of Caucasians with all leukaemia display chronic lymphocytic leukaemia. The incidence of disease in Eastern Europe and the USA is high, while chronic leukaemia is rare in Asia and Africa.

The defined hematopoietic neoplasm of the World Health Organization defines the chronic lymphocytic leukaemia and the small lymphocytic lymphoma (SLL)
is only distinguished in terms of leukemia. Chronic lymphocytic leukemia is, by definition, often a neoplastic B-cell disease, while a person's lymphocytic entity does not.

Chronic lymphocytic leukemia cells coexpress CD5, the surface antigen, along with the CD19, CD20 and CD23 B cell antigens, for at least 3 months. The chronic diagnosis for lymphocytic cellular Leukemia needs 5 lymphocytes x 109/LB to be present in the peripheral blood. The expression of either K or L immunoglobulin light chains is limited to any leukaemia clone. Autoimmune phenomena are a well-known complication of lymphoproliferative diseases. Three autoimmune hematologic conditions frequently associated with chronic lymphocytic leukemia are autoimmune haemolytic anaemia, idiopathic thrombocytopenic purpura, and pure red cell aplasia.

Of these, autoimmune haemolytic anaemia is the most frequent autoimmune disorder and its pathogenesis complicating the course of chronic lymphocytic leukaemia remains a matter of considerable mystery. Establishing a relationship between autoimmune haemolytic anaemias and chronic lymphocytic leukaemia will help the clinicians in modifying the treatment and to screen all chronic lymphocytic leukaemia patients for autoimmune haemolytic anaemia to alter timely management. Patients presenting with WAIHA present a perplexing problem for the blood bank because transfusion is commonly needed but it is to be avoided when possible because it can increase the haemolysis. Transfusion is reserved for situations that are life-threatening.

MATERIALS AND METHODS

This descriptive cross sectional study was conducted at Department of Pathology and Oncology, King Edward Medical University and Institute of Nuclear Medicine & Oncology Lahore from 1st January 2013 to 31st December 2016. A total of 100 adult patients with chronic lymphocytic leukemia were enrolled. All patients age above 18 years to 85 years, both males and females and newly diagnosed cases and cold cases of chronic lymphocytic leukemia that have not taken any treatment were included. Patients on treatment or having being treated with chronic lymphocytic leukemia, received transfusion within last three months, known cases of autoimmune disorders like systemic lupus erythematosus, lupus nephritis, pemphigus vulgaris and giant cell arthritis, taking drugs known to cause haemolytic anaemia like quinidine, penicillin, and methyl dopa and steroid therapy were excluded. A thorough and methodical history and examination of all the diagnosed lymphoma patients was recorded. For every patient a fresh 3 ml blood sample was collected. A complete blood count was carried out using Automated Haematology Analyzer (Sysmex KX-21) and peripheral blood smears were prepared using Wright Giemsa stain to establish whether anaemia is present or not. Direct antiglobulin test using antihuman globulin (Coombs reagent) was done to determine the immune cause of anaemia. Bilirubin and Lactate dehydrogenase levels were measured using Beckman coulter. The antibody screening was done using 3 cell screening pannel of DIA cell and antibody typing was done using 11 cell ID pannel of DIA cell. Data was entered and analysed on SPSS version 20.

RESULTS

There were 82 (82%) males and 18 (18%) females with mean age of the patients was 65.8±1.5 years (Table 1). The mean haemoglobin of all chronic lymphocytic leukaemia patients was 9.8±2.62 g/dl and further stratification showed that most number of patients fell in the group of 11.1-14 g/dl. Among the total patients, 73.33% had Coombs test negative and 26.67% had a positive result. However, it was noted that those who had Coombs positive had a lower level of haemoglobin with a mean of 7.69±2.3 g/dl and with maximum number of patients were in range of 8.1-11 g/dl. The antibody was of the IgG class in 85 of patients (85%) and C3d was present in 77 of them, IgM class in 15 patients (15%). Out of 15 only 8 showed presence of C3d (Table 2).

Table 1: Demographic information of the patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>82</td>
<td>82.0</td>
</tr>
<tr>
<td>Female</td>
<td>18</td>
<td>18.0</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40-50</td>
<td>19</td>
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<tr>
<td>51-60</td>
<td>17</td>
<td>17.0</td>
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<tr>
<td>61-70</td>
<td>31</td>
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<tr>
<td>71-80</td>
<td>30</td>
<td>33.0</td>
</tr>
<tr>
<td>81-90</td>
<td>3</td>
<td>3.0</td>
</tr>
</tbody>
</table>

Table 2: Means of the different variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin</td>
<td>9.8 g/dl±2.62</td>
</tr>
<tr>
<td>Coombs positive</td>
<td>7.69 g/dl±2.3</td>
</tr>
</tbody>
</table>

DISCUSSION

The results of this study showed a frequency of autoimmune haemolytic anaemia in our patients of 22.66%. The mean age of the patients in our study was 65.8±1.5 years with most of patients falling in the group of 71-80 years. While in another local study by Elsan et al the mean age of cohort was 62.84 years. The maximum number of patients presented in the 7th decade (45.2%). In another study by Diehl reported the average age was 69.6 years with a peak incidence in the age bracket of 70–79 years.
The majority of the patients in our study were male i.e. 81.33% with a male to female ratio of 4.3:1. In one of the local study conducted at KPK by Hamayun, all cases reported were that of males. Similar to these results of 100% male predominance was found in another local study of leukaemic patients by Aziz at al. The study by Ehsan showed similar results of gender distribution with a male to female ratio of 4.6:1. Oppezo et al conducted a study showing that 63% of the population under study was male. In another study conducted by Goldin et al on a cohort of 660 showed that male population suffered from CLL twice as more. Our study showed that patients with Coombs positive presented with advanced stage of 3 and 4. This is in concordance to the study by Kyasa et al which establishes that DAT positive is a poor prognostic factor. In another study by Moreno et al male sex and advanced disease have been classically associated with autoimmune cytopenia. Barcellini et al also concludes in the study that Coombs positive is bad prognostic factor and patients present usually with advanced stages.

In this study patients were divided in two groups. Half of the patients were below 60 years and half of the patients more than 60 years. No significant relationship (p value = 0.136) was found between age and autoimmune anaemia in chronic lymphocytic leukaemia patients. The study by Flowers also showed that age had no role in patients developing the complications of chronic lymphocytic leukaemia. However, a study by Nicora showed that with advancing age the complications of chronic lymphocytic leukaemia were also increased.

In our study 85 of the patients had IgG and 15 had IgM which in concordance to a study conducted by Wilson and Chabot. In selecting blood for transfusion, precision can also be helpful. Some staff choose to transfuse RBCs that are autoantibody friendly. In few cases, any blood donor is typically incompatible with WAIHA patients. Any transfused blood being administered in the crosspatch is thus considered "least incompatible." Because of the low number of White Cells in this blood portion, leukocyte-reduced RBCs are the preferred blood product. Tiny volumes (100mL) of Leuco-filtered blood are steadily transfused and the patient is monitored for any adverse effects.

CONCLUSION

Frequency of autoimmune haemolytic anaemia is 22.66% among chronic lymphocytic leukaemia patients which reflects that autoimmune complications are significantly high with chronic lymphocytic leukaemia. Antibody detection and specificity may also be helpful in selecting blood for transfusion.

REFERENCES

Examine the Outcomes of Dynamic Hip Screw Fixation in Patients with Intertrochanteric Femur Fractures

Attiq-ur-Rehman¹, Karim Bakhsh¹ and Muhammad Ishaq²

ABSTRACT

Objective: To examine the outcomes of dynamic hip screw fixation in patients presented with intertrochanteric femur fractures.

Study Design: Retrospective study.

Place and Duration of Study: This study was conducted at the Department of Orthopedic, Bolan Medical College Hospital, Quetta from January 2019 to March 2020.

Materials and Methods: Thirty patients of both genders with ages 20 to 70 years presented with intertrochanteric femur fractures were enrolled. Patients demographic including age, sex and side of fracture were recorded. All patients received dynamic hip screw placement under general anesthesia. Radiological assessment was done. Follow-up was taken at 12weeks and 24 weeks postoperatively. Functional outcomes were assessed by Harris Hip Scoring (HHS) system. Post-operative wound infection, union of bone, range of hip motion, shortening of limb was examined. Patient’s satisfaction was recorded at final follow-up.

Results: Eighteen (60%) were males and 12 (40%) were females. 5 (16.67%) patients were ages 20 to 40 years, 14 (46.67%) patients were ages 41 to 60 years and 11 (36.67%) patients had ages above 60 years. 1 (3.33%) patients had limb shortening more than 2cm. Wound infection found in 2 (6.67%) patients. There was 1 (3.33%) patient with non-union. 22 (73.33%) patients had excellent, 4 (13.33%) patients had good, 2 (6.67%) patients had fair and no patient with poor outcome by HHS. 21 (%) patients were very satisfied.

Conclusion: Dynamic hip screw placement for intertrochanteric femur fractures is better and very effective treatment modality with fewer rate of complications.

Key Words: Intertrochanteric Femur Fracture, Dynamic Hip Screw, Functional Outcomes.

Citation of article: Rehman A, Bakhsh K, Ishaq M. Examine the Outcomes of Dynamic Hip Screw Fixation in Patients with Intertrochanteric Femur Fractures. Med Forum 2020;31(9):107-110.

INTRODUCTION

Intertrochanteric fractures are fractures that involve the proximal region of the femur from the extra capsular part of the femoral neck to the transverse line at the level of the distal end of the lesser trochanter.¹ Nearly 90% of these fractures occur in patients older than 65 years. They are more common in women than in men with ratio 3:1. Other risk factors include white race, neurological impairment, malnutrition, impaired vision, malignancy, and decreased physical activity.²

Intertrochanteric fractures are predominantly seen following low energy injuries in elderly women due to osteoporosis and they are associated with high morbidity and mortality especially in patients with medical comorbidities whose declining health status is further worsened by trauma.³,⁴

Successful treatment of intertrochanteric fractures depends on many factors including the age of patients, the patients’ general health, the time from fracture to treatment, concurrent medical illness and the stability of fixation.⁵ There are various types of hip fracture fixation devices available for treatment of intertrochanteric fractures. Dynamic hip screw (DHS) is the gold standard device of fixation of this fracture, regardless of number of parts, by which all other fixation devices are to be measured. This is because of its telescoping properties, which allows impaction of the fracture site (controlled collapse), thereby achieving bone-on-bone stability and reducing chances of implant failure.⁶,⁷

Numerous internal fixation devices have been used to stabilize intertrochanteric femoral fractures. These devices can be divided into 2 categories: extramedullary fixation devices and intramedullary fixation devices. It is generally accepted that dynamic hip screw (DHS) is the implant of choice in the treatment of stable intertrochanteric femur fractures.⁸ For unstable intertrochanteric femoral fractures, the...
commonly used extramedullary fixation devices, such as DHS, dynamic condylar screw (DCS), and angular blade plates are often problematic.\(^9\) The importance of a well-performed surgical treatment in hip fracture care is undisputable; however, treating the patients from a holistic point of view is probably even more important in order to improve the overall outcome for these patients.\(^{10}\)

The present study was conducted aimed to examine the outcomes of dynamic hip screw placement in patients with intertrochanteric fractures.

MATERIALS AND METHODS

This retrospective case series study was conducted at Department of Orthopedic, Bolan Medical College Hospital Quetta from 1\(^{st}\) January 2019 to 31\(^{st}\) March 2020. A total of 30 patients of both gender with ages 20 to 70 years presented with intertrochanteric femur fractures were enrolled. Patients demographic including age, sex and side of fracture were recorded. Causes of fractures were also recorded. Patients with pathological fractures, unstable intertrochanteric fractures, non-operatively treated fractures, bed-bounded patients and patients with no consent were excluded. All patients received dynamic hip screw placement under general anesthesia. Radiological assessment was done preoperatively and postoperatively. Functional outcomes were assessed by Harris Hip Scoring (HHS) system. Post-operative wound infection, union of bone, range of hip motion, shortening of limb was examined. Patient’s satisfaction was recorded at final follow-up. Follow-up was taken at 12 weeks and 24 weeks postoperatively. Data was analyzed by SPSS 24.0. Chi-square test was applied to compare the preoperative and postoperative findings of HHS. P-value <0.05 was set at statistically significant.

RESULTS

There were 18 (60\%) were males and 12 (40\%) were females. 5 (16.67\%) patients were ages 20 to 40 years, 14 (46.67\%) patients were ages 41 to 60 years and 11 (36.67\%) patients had ages above 60 years. 16 (53.33\%) patients had left side fracture and 14 (46.67\%) had right side fracture. Slip on ground were the most common etiology found in 13 (43.33\%) followed by road traffic accident and fall from height in 11 (36.67\%) and 6 (20\%) patients (Table 1). According to the Harris Hip Score, it was 18.8±23.5 preoperatively, at postoperative 12 weeks 65.4±10.7 and at 24 weeks it was 93.4±11.6 (p<0.05) (Tables 2-3). At final follow up, we found 24 (80\%) patients had excellent, 4 (13.33\%) patients had good, 1 (3.33\%) patients had fair and 1 (3.33\%) patient with poor outcome by HHS (Table 4).

There was 1 (3.33\%) patient with limb shortening more than 2cm. Wound infection found in 2 (6.67\%) patients, 1 (3.33\%) patient with screw cut-out (Table 5).

According to the patients satisfaction scoring, we found 26 (86.67\%) patients were strongly satisfied, 2 (6.67\%) were satisfied and 2 (6.66\%) were not satisfied (Table 6).

Table No.1: Demographic information of the patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
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</tr>
<tr>
<td>Male</td>
<td>18</td>
<td>60.0</td>
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<tr>
<td>Female</td>
<td>12</td>
<td>40.0</td>
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<tr>
<td>Age (years)</td>
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<td></td>
</tr>
<tr>
<td>20 – 40</td>
<td>5</td>
<td>16.67</td>
</tr>
<tr>
<td>41 – 60</td>
<td>14</td>
<td>46.66</td>
</tr>
<tr>
<td>&gt; 60</td>
<td>11</td>
<td>36.67</td>
</tr>
<tr>
<td>Fracture side</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>16</td>
<td>53.33</td>
</tr>
<tr>
<td>Right</td>
<td>14</td>
<td>46.67</td>
</tr>
<tr>
<td>Cause of fracture</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slip on ground</td>
<td>13</td>
<td>43.33</td>
</tr>
<tr>
<td>RTA</td>
<td>11</td>
<td>36.67</td>
</tr>
<tr>
<td>Fall from height</td>
<td>6</td>
<td>20</td>
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Table No.2: Comparison of Harris Hip Score (HHS) preoperative and postoperative 12\(^{th}\) week

<table>
<thead>
<tr>
<th>HHS</th>
<th>Preoperative</th>
<th>Postoperative 12(^{th}) week</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>18.8±23.5</td>
<td>65.4±10.7</td>
<td>0.0001</td>
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Table No.3: Comparison of Harris Hip Score (HHS) preoperative and postoperative 24\(^{th}\) week

<table>
<thead>
<tr>
<th>HHS</th>
<th>Preoperative</th>
<th>Postoperative 24(^{th}) week</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>18.8±23.5</td>
<td>93.4±11.6</td>
<td>0.0001</td>
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Table No.4: At final follow-up findings by Harris Hip Score (HHS)

<table>
<thead>
<tr>
<th>HHS</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent (90-100)</td>
<td>24</td>
<td>80.0</td>
</tr>
<tr>
<td>Good (80-89)</td>
<td>4</td>
<td>13.34</td>
</tr>
<tr>
<td>Fair (70-79)</td>
<td>1</td>
<td>3.33</td>
</tr>
<tr>
<td>Poor (0-69)</td>
<td>1</td>
<td>3.33</td>
</tr>
</tbody>
</table>

Table No.5: Postoperative complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limb Shortening</td>
<td>1</td>
<td>3.0</td>
</tr>
<tr>
<td>Wound Infection</td>
<td>2</td>
<td>3.67</td>
</tr>
<tr>
<td>Screw Cut-out</td>
<td>1</td>
<td>3.33</td>
</tr>
</tbody>
</table>

Table No. 6: Patient’s satisfaction

<table>
<thead>
<tr>
<th>Variable</th>
<th>No.</th>
<th>%</th>
</tr>
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<tr>
<td>Strongly satisfied</td>
<td>21</td>
<td>70%</td>
</tr>
<tr>
<td>Satisfied</td>
<td>7</td>
<td>23.33%</td>
</tr>
<tr>
<td>Not satisfied</td>
<td>2</td>
<td>6.67%</td>
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</table>

DISCUSSION

Intertrochanteric fractures are the most common femoral fractures and can cause mortality and
morbidity. In elderly patients hip fractures are common with high rate of mortality and morbidity. Dynamic hip screw procedure considered as a procedure of choice for the treatment of intertrochanteric femur fractures with high rate of union of bone. The present study was conducted to examine the outcomes of dynamic screw placement in patients with intertrochanteric fractures. In our study the union rate was 96.67%. Many of previous studies reported bone union rate was 88-98%. In this study total 30 patients of intertrochanteric fractures were included. Mostly patients were male 60% as compared to females 40% and 83.33% patients were ages 41 to 70 years. These results were similar to several previous studies conducted regarding intertrochanteric fractures, in which most of the patients were males as compared to females with majority of patients had elderly ages. In our study we found the most common cause of fracture was slip on ground and fall from height in 11 (36.67%) and 6 (20%) patients. These results were comparable to many other studies.

In the present study, according to the Harris Hip Score, we found significant difference in term of pre and postoperatively (P=0.05). The values obtained, 18.8±23.5 preoperatively, at postoperative 12 weeks 65.4±10.7 and at 24 weeks it was 93.4±11.6. A study conducted by Arojuraye et al reported statistically significant differences between the pre-operative Harris hip score and the Harris hip scores at 3 months and 6months respectively (P<0.05). We found 24 (80%) patients had excellent, 4 (13.33%) patients had good, 1 (3.33%) patients had fair and 1 (3.33%) patient with poor outcome by HHS. There was 1 (3.33%) patient with limb shortening more than 2cm. Wound infection found in 2 (6.67%) patients, 1 (3.33%) patient with screw cut-out. These results were similar to multiple studies in which majority of patients had excellent HHS 75 to 90% and few rate of complications 2-10%. This study showed that patients satisfaction scoring, we found 21 (70%) patients were strongly satisfied, 7 (23.33%) were satisfied and 2 (6.66%) were not satisfied. Arojuraye et al reported 62.5% patients were very satisfied, 31.3% patients were satisfied and 6.3% patients were dissatisfied.

**CONCLUSION**

Dynamic hip screw placement for intertrochanteric femur fractures is better and very effective treatment modality with fewer rate of complications. The bone union rate was 96.67% with higher rate of patient’s satisfaction and good functional outcomes.

**Author’s Contribution:**

Concept & Design of Study: Attiq-ur-Rehman
Drafting: Karim Bakhsh
Data Analysis: Muhammad Ishaq

**REFERENCES**


Incidence of Brain Tumours in Children and Adults in Pakistan

Nauman Idris Butt¹, Fatima Kashif², Faisal Iqbal³, Shafiq Ur Rehman⁴ and Kamran Hamid⁵

ABSTRACT

Objective: To study the incidence of Brain Tumours in Children and Adults in Pakistan

Study Design: Retrospective Study

Place and Duration of Study: This study was conducted at the Pathology Department of Idris Teaching Hospital Sialkot and Aziz Bhatti Teaching Hospital Gujrat from January 2016 to February 2020.

Materials and Methods: The histopathology records of all patients with brain tumors were reviewed which were received, diagnosed and operated for brain tumors. In addition to types and site of the tumor, patient demographics including sex and age were also recorded. To highlight the sex distribution and age frequency amongst each age group, the age of the patients was divided in two broad groups 1 (0-14 years) and 14-82 years. The written informed was taken before collecting the data from each patient and permission of Ethical Committee was also considered before collecting the data and publishing in medical journal. The data was analyzed for results by SPP version 10.

Results: Incidence of Benign 16 (30.76%) Small Round Blue Cell Tumor 09 (17.30%) Medulloblastoma 11 (21.15%) High grade glioma 06 (11.53%) Low grade glioma 07 (13.46%) Glioblastoma multiform 03 (5.76%) Total 52 (100%). Incidence of GBM 27 (21.95%) Meningioma 25 (20.32%) Benign 25 (20.32%) Low grade glioma 23 (18.69%) Metastatic carcinoma 05 (4.06%) High grade glioma 04 (3.25%) DLBCL 02 (1.62%) Mesenchymal chondrosarcoma 03 (2.43%) Non diagnostic 09 (7.31%). One hundred seventy-five patients with brain tumors, of ages between 2-82 years had underwent surgery during the study period. Out of these, 154 (88%) were males and 21 (12%) were females. Male to female ratio was 13.63:1. The mean age of patients was 6.73 (±0.21) years. A distinct overall male predominance was noted in all tumor types.

Conclusion: Population-based studies were required to determine the cancer burden due to pediatric malignancies of the brain in this population and for the morphological categorization of brain tumors in Pakistan. Conventional hematoxylin e-eosin staining is the mainstay for pathological diagnosis in most of the cases, however Immuno histochemistry (IHC) has a major role in differential diagnosis and improving diagnostic accuracy in difficult cases not only in general surgical pathology but also in neurooncologic pathology.

Key Words: Incidence, Brain Tumours, Pakistan

INTRODUCTION

Occurrence of cerebrum tumors is identified with age, with the most noteworthy frequency in more established men and women¹. In youth mind tumors are the second most normal diseases after leukemia, representing in excess of a fourth of all tumors analyzed in youngsters Although a dominant part of these tumors happen in grown-ups, some particular histological sorts which are basic in adolescence are uncommon in adults²,³. All the more significantly, there are signs that pediatric and grown-up glial tumors have contrasts in their sub-atomic science and conduct. These have significant ramifications for future research, treatment and prognosis⁴. In numerous pieces of the world, they are not just the most widely recognized dangerous strong tumors seen before the age of 20 years, yet in addition a biggest reason for youth malignancy mortality in the age group 0-1⁴. Early location and improvement in remedial modalities have brought about longer endurance. It’s shocking that treatments effecte affect the cerebrum tissue. Longer stabilities are regularly connected with neurological, subjective and endocrine issue and diminished nature of life⁵. Survivors are at an expanded danger of building up a second neoplasm later in life⁶. In writing there are overall varieties in the example of cerebrum tumor as for occurrence, sexual orientation, anatomical area and recurrence of explicit histological sorts. Area and histological sorts, to an enormous degree, impact treatment choices, out-come and hazard factors. Information on these parameters are helpful for arranging of social insurance conveyance framework.
and future research. Generally morphological measures are useful for diagnosing the vast majority of these tumors however in situations where tumors are ineffectively separated or example gave is restricted, Immunohistochemistry and radiological assessment is extremely useful in arriving at a precise diagnosis.

MATERIALS AND METHODS
For this study data of one hundred seventy five patients was collected from the Pathology department of Idris Teaching Hospital Sialkot and Aziz Bhatti Teaching Hospital Gujrat Pakistan. The histopathology records of all patients with brain tumors were reviewed which were received, diagnosed and operated for brain tumors during January 2016 to February 2020. In addition to types and site of the tumor, patient demographics including sex and age were also recorded. To highlight the sex distribution and age frequency amongst each agegroup, the age of the patients was divided in two broad groups 1 (0-14 years); and 14-82 years.
The written informed was taken before collecting the data from each patient and permission of Ethical Committee was also considered before collecting the data and publishing in medical journal. The data was analyzed for results by SSPP version 10.

Inclusion criteria: All the patients having brain tumors were included in this study.

Exclusion criteria: All the patient without brain tumor were excluded from the study.

RESULTS
Table No: 1 Childhood brain tumours distribution

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of Patients</th>
<th>Percentage %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>16</td>
<td>30.76 %</td>
</tr>
<tr>
<td>Small Round Blue Cell Tumor</td>
<td>09</td>
<td>17.30 %</td>
</tr>
<tr>
<td>Medulloblastoma</td>
<td>11</td>
<td>21.15 %</td>
</tr>
<tr>
<td>High grade glioma</td>
<td>06</td>
<td>11.53 %</td>
</tr>
<tr>
<td>Low grade glioma</td>
<td>07</td>
<td>13.46 %</td>
</tr>
<tr>
<td>Glioblastoma multiform</td>
<td>03</td>
<td>5.76 %</td>
</tr>
<tr>
<td>Total</td>
<td>52</td>
<td>100 %</td>
</tr>
</tbody>
</table>

Incidence of Benign (16 (30.76%)) Small Round Blue Cell Tumor 09 (17.30%) Medulloblastoma 11 (21.15%)
High grade glioma 06 (11.53%) Low grade glioma 07(13.46%) Glioblastoma multiform 03(5.76%) Total 52(100%) as shown in table no 1.

Incidence of GBM 27(21.95%) Meningioma 25(20.32%) Benign 25(20.32%) Low grade glioma 23(18.69%) Metastatic carcinoma 05(4.06%) High grade glioma 04(3.25%) DLBCL 02(1.62%) Mesenchymal chondrosarcoma 03(2.43%) Non diagnostic 09(7.31%) as shown in table no 2

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of Patients</th>
<th>Percentage %</th>
</tr>
</thead>
<tbody>
<tr>
<td>GBM</td>
<td>27</td>
<td>21.95 %</td>
</tr>
<tr>
<td>Meningioma</td>
<td>25</td>
<td>20.32 %</td>
</tr>
<tr>
<td>Benign</td>
<td>25</td>
<td>20.32 %</td>
</tr>
<tr>
<td>Low grade glioma</td>
<td>23</td>
<td>18.69 %</td>
</tr>
<tr>
<td>Metastatic carcinoma</td>
<td>05</td>
<td>4.06 %</td>
</tr>
<tr>
<td>High grade glioma</td>
<td>04</td>
<td>3.25 %</td>
</tr>
<tr>
<td>DLBCL</td>
<td>02</td>
<td>1.62 %</td>
</tr>
<tr>
<td>Mesenchymal chondrosarcoma</td>
<td>03</td>
<td>2.43 %</td>
</tr>
<tr>
<td>Non diagnostic</td>
<td>09</td>
<td>7.31 %</td>
</tr>
<tr>
<td>Total</td>
<td>123</td>
<td>100 %</td>
</tr>
</tbody>
</table>

Table No.3: Age and Gender distribution

<table>
<thead>
<tr>
<th>Age (Years)</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-14</td>
<td>15</td>
<td>7</td>
</tr>
<tr>
<td>15-30</td>
<td>25</td>
<td>5</td>
</tr>
<tr>
<td>31-45</td>
<td>25</td>
<td>3</td>
</tr>
<tr>
<td>46-60</td>
<td>30</td>
<td>5</td>
</tr>
<tr>
<td>61-76</td>
<td>31</td>
<td>7</td>
</tr>
<tr>
<td>77-82</td>
<td>30</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>154</td>
<td>21</td>
</tr>
</tbody>
</table>

One hundred seventy five patients with brain tumors, of ages between 2-82 years had underwent surgery during the study period. Out of these, 154(88%) were males and 21(12%) were females. Male to female ratio was 13.63:1. The mean age of patients was 6.73 (±0.21) years. A distinct overall male predominance was noted in all tumor types.

DISCUSSION
The current investigation was intended to decide the recurrence of Brain Tumors from January 2010 to February 2014. Our examination uncovered male prevalence with by and large male to female proportion of 13.63:1, which is in accordance with past studies. As it is a medical clinic based examination, it is preposterores to expect to figure tumor rate. In past investigations a moderately lower recurrence was accounted for. Grover and Hardas announced 9% recurrence of youth mind tumors.
Present examination uncovered the greater part of the patients in age bunch 6-8 which is about as per a past report done by Ahmed et al who revealed most cases in age bunch 5-9. Anyway Velemia and Percy; and Memon et al detailed most cases in lower age group. In our examination mean age for tumor occurrence was 6.73. The mean age was 6 years in a past report revealed by Farwell et al while Ahmed et al and Mehrzin et al announced mean age as 8.8 and 8.7 years separately which is higher than our examination. Medulloblastoma was the most successive
tumor in youngsters as indicated by our examination establishing 24% of complete cases and is equivalent to concentrate by Young et al and Ahmed et al, where it was additionally the main tumor type\(^{10,18}\). Some different investigations have detailed astrocytoma as the most well-known youth tumor dissimilar to our study\(^{11,19}\). Our investigation repudiates with contemplates done by Mehrazine et al, Rehman et al and Khan et al who revealed meningioma, neuroma and gliomas as the most ruling kinds of youth tumors\(^{12,14,19}\). The greater part of the studies\(^{10,11,19}\) indicated roughly the comparable %age of ependymoma as detailed in the current investigation (9.5%). In some studies\(^{14,17}\) lower rates of ependymoma is appeared. The present examination is a solitary establishment study and needs wary translation. Morphology is the way in to the conclusion and sub typing of these biopsies; in any case, this ought to be joined with clinical history, radiological connection, and proper examining. Old style morphological highlights by and large consider right finding. Challenges may emerge when tumor show irregular morphology, are, ineffectively separated or blended sort. Metastatic tumors from different locales can be of indicative difficulties. In such cases Immuno histochemistry is very useful in setting up right diagnosis\(^{20}\). Changes embraced with respect to analytic and treatment since mid-1970s have brought about improved endurance rates for patients analyzed as Medulloblastoma, oligodendroglioma, and astrocytoma, particularly controlling for age at determination. Glioblastoma multiform keeps on being the most obstinate essential mind tumor\(^{21}\). In grown-ups the astrocytomas were the commonest tumors comprising 47% and meningioma was the second most successive tumor 21%. This is similar to worldwide statistics\(^{22}\). Morphology alone had the option to analyze the majority of the cerebrum tumors. In kids for instances of Medulloblastoma and little round blue cell tumor Immunohistochemistry was required for the affirmation of the conclusion. In grown-ups Immunohistochemistry was required in instances of metastatic carcinomas and lymphomas. So as to get a corroborative finding a board of Immunohistochemical stains involving CK, S100, GFAP, EMA, LCA, CD20, CD56, chromogranin and synaptophysin was used\(^{23}\). Imrana Tanvir, Rahat Malik, Rizwan Ullah Kh.

CONCLUSION

Population-based studies are required to determine the cancer burden due to pediatric malignancies of the brain in this population and for the morphological categorization of brain tumors in Pakistan. Conventional hematoxylin-eosin staining is the mainstay for pathological diagnosis in most of the cases, however IHC has a major role in differential diagnosis and improving diagnostic accuracy in difficult cases not only in general surgical pathology but also in neurooncologic pathology.

Author's Contribution:
Concept & Design of Study: Nauman Idris Butt
Drafting: Fatima Kashif, Faisal Iqbal
Data Analysis: Shafiq Ur Rehman, Kamran Hamid
Revisiting Critically: Nauman Idris Butt, Fatima Kashif
Final Approval of version: Nauman Idris Butt

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

REFERENCES

11. Memon F, Rath SL, Memon MH. Pattern of solid paediatric malignant neoplasm at LUMHS,
Causes of Admission and Outcome Among Newborns in Neonatology Ward of Mardan Medical Complex Mardan Khyber Pakhtunkhwa, Pakistan

Kiramat Ullah, Mohammad Fazil, Qasim Khan and Sumera Akram

ABSTRACT

Objective: To study the main causes of admission and outcome among newborns in Nursery ward of Mardan Medical Complex Mardan Khyber Pakhtunkwa, Pakistan.

Study Design: Retrospective descriptive study

Place and Duration of Study: This study was conducted at the Mardan Medical Complex Neonatology Unit from January 2019 to December 2019.

Materials and Methods: Data of all the neonatal admissions in the nursery unit was recorded in Mardan Medical Complex neonatology unit and analyzed for age, sex, the reason for admission, duration of hospital stay and the final outcome of these patients.

Results: A total of 4759 neonates were admitted to the neonatal unit Mardan Medical Complex. Among them, males were 2285 (48.07%) and females were 2474 (51.99%). The average length of stay was 6.2 days (SD 6 days). According to the data neonatal sepsis represent about 30.95% of all admission in 2019. Neonatal jaundice accounted for 15.17%. Birth asphyxia (15.67%), preterm constitute 10.29%, meconium aspiration syndrome was 5.77%, hypoxic ischemic encephalopathy 4.60%, respiratory distress syndrome 9.81%, hypoglycemia 3.2%, hypothermia 2.64%, neonatal seizure 1.22%, tetanus 0.19% and others constitute 2.33% of the admitted cases. Among total admissions 3801 (79.86%) patient were discharged with a satisfactory condition while 958 (20.13%) patient died. The highest number of admitted patient was observed in the month of July 2019 while highest death rate was observed in month of August 2019.

Conclusion: This study conclude that the most common causes of the neonatal admission were neonatal sepsis, neonatal jaundice (NNJ), preterm, meconium aspiration syndrome, birth asphyxia, respiratory distress syndrome, hypoxic ischemic encephalopathy, hypoglycemia, hypothermia, neonatal seizure and tetanus. The commonest cause for the mortality was neonatal sepsis, birth asphyxia and neonatal jaundice. There is need of increased awareness in health workers who conduct deliveries at home or in home for time referral to tertiary level hospital.

Key Words: Newborns; Admission; Outcome; Awareness

Citation of article: Kiramat Ullah, Fazil M, Khan Q, Akram S. Causes of Admission and Outcome Among Newborns in Neonatology Ward of Mardan Medical Complex Mardan Khyber Pakhtunkhwa, Pakistan. Med Forum 2020;31(9):115-119.

INTRODUCTION

As neonate face a lot of problems during perinatal period hence it is recognized as the most dangerous period. The high vulnerable time for infant is the neonatal period because in neonatal period the child are completing many physiological adjustments that are required for extra-uterine existence. In developing countries 98% of the death in total death of nine million children in world is during perinatal and neonatal period. The contribution of neonatal mortality ranged from 40-70% of infant mortality. Two-third of the infant death in India is due to neonatal death. In the first two days of life about 45% of death occur. Birth asphyxia, sepsis, congenital abnormalities, prematurity, low birth weight and surgical problems are the major causes for neonatal mortality in India. The mortality rate can be decreased by improving the neonatal care. Prematurity and malformation are the major cause of death in advanced countries while in less developed countries the most important causes of neonatal death are infections (29%), prematurity (29%), asphyxia (23%), congenital malformations (8%), and other (11%) during antepartum or intrapartum approximately half of the perinatal death occur while the rest of the death occur in first week of life in most developing nation state. In developing countries the perinatal and neonatal death occur due to many factors
including poor maternal health, adverse social conditions, and inadequate care during pregnancy, delivery, and the immediate postpartum period1. Therefor it is important to measure and monitor the perinatal morbidity and mortality to develop different strategies to improve the perinatal heath care at various level. The instability of life during this period, of all the death occurring, is due to high neonatal mortality and morbidity rate. During the first year of life in the United States, two-thirds are in a birth condition. The death rate for the first year is not comparable by the Rate in any other lifetime to seventh decade 2,4.

There are many causes of newborn admission to neonatal unit as high-risk infants other than prematurity as patients with genetic disorder, blood group sensitization, multiple gestation, intrauterine growth restriction, neonatal jaundice, mother illness such as hypertension, diabetes mellitus and some drug administration during pregnancy, respiratory distress, premature rupture of membrane, body weight either Less than 2.500 or greater than 4.000g or birth less than 37 or more than 42 weeks of gestation and congenital malformation2. Number of studies have been done on the causes of admission of newborn in which majority of admission is due to low birth weight followed by neonatal infection 3,5,6. The important causes for the increased mortality in newborn admission is due to prematurity followed by birth asphyxia than neonatal infection7. The high mortality rate of neonate in a country is reflected by many factors including poor availability of quality and quantity of set-up and proper utilization of neonatal care of that country. To define the causes for admission and outcomes among newborn in Pakistan a very limited data is available. We therefore sought to conduct the study in neonatal unit of Mardan Medical complex Mardan Khyber Pakhtunkhwa, Pakistan to determine the causes and outcomes of the admitted newborn. This study will help us in making guidelines and will also prove very fruitful to local health pediatrician and researchers in minimizing mortalities and morbidities associated with the different diseases among newborn patient. This study will be helpful in finding all the gaps in the required infrastructure of neonatal unit of Mardan Medical complex Mardan Khyber Pakhtunkhwa, Pakistan

MATERIALS AND METHODS

This study was done at a neonatal unit of Mardan Medical complex Mardan Khyber Pakhtunkhwa, Pakistan. The study was conducted from 1st January 2019 to 31st December 2019. A hospital based retrospective study was 4759 neonates admitted in the neonatal unit of Mardan Medical complex Mardan Khyber Pakhtunkhwa, Pakistan.

Inclusion Criteria was all newborns with available data admitted in the Neonatal Unit while the Exclusion criteria was Individual recordings in the register which were not properly filled were omitted.

Data collection technique: The data source for our study was the neonatal unit registers at Mardan Medical complex Mardan Khyber Pakhtunkhwa, Pakistan which comprised of neonate information recorded at admission such as date of admission, age, weight of the child, status at birth, diagnosis, treatments given, outcome status and records of maternal information like parity, antenatal follow up, gestational age and mode of delivery. All these data were collected using a uniform extraction format developed by taking in to account all the relevant variables in the standard neonatal unit registers. Mostly clinical sign and symptoms were the base for diagnosis or based on WHO definition for prematurity (live born Neonates delivered before 37 weeks from 1st day of last menstrual period(LMP))8. Serum bilirubin along with G6PD estimation was done for the diagnosis of neonatal jaundice. Clinical grounds together with the positive blood culture and CSF examination was used for the diagnosis of the neonatal sepsis. Samat-staging was base for the clinical diagnose of birth asphyxia.

RESULTS

The total number of babies admitted to neonatal unit of Mardan Medical complex Mardan KPK from fist January 2019 to 31st December 2019 was 4759 babies Among them, males were 2285 (48.07%) and females were 2474 (51.99%). (Table 1) The average length of stay was 6 days (SD 6 days). (Table 2) Neonatal sepsis was the main cause of admission to neonatal unit. Out of 4759 admitted newborn 1470 newborn (30.95%) were admitted due to neonatal sepsis. Neonatal sepsis was followed by Birth asphyxia (15.67), Neonatal jaundice accounted for 15.17%), preterm constitute 10.29%, respiratory distress syndrome (9.81%), meconium aspiration syndrome was 5.77%, hypoxic ischemic encephalopathy 4.60%, hypothermia 2.64%, hypoglycemia 1.32%, neonatal seizure 1.22%, tetanus 0.19% and others constitute 2.33% of the total admitted cases. (Table 3) Among total 4759 admitted neonate 3801 (79.86%) patient were discharged to their home with a satisfactory condition while 958 (20.13%) patient expired. (Figure 1) Those among the expired patients 958 (20.13%), the major causes of death was neonatal sepsis that constitute 218 patient (22.73%). The other causes of death followed by neonatal sepsis were preterm constitute 22.21%, Birth asphyxia (18.35%), respiratory distress syndrome (14.28%), meconium aspiration syndrome was 7.92%, hypoxic ischemic encephalopathy 6.04%. Neonatal jaundice accounted for 4.06%, hypothermia 0%, hypoglycemia 0% neonatal seizure 0%, tetanus 0.93% and others constitute 3.33% of the total expired cases. (Table 4).
Table No.1: The total number of babies admitted gender wise to the neonatal unit in Mardan Medical Complex

<table>
<thead>
<tr>
<th>Gender</th>
<th>Total No</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>2285</td>
<td>2474</td>
<td>4759</td>
</tr>
<tr>
<td>percentage</td>
<td>(48.07%)</td>
<td>(51.99%)</td>
<td></td>
<td>100%</td>
</tr>
</tbody>
</table>

Table No.2: Length of stay in the neonatal unit in Mardan Medical Complex

<table>
<thead>
<tr>
<th>No.</th>
<th>Max</th>
<th>Min</th>
<th>Range</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>Variance</th>
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<tbody>
<tr>
<td>4759</td>
<td>31</td>
<td>1</td>
<td>30</td>
<td>6.22</td>
<td>6.0</td>
<td>36.0</td>
</tr>
</tbody>
</table>

Table No.3: Causes of admissions to the neonatal unit in Mardan Medical Complex

<table>
<thead>
<tr>
<th>Causes of admission</th>
<th>Frequency</th>
<th>percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonatal sepsis</td>
<td>1473</td>
<td>30.95%</td>
</tr>
<tr>
<td>Preterm</td>
<td>490</td>
<td>10.29%</td>
</tr>
<tr>
<td>Birth asphyxia</td>
<td>746</td>
<td>15.67%</td>
</tr>
<tr>
<td>Respiratory distress syndrome</td>
<td>467</td>
<td>9.81%</td>
</tr>
<tr>
<td>Meconium aspiration syndrome</td>
<td>275</td>
<td>5.77%</td>
</tr>
<tr>
<td>Hyponic ischemic encephalopathy</td>
<td>219</td>
<td>4.60%</td>
</tr>
<tr>
<td>Neonatal jaundice</td>
<td>722</td>
<td>15.17%</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>126</td>
<td>2.64%</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>63</td>
<td>1.32%</td>
</tr>
<tr>
<td>Neonatal seizure</td>
<td>58</td>
<td>1.22%</td>
</tr>
<tr>
<td>Netanus</td>
<td>9</td>
<td>0.19%</td>
</tr>
<tr>
<td>Others</td>
<td>111</td>
<td>2.33%</td>
</tr>
<tr>
<td>Total</td>
<td>4759</td>
<td>100%</td>
</tr>
</tbody>
</table>

Table No.4: Disease wise mortality pattern among neonates admitted to Mardan Medical Complex

<table>
<thead>
<tr>
<th>Causes of admission</th>
<th>Frequency (N)</th>
<th>Death</th>
<th>%age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonatal sepsis</td>
<td>1473</td>
<td>218</td>
<td>22.73%</td>
</tr>
<tr>
<td>Preterm</td>
<td>490</td>
<td>213</td>
<td>22.21%</td>
</tr>
<tr>
<td>Birth asphyxia</td>
<td>746</td>
<td>176</td>
<td>18.35%</td>
</tr>
<tr>
<td>Respiratory syndrome</td>
<td>467</td>
<td>137</td>
<td>14.28%</td>
</tr>
<tr>
<td>Meconium aspiration syndrome</td>
<td>275</td>
<td>76</td>
<td>7.92%</td>
</tr>
<tr>
<td>Hyponic ischemic encephalopathy</td>
<td>219</td>
<td>58</td>
<td>6.04%</td>
</tr>
<tr>
<td>Neonatal jaundice</td>
<td>722</td>
<td>39</td>
<td>4.06%</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>126</td>
<td>0</td>
<td>0.00%</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>63</td>
<td>0</td>
<td>0.00%</td>
</tr>
<tr>
<td>Neonatal seizure</td>
<td>58</td>
<td>0</td>
<td>0.00%</td>
</tr>
<tr>
<td>Tetanus</td>
<td>9</td>
<td>9</td>
<td>0.93%</td>
</tr>
<tr>
<td>Others</td>
<td>111</td>
<td>32</td>
<td>3.33%</td>
</tr>
<tr>
<td>Total</td>
<td>4759</td>
<td>959</td>
<td>100%</td>
</tr>
</tbody>
</table>

DISCUSSION

This study was done to find out the reason for newborn admission and outcome of the causes in children ward of Mardan Medical Complex Khyber Pakhtunkhwa, Pakistan from 1st January 2019 to 31st December 2019. In many developing countries low birth weight is a major health problem. The results obtained from our study shows that the maximum number of newborn patient (30.95%) admitted was due to neonatal sepsis and this in contrast to the other study done in Pakistan by Fazlur R et al. in which the number of maximum patient admitted was due to low birth weight (41.20%). This is also in contrast to another study done by Parkash J et al. in which the number of maximum patient admitted was also due to low birth weight (55.4%). In developing countries neonatal infection are the major cause for neonatal morbidity and neonatal mortality. The percentage of neonatal sepsis (30.95%) in our study is comparable to the study done by Fazlur R et al. in which neonatal sepsis constitute 26.03% while lower than another study done in Karachi by Parkash J et al (45.21%), and less than the study done by M Hoque et al. (21.0%) and lower than M Hoque et al. (38.2%). Use of unsterile delivery practices and poor obstetric care were the main predisposing factors for neonatal infection. Birth asphyxia and neonatal jaundice are next main causes of newborn admission in our study that constitute 15.67%, 15.17% correspondingly. Birth asphyxia result of our study 15.67% is comparable to a study done by Fazlur R et al. (16.52%) and higher than Raghvendra N (12%) and lower than M Hoque et al. (38.2% and 15%). Use of unsterile delivery practices and poor obstetric care were the main predisposing factors for neonatal infection. Birth asphyxia in Rawalpindi is reported 31%.
Neonatal jaundice constitute 15.17% of the admitted newborn which shows a lower value then the other study done by Fazlur R et al (20%)\textsuperscript{6}. From Lahore neonatal jaundice was reported 8.33%\textsuperscript{16}, and from Bangladesh it was reported 30.71%\textsuperscript{16}. According to our study 3801 (79.86%) patient were discharged satisfactorily to their home after proper treatment. This high percentage of discharge newborn patient may be due to better awareness amongst workers of health and all the potential management in spite of having limited resources. According to our study the neonatal mortality was 20.13% which is higher than other study done by Fazlur R et al.\textsuperscript{7} in which 14.87% mortality was recorded while our mortality rate was lower than another study done by Parkash J et al\textsuperscript{6} in which 25.85% mortality was recorded. Another study was done in Lahore in which a very high mortality rate 34% was recorded\textsuperscript{18} which is very high than our study. The mortality rate of the neonate depends upon mainly the critical condition of the neonate at the time of admission\textsuperscript{19}. According to our study the major cause of the neonatal death was neonatal sepsis which is 22.73% followed by birth asphyxia which constitute 22.21%. our these results of neonatal sepsis and birth asphyxia are in accordance with the study done by Fazlur R et al.\textsuperscript{7} which recorded 14.1% and 21% respectively. According to the study done by Parkash J et al\textsuperscript{6} in Karachi, the reported mortality rate due to neonatal infection is much higher (46.44%) than our study while same results were figured in a study from India\textsuperscript{20}. Furthermore, in our study the average length of stay of neonate admitted to our neonatal unit was 6.2 days which is in accordance to a study done by M Hoque et al.\textsuperscript{14} in which an average stay of 9.2 days was reported. Immediate intervention and early recognition of neonatal problems led to rare complication and sequelae. In order to get better outcomes, it is necessary to do thorough examination of neonate just after birth for early recognition and timely referral of surgical condition.

CONCLUSION

According to our study the number of admitted neonate due to neonatal sepsis are comparatively high as compared to other causes of admission. The mortality rate in our study was generally low but higher for the neonate with neonatal sepsis. These results are in accordance with the other studies from the developing countries. The death rate are avoidable significantly due to postpartum, intrapartum and antenatal care. The major factor for the neonatal infections are the home based delivery done by traditional birth attendant under un-hygienic condition. Use of un-sterile delivery practices and poor obstetric care are the main predisposing factors for neonatal infection. In order to reduce the high case morbidity and mortality it is mandatory to have antenatal and intrapartum monitoring, referred on time and resuscitation at the time of birth. There is need of increased awareness in health workers who conduct deliveries at private clinic or in home for time referral to tertiary level hospital.

Author’s Contribution:
Concept & Design of Study: Kiramat Ullah
Drafting: Mohammad Fazil
Data Analysis: Qasim Khan, Sumera Akram
Revisiting Critically: Kiramat Ullah, Mohammad Fazil
Final Approval of version: Kiramat Ullah

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

REFERENCES

PCR Based Identification of Staphylococcus. Aureus Isolated from Different Operation Theaters of Tertiary Care Hospital and Antibiotic Susceptibility by Disk Diffusion Method

Muhammad Waseem¹, Noreen Sarwar², Mizna Arif³, Rabiya Jamil¹ and Ayesha Sajjad¹

ABSTRACT

Objective: To isolate the presence of Staphylococcus. aureus from different operation theaters and confirmation by the help of PCR and to determine the antibiotic susceptibility pattern by disk diffusion method.

Study Design: Clinical Study

Place and Duration of Study: This study was conducted at the Institute of Microbiology and Biotechnology Department, University of Lahore, Pakistan from September 2016 to March, 2017.

Materials and Methods: To evaluate contamination in various operation theaters from Tertiary Care Hospital at Lahore city. Air contamination of operation theatre was evaluated by settle plate method. Petri plates containing media were opened on different places that include window, instrument table, and entrance and OT table for about 15 minutes. Total 12 media containing petri plates were opened at different levels in each operation theatre and incubated for 24 hours at 37°C. Antibiotic susceptibility done by disk diffusion method and molecular identification was also done.

Results: To detect antimicrobial resistance, mecA and vanA gene were amplified and molecular identification of S. aureus was done by TStaG gene. 14 out of 16 samples were positive for TStaG gene, 8/8 were positive for mecA and 0/7 for vanA gene.

Conclusion: S. aureus is commonly present in all operation theatres and causes a lot of lethal infections thus proper sterilization/disinfection and proper antibiotic selection is required for its treatment.

Key Words: Nosocomial infection, Operation theatre, Staphylococcus aureus, Hospital acquired infections.


INTRODUCTION

The prevalence of nosocomial infections (NI) is increasing day by day and contamination of operation theatres (OT) is one of the important causes. In developing countries, these infections are involved in causing lethal problems. A study revealed that (HAI) ranges from 2.5 to 14.8%. In Asia and Africa 40% of cases are due to NI. The most common pathogens involved in causing NI are S. aureus, S. epidermidis, Vancomycin resistant Enterococci, E.coli, Bacillus cereus, Klebsiella pneumonia and P. aeruginosa. The most important bacteria is S. aureus. From 1999 to 2005 the no. of cases admitted due to methicillin resistant Staph. aureus was 477927 that increased from 127036 to 278203. Another cause of bacteremia, cardiovascular infections and pneumonia is S. aureus. Major cause of morbidity and mortality in hospitals all around the world is Methicillin Resistant S. aureus (MRSA). It is proved that environment is an essential part in developing resistance in microorganisms i.e. Staphylococcus survives in dry environment and can stick in clinical areas that are not cleaned properly.

Multiple ways are involved in spreading contamination in operation theatres like unfiltered air, ventilation system, collection bags, drainage of wounds, indoor traffic, gown, transportation of patients, surgical team, gloves, inadequate sterilized instruments and foot wear.

In Asia and Africa 40% of cases are due to NI. The most common pathogens involved in causing NI are S. aureus, S. epidermidis, Vancomycin resistant Enterococci, E.coli, Bacillus cereus, Klebsiella pneumonia and P. aeruginosa. The most important bacteria is S. aureus. From 1999 to 2005 the no. of cases admitted due to methicillin resistant Staph. aureus was 477927 that increased from 127036 to 278203. Another cause of bacteremia, cardiovascular infections and pneumonia is S. aureus.

Major cause of morbidity and mortality in hospitals all around the world is Methicillin Resistant S. aureus (MRSA). It is proved that environment is an essential part in developing resistance in microorganisms i.e. Staphylococcus survives in dry environment and can stick in clinical areas that are not cleaned properly.

The most effective antibiotic considered against
S. aureus is Vancomycin but now resistance is developing against it. There are number of PCR- based methods reported that are used for specific detection of these bacteria. Airborne bacteria in Operation Theater can be reduced upto 13- fold e.g. contamination through wound would reduce up to 50%. It all depends on proper disinfection, regular fumigation and proper disinfection of OT. This research was designed to isolate the occurrence of staphylococcus aureus in Operation Theater environment and also check antibiotic sensitivity through disk diffusion method.

**MATERIALS AND METHODS**

This study was carried out at Institute of Microbiology and biotechnology Department, University of Lahore, Pakistan from September 2016 to March, 2017. **Sample Collection:** Air contamination of operation theatre was evaluated by settle plate method. Petri plates containing media were opened on different places that include window, instrument table, and entrance and OT table for about 15 minutes. Total 12 media containing petri plates were opened at different levels in each operation theatre and incubated for 24 hour at 37°C.

**Isolation and Identification:** For isolation and identification of bacteria colonies with different morphology were taken and carefully streaked on nutrient agar plates. **Microscopy and Gram Staining:** Microscopy and Gram staining was performed for well isolated colonies on Nutrient agar, MacConkey's agar and Blood agar. **Confirmation by Biochemical Tests:** To differentiate between Staphylococci or Streptococci catalase and coagulase test were performed. All species of Staphylococcus were positive for catalase test and therefore differentiated from catalase negative Streptococci species. S. aureus is coagulase positive. **Antibiotic Susceptibility Testing:** Disk diffusion method was used to evaluate antimicrobial susceptibility of Staphylococcus aureus. Fresh Staphylococcus aureus colonies were inoculated in 5ml of normal saline and turbidity was compared with 0.5M MacFarl and standard solution. With the help of sterile cotton swabs inoculum was inoculated on Muller Hinton Agar plates, then discs were applied on it at left at 37°C for 24 hours.

**Molecular Identification:** Molecular identification of S. aureus was done by TStaG gene amplification while to detect antimicrobial resistance against methicillin and vancomycin, mecA and vanA gene were amplified respectively.

**RESULTS**

**Morphological and Biochemical Test:** Staphylococcus aureus: is a gram +ve cocci with thick cell wall of peptidoglycan, facultative anaerobe, non-motile and non-spore forming bacteria. S. aureus produce circular pinhead convex yellowish colonies on nutrient agar, microscopically bunch of gram +ve cocci, produce bright yellow colonies on mannitol salt agar, produce beta hemolysis on blood agar, gave catalase and coagulase test positive. S. aureus occur as commensals on human skin and major pathogen cause nosocomial infection.

**Molecular Identification of Isolated Bacteria:** For molecular identification of S. aureus, 16 samples among 53 isolated S. aureus samples were picked for molecular identification. 14 out of 16 samples were amplified TStaG (370 bp) gene specific for S. aureus hence positive for this gene. For methicillin resistant S. aureus strains mecA gene amplification was done and all 8 samples picked randomly were positive for mecA gene. While for vancomycin resistant strains of S. aureusvanA gene was amplified but none of the sample amplified vanA gene hence no vancomycin resistant S. aureus was present.

**Table No. 1: Primer sequence for S. aureus identification, methicillin and vancomycin resistant genes**

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Targeted gene</th>
<th>5’ to 3’ primer sequence</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>R- TT. AC. CA. TT. TC. AG. TA. CC. TT. CT. GG. TA. A</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>mecA</td>
<td>F- AA. AA. TC. GA. TG. GT. AA. AG. GT. TG. GC</td>
<td>(Pournajaf et al., 2014)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R- AG. TT. CT. GG. AG. TA. CC. GG. AT. TT. GC</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>vanA</td>
<td>F- AT. GA. AT. AG. AA. TA. AA. AG. TT. GC</td>
<td>(Saadatet al., 2014).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R- TC. AC. CC. CT. T T. AA. CG. CT. AA.TA</td>
<td></td>
</tr>
</tbody>
</table>

**Table No.2: PCR Conditions for S. aureus identification and antibiotic resistant genes**

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Targeted gene(primer)</th>
<th>Initial denaturation</th>
<th>35 cycles of repeated</th>
<th>Final extension</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Denaturation</td>
<td>Annealing</td>
<td>Extension</td>
</tr>
<tr>
<td>1</td>
<td>TStaG</td>
<td>95°C 4 mint</td>
<td>95°C 1 mint</td>
<td>57°C 1 mint</td>
</tr>
<tr>
<td>2</td>
<td>mecA</td>
<td>95°C 5 mint</td>
<td>94°C 1 mint</td>
<td>55°C 1 mint</td>
</tr>
<tr>
<td>3</td>
<td>vanA</td>
<td>98°C 2 mint</td>
<td>98°C 30 sec</td>
<td>48°C 90 sec</td>
</tr>
</tbody>
</table>
Figure No. 1(A): Gram positive cocci with bunch like appearance (Staphylococci) (B): Gram positive cocci bacteria in the form diplo cocci and tetrad (Micrococcus) (C): Gram positive rods bacteria (B. cereus) (D): Gram positive cocci bacteria in the form of short chains (Enterococci).

(A) Different growth morphologies on Nutrient agar (B) S. aureus showing β hemolysis on blood agar.(C) S. aureus showing yellow growth on MSA

Antibiotic Sensitivity Test:

Figure No. 3(A): Vancomycin with reduced susceptibility (B) Methicillin sensitive (C) Vancomycin with reduced susceptibility and methicillin resistant.

Figure (A) shows Agarose gel electrophoresis of PCR product using TStaG primer, L: DNA ladder 1000bp, lanes 1,2,3,4, DNA positive samples showing 370bp DNA bands. Figure B shows Agarose gel electrophoresis of PCR product using mecA primer, L: DNA ladder 1000bp, lanes 1,2,3,4, DNA positive samples showing 512bp DNA bands. Figure C shows Agarose gel electrophoresis of PCR product using vanA primer, L: DNA ladder 1000bp, lane 3 DNA positive sample showing 500 and 900 bp non-significant DNA bands.
DISCUSSION

Nosocomial infections caused by different microbes (commonly bacteria) are a real threat in developing nations where hygienic conditions are poor. More than half of the nosocomial infections are due to bacterial contamination i.e. bacteria present on skin, clothes, aerosol drops can contaminate OT air and also deposit on surfaces\(^1\). Diseased carrier patients and dirty wounds also contaminate operation theatres.\(^8\) Bacterial agents commonly responsible for nosocomial infections include S.aureus, Streptococcus species, CoNS, P.aeruginosa, B. cereus, Enterococci, E. coli.\(^9\) This study was designed for the evaluation of contamination at diverse or various Operation Theaters of a tertiary care from Lahore city. Evaluation was done by using settle plate method at different places of OTs such as entrance, OT table, window and instrument table. Microbial contamination of five different operation theater of a tertiary care hospital was checked. Among the isolated bacteria gram positive cocci i.e Staphylococcus aureus was identified in high percentage. S. aureus is a nosocomial causative pathogen, emergence of vancomycin (effective drug for S.aureus) resistant strain in different part of world is challenging.\(^10\) S.aureus amplified for TStaG gene specific for S. aureus. 13 out of 15 randomly selected samples were positive for the TStaG gene, producing 370bp product. Similar result was observed in previous studies of 7, 19, hence confirming S. aureus. For detection of MRSA strain mecA gene was amplified for 8 isolates. All S. aureus strains were positive for mecA gene producing 533 bp band as observed in previous study.\(^11\) Not a single MRSA strain amplified vanA resistance gene for vancomycin hence confirming absence of vancomycin resistance strain among MRSA. Although there is reports of reduced susceptibility and resistance to vancomycin but in present study it was confirmed that no strain possesses vancomycin resistant vanA gene. Antibiotic resistance of S. aureus by Disk Diffusion Method against different antibiotics was as follow: for Levofloxacin 4/53 (7.55%), for Ceftriaxone 2/53 (3.8%) for Azithromycin 15/53 (28.3%), Amoxicillin/clavulanate 18/53 (34%), for Methicillin 40/53 (75.5%) and Vancomycin 11/53 (20.75%). In present study antibiotic susceptibility showed that Ceftriaxone and levofloxacin are the most effective drugs with least resistance percentages of 3.8 and 7.5 respectively, these finding also observed in this study.\(^12\)

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Targeted gene of Staphylococcus aureus</th>
<th>Amplicon size (bp)</th>
<th>Positive samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>StaG</td>
<td>370 bp</td>
<td>14/16</td>
</tr>
<tr>
<td>2</td>
<td>mecA</td>
<td>533 bp</td>
<td>8</td>
</tr>
<tr>
<td>3</td>
<td>vanA</td>
<td>032 bp</td>
<td>0/7</td>
</tr>
</tbody>
</table>

also confirmed by 46 PCR detection of mecA gene. Although percentage of methicillin resistance S. aureus is different around the globe but in previous study that percentage of around 55% was observed and also present that MRSA strains was sensitive to vancomycin. Vancomycin resistant MRSA are real challenge in wait but in present study all Methicillin resistant isolates are sensitive to vancomycin. Amplification of vanA gene also confirmed the susceptibility test as not a single isolates produce require band of 1032. Instead non-specific bands of size between 500- 900bp might be indicating emergence of resistance.

CONCLUSION

Nosocomial infection can be reduced by proper sterilization of instruments and fumigation of operation theatre which can kill the deadly bacteria i.e S.aureus. This study showed that the vancomycin resistant gene is so far not present and S.aureus can be treated with vancomycin. So selection of proper antibiotic and cleanliness of operation theatre is very important.

Author’s Contribution:

Concept & Design of Study: Nureen Sarwar
Drafting: M Waseem
Data Analysis: Rabiya Jamil, Ayesha Sajjad
Revisiting Critically: Mizna Arif
Final Approval of version: Nureen Sarwar

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

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5. Sexton T, Clarke P, O’neill E, Dillane T, Humphreys H. Environmental reservoirs of methicillin-resistant Staphylococcus aureus in
Assessment of Positive Troponin I in Non-Acute Coronary Syndrome Critically Ill Patients
Sarfraz Ali Mangi, Faisal Ahmed, Naveen Roy, Rubina Khan, Imran Khan Sandeelo and Sumayya Zaman

ABSTRACT

Objective: To determine the frequency of positive Troponin I in non-acute coronary syndrome critically ill patients, at a tertiary care hospital, Karachi.

Study Design: Descriptive / cross sectional study

Place and Duration of Study: This study was conducted at the Cardiology Unit at Liaquat National Hospital Karachi from June 2019 to Dec 2019.

Materials and Methods: Total 148 patients of either gender with age between 35 to 70 years, diagnosed as critical illness were included. Non-ACS was diagnosed through ECG and echocardiography findings. Blood sample was taken for a troponin I test. Outcome variable was diagnosis of elevated Troponin I level. SPSS version 21 used for data analysis. Mean±SD were calculated for quantitative variables. Qualitative variables presented as frequency and percentages. Chi square test was applied and p-value ≤0.05 was taken as significance.

Results: There were 111 male and 37 female patients. The mean age was 51.15±9.76 years. The mean troponin-I score was 3.08±7.47 ng/mL with range 50.7(0.3–51.0). The elevated troponin-I was observed in 84(56.8%) patients. The result showed that age was significantly association with elevated troponin but gender, duration of illness, hypertension, and smoking status were not significantly association.

Conclusion: In conclusion there was high prevalence of cardiac troponin-positive patients admitted with critical illness other than ACS. It increases with the increase in age, predominant in male gender but no significant association with risk factors was noted.

Key Words: Positive Troponin I, Non-Acute Coronary Syndrome, Critically Ill Patients


INTRODUCTION

It is important to determine the extent of disease and outcome of critical patients as it affects management approaches. There are many individual risk factors that predict the intensive care unit (ICU) mortality and can be judged by multiple investigations such as highly elevated troponin-I in critically ill patients. Several reports have shown that cardiac involvement is a significant factor in deciding the outcome of critical patients. For critically sick patients the pathophysiology of myocardial injury is considered to be multi-factorial, including the underlying disease mechanism, hypoxemia, acidosis, and therapeutic maneuvers.

This is estimated that some degree of myocardial damage can complicates as many as 15 per cent of ICU admissions and as many as 85 per cent of patients with sepsis may have elevated cardiac troponin. Multiple studies have measured the prognostic importance of elevated cTnI in chronically ill patients without ACS. While some have proposed that cTnI levels correlate with myocardial damage and bad outcomes, others were unable to validate this association. Troponin I and troponin T cardiac isoforms are highly active and are common indicators for myocardial damage, as the main Diagnostic biomarker of an acute myocardial injury. Cardiac troponins are also important prognostic indicators in acute coronary syndrome and other diseases such as sepsis, septic shock, acute stroke and pulmonary embolism. The increased levels of troponin suggest a worse prognosis epically in SIRS, sepsis and/or septic shock. The elevations of the serum troponin aren't usually due to an acute coronary syndrome. Multiple ICU conditions such as cardiac failure, pulmonary embolism, atrial fibrillation, acute right heart overload, cardiopulmonary resuscitation trauma, myocarditis, pericarditis, sepsis, hypovolemia, electrical cardioversion, renal failure and myocardial
Contusion may lead to serum troponin elevations. Therefore, the secretion and accumulation of troponin is not sufficient by itself to establish an ACS diagnosis. Troponin can be elevated in:
1) Sustained ischemia, with permanent damage to myocytes. The cell membrane degrades, followed by phasing out cytosolic complexes.
2) Conditions allowing increased permeability of the myocyte membrane.
3) Myocardial depressive factors generated during sepsis cause free troponin degradation to components of less molecular weight.
4) Wall stress can cause microinjury and microinfarction to the ventricles.

Higher troponin levels in the absence of ACS will trigger an assessment of an alternative diseaselike pulmonary embolism, renal failure, pneumonia, and sepsis.11,12 Regardless of the origin, elevated troponin levels are likely to have prognostic significance in critically ill patients.13 Apart from having the diagnostic value in myocardial infarction the troponin I is found to have prognostic value in sepsis and critically ill patients. Though sepsis is common presentation in ICU patients with high mortality rate in Pakistan; therefore Troponin I can be used as to assess prognosis in local patients. There is no research study done on such patients locally. This is why the current study is proposed. The results of this study will provide statistics on magnitude of raised serum Troponin I in sepsis and critically ill patients. If serum Troponin I found significantly raised and associated with increased mortality, the study will suggest recommendations for routine screening and aggressive critical care of such patients.

MATERIALS AND METHODS

This single centre, cross-sectional, non probability consecutive study was performed between June 2019 and Dec 2019. The inclusion criterion research population was either gender of 35 to 70 years of age, diagnosed of cases of acute coronary syndrome and de novo lesion (> 70 percent lesion) in a native coronary artery after coronary angiography, in outpatient facilities and inpatients attending cardiology unit at Liaquat National Hospital Karachi. The data were collected after taking permission from Ethical review committee of the Liaquat National Postgraduate Medical Centre Karachi. Approval of synopsis was taken from the College of Physicians and Surgeons of Pakistan. Patients who are brought to intensive care unit with suspicion of critically illness were approached. The patient whose immediate attendant provides the written consent was included in the study. The purpose and procedure of the study were explained and detailed history and physical examination (including pulse, BP, Temperature etc) were done before taking consent. Non-acute coronary syndrome was diagnosed through ECG & echocardiography findings as per operational definitions. It was followed by drawing blood sample, taken from the peripheral vein to perform a troponin I test. Pre-approved proforma was used to collect and document data. Data were collected on demographic variables like gender, name, residence, age, GCS score, level of Troponin I and duration of illness. Outcome variable was diagnosis of elevated Troponin I level. Standard treatment protocols were followed for each patient. Participants in the study were enrolled in a way that confounding factors were controlled by strictly following the selection criteria.

Statistical analysis: Data were analyzed after entering into SPSS version 21. Continuous variables like age, duration of illness, GCS score, level of Troponin I were analyzed as mean ± Standard deviation. Categorical variable like gender, diagnosis of elevated Troponin I level were expressed in frequency & proportions. Age, gender, duration of illness, GCS score were stratified to analyze the effect of these variables on outcome. It was followed by applying the Chi-square test with a P value ≤0.05 was taken as significant.

RESULTS

Total 148 patients of either gender with age between 35 to 70 years, who were diagnosed as critically ill with duration ≥24 hours up to 7 days, were included in this study to determine frequency of positive Troponin-I in non-acute coronary syndrome. Stratification was accomplished, and post-stratification chi square testing was applied to observe the effect of modifiers on the result. The value of P ≤0.05 was considered to be substantial.

The results revealed that there were 111 male and 37 female patients. [Table-2]. The mean age of participants at study was 51.15±9.76 years, with a range of 35(35–70) years. The age distribution is given in Graph-1. The comprehensive descriptive age statistics are given in Table-1. The age in two classes was stratified. 71 patients were under 50 years of age and 77 patients were over 50 years of age.[Graph-1]

The mean duration of illness was 2.57±0.57 days, with range 2(2–4) days. [Table-1].

The mean GCS score was 3.64±1.25, with range 4(2–6). [Table-1]

The results showed that 41.9% patients were hypertensive and 55.4% patients were smokers. Table-2

The mean troponin-I level was 3.08±7.47 ng/mL with range 50.7(0.3–51.0). [Table-1]. With reference to the troponin-I levels it was revealed that elevated troponin was observed in 56.8% patients. [Graph-2]

The descriptive statistics for age, duration of illness, and GCS score according to elevated troponin-I was also calculated. The results showed that among patients with elevated troponin-I mean age was 49.65±9.33
years, mean duration of illness was 2.58±0.54 days, and mean GCS score was 3.86±1.30. The detailed descriptive statistics are presented in Table-13, Table-14 and Table-15 respectively. Stratification with respect to age, duration of illness, gender, GCS score, hypertension, and smoking status was done to check effect of these modifiers on outcome i.e. elevated troponin-I levels. Post stratification Chi square test was measured and p-value ≤0.05 was considered as significant. The result showed among total patients who were observed elevated troponin, 64 were male patients and 20 were female patients. [Graph-2]. The association was not significant with gender (p=0.702). There were 47 patients of age ≤50 years and 37 patients of age >50 years. [Graph-2] The association of age was found significant (p=0.026). Among these patients of elevated troponin-I, GCS score was ≤4 in 40 patients and it was >4 in 44 patients. The association of was found significant (p=0.017). Total 35 patients were hypertensive and 50 patients were smokers. The association was not found significant among hypertension (p=0.949) and also with smoking (p=0.248).

**Table No.1: Descriptive statistics of age, duration of dyspepsia**

<table>
<thead>
<tr>
<th>Statistics</th>
<th>Age (Years)</th>
<th>Duration of illness (days)</th>
<th>GCS Score</th>
<th>Troponin I level (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimum</td>
<td>35</td>
<td>2</td>
<td>2</td>
<td>0.3</td>
</tr>
<tr>
<td>Maximum</td>
<td>70</td>
<td>4</td>
<td>6</td>
<td>51.0</td>
</tr>
<tr>
<td>Mean</td>
<td>51.15</td>
<td>2.57</td>
<td>3.64</td>
<td>3.08</td>
</tr>
<tr>
<td>Std. Deviation</td>
<td>9.76</td>
<td>0.57</td>
<td>1.25</td>
<td>7.47</td>
</tr>
</tbody>
</table>

**Table No.2: Frequency distribution of gender, hypertension, smoking status, elevated Troponin I level(n=148)**

<table>
<thead>
<tr>
<th>Gender</th>
<th>Frequency(n)</th>
<th>Percentage (%)</th>
</tr>
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<tbody>
<tr>
<td>Male</td>
<td>111</td>
<td>75.0%</td>
</tr>
<tr>
<td>Female</td>
<td>37</td>
<td>25.0%</td>
</tr>
<tr>
<td>Total</td>
<td>148</td>
<td>100%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hypertension</th>
<th>Frequency(n)</th>
<th>Percentage(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>YES</td>
<td>62</td>
<td>41.9%</td>
</tr>
<tr>
<td>NO</td>
<td>86</td>
<td>58.1%</td>
</tr>
<tr>
<td>Total</td>
<td>148</td>
<td>100%</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Smoking status</th>
<th>Frequency (n)</th>
<th>Percentage(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>YES</td>
<td>82</td>
<td>55.4%</td>
</tr>
<tr>
<td>NO</td>
<td>66</td>
<td>44.6%</td>
</tr>
<tr>
<td>Total</td>
<td>148</td>
<td>100%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Elevated Troponin I level</th>
<th>Frequency (n)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>YES</td>
<td>84</td>
<td>56.8%</td>
</tr>
<tr>
<td>NO</td>
<td>64</td>
<td>43.2%</td>
</tr>
<tr>
<td>Total</td>
<td>148</td>
<td>100%</td>
</tr>
</tbody>
</table>

**DISCUSSION**

For critically ill patients with mechanical ventilation elevated cTnI is associated with higher mortality and longer duration. Cardiac troponin I and T are the most widely known and sensitive laboratory markers of myocardial tissue damage, and can increase in patients with many other diseases than acute coronary syndrome.1,5 In a study14,17 (55 percent) of 58 patients admitted to two intensive medical care units as a result of serious diseases other than ACS, or 32 (63 percent) of 51 patients admitted for sepsis, SIRS, or septic shock, were troponin-positive. Mortality in troponin-positive patients was fourfold higher and LVEF considerably lower compared to troponin-negative patients. It is the first research in which the majority of troponin-positive patients attempted to systematically eliminate severe coronary artery disease by autopsy or stress echocardiography.14 Our results showed that the elevation of troponin could be used as a potential risk factor for mortality for patients in intensive care without coronary artery disease. This is interesting that
there was no substantial difference in SAPS between troponin-positive and negative patients while a slightly higher percentage of shock-presenting patients were troponin-positive relative to those without shock. Elevated rates of cTnl also correlate with reduced left ventricular activity in both non-coronary and coronary patients. Cardiac dysfunction in sepsis is relatively well known and has been associated with poor prognosis. In addition, a small recent study indicated that 44 percent of patients with extreme sepsis had systolic dysfunctions. Their data showed that there is a stronger association between elevated cTnl and mortality in patients over 65, which is likely to be due to the degree, and probably reversibility, of myocardial injury in this age group. An significant finding from this study was that the majority of deaths among younger patients occurred during the first five days, while the majority of deaths (60 percent) occurred in the elderly population during this time period. Several non-coronary medical trials dealt with the prognostic significance of elevated cTnl. Elevated cTnl correlated with poor outcome in selected groups such as patients with COPD and hemodialysis. A research in individuals with emergency department found that there is a significant correlation between elevation and outcome of cTnl. Relos et al.22 evaluated ICU patients, suggesting that moderate serum troponin I levels below the threshold for diagnosing acute myocardial infarction, which is associated with recurrent myocardial damage in critically ill patients and higher mortality rates and longer hospital and duration of ICU stay. A significant correlation between death rates and elevated cTnl was observed in studies involving critically ill medical patients without coronary disease. However, the sample size was very small (58 patients) and most patients had sepsis (88%), restricting the interpretation of these results. Like those research. Kollef et al.11 indicated that cTnl serial measurements do not contribute independently to predicting hospital mortality beyond that given by clinically recognised cardiac dysfunction. Nevertheless, as previously suggested, elevated cTnl was previously associated with left ventricular function. The difficult interpretation of non-coronary troponin rises reflects the limited understanding of the etiology of myocardial cell injury. It is clear how an acute coronary event or an oxygen supply-demand imbalance can render heart cells ischemia and how the subsequent necrosis leads to troponin release into the plasma. It is less clear how a diverse group of disease processes can result in troponin leaks with no evidence of coronary disease, and why this should be such a consistent predictor of poor outcomes. In Alattasiet al.24 study the association of increased mortality with increased troponin level was observed whether patients had underlying advanced heart failure or not.

Our study results are comparable with the above stated literature findings. In our study ratio of male patients was very high as with female patients. More patients were found with age ≥ 50 years. The duration of illness before reporting was 2 to 4 days. The mean troponin-I was 3.08±7.47 ng/mL with range 50.7(0.3–51.0) hence by the criteria elevated troponin was observed in 84(56.8%) patients. As male patients are more in our study, elevated Troponin was also found more in males rather than females, but the difference was not significant. More patients were aged ≥ 50 years in our study but the elevated Troponin I was observed more in patients with age ≤50 years and the association of age was found significant. Smoking status and hypertension was not associated with elevated Troponin I among non ACS patients.

CONCLUSION

The study results showed high prevalence of cardiac troponin-positive patients admitted with critical illness other than ACS. It increases with the increase in age, predominant in male gender but no significant association with risk factors was noted. We conclude that troponin elevation may be used as an early marker of severity of illness and outcome, particularly in older patients, male gender and patients with low GCS score.

Author’s Contribution:
Concept & Design of Study: Sarfraz Ali Mangi
Drafting: Faisal Ahmed, Naveen Roy
Data Analysis: Rubina Khan, Imran Khan Sandeeel, Sumayya Zaman
Revisiting Critically: Sarfraz Ali Mangi, Faisal Ahmed
Final Approval of version: Sarfraz Ali Mangi

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

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4. Kakihana Y, Ito T, Nakahara M, Yamaguchi K, Yasuda T. Sepsis-induced myocardial dysfunction:
Frequency of Left Main Coronary Artery Disease in Patients Having ST-Elevation in Lead AVR on Electrocardiogram Presenting with Acute Coronary Syndrome


ABSTRACT

Objective: To determine the frequency of left main coronary artery disease in patients presenting with acute coronary syndrome having ST elevation in lead avR.

Study Design: Descriptive/ cross sectional study

Place and Duration of Study: This study was conducted at the Department of Cardiology, Liaquat National hospital, Karachi from March 2019 to September 2019.

Materials and Methods: Total 246 patients presented with acute coronary syndrome had ST elevation in lead avR > 0.5 mm on ECG were included. Demographic data were recorded. All patients underwent coronary angiography to diagnose coronary artery disease. SPSS version-21 was used. Descriptive statistics were calculated. Stratification was done and chi square test was applied. P-value ≤0.05 was taken as significance.

Results: There were 174 male and 72 female patients. The mean duration of chest pain was 45.01±14.40 minutes. 42.3% were diabetic, 58.9% were hypertensive, 37.8% were smokers, and 42.3% were obese. The left main stem disease was observed in 201(81.7%) patients and its significant association was observed with smoking and obesity with p<0.05.

Conclusion: The ST-segment elevation on lead aVR was an important predictor of occurrence of left main disease in patients with ACS.

Key Words: Left Main Coronary Artery Disease, Electrocardiography, ST Elevation In Lead avR, Angiocardiography

Citation of article: Roy N, Ahmed F, Shakir MA, Mangi SA, Sandeelo IA, Kakepoto N. Frequency of Left Main Coronary Artery Disease in Patients having ST-Elevation in Lead AVR on Electrocardiogram Presenting with Acute Coronary Syndrome. Med Forum 2020;31(9):130-135.

INTRODUCTION

Coronary artery illness is among the top causes of mortality in the globe. Acute coronary syndrome comprises of ST-elevation myocardial infarction, unstable angina and non-ST elevation myocardial infarction. Identification of clinical and electrocardiographic characteristics predictive of severe left main coronary artery disease is critical, especially in individuals diagnosed with an acute coronary syndrome.

A severe left main stem stenosis is known to be a lesion comprising over 50 percent of the vessel diameter. Left main stem stenosis usually occurs in 3 percent to 5 percent of all individuals undergoing coronary angiography and in 30 percent of coronary artery bypass grafting patients.

This is associated with multi-vessel coronary artery disease about 70 per cent of the time as present. Majority of individuals are symptomatic and at significant risk of coronary problems, since this vessel's occlusion reduces the flow of at least 75% of the left ventricle, whether it is covered by collateral flow or patent bypass grafting to either the left anterior descending artery or left circumflex arteries. Studies carried out before revascularization with coronary artery bypass graft became the standard of treatment showed a weak prognosis for these patients, with survival of three years as low as 37 per cent. Coronary artery bypass graft is associated with slightly improved coronary outcomes including survival as compared directly to conventional treatment.

For one study, the finding on electrocardiogram of the ST-segment elevation for lead avR bis V1 separated the left main stenosis group from the left anterior...
descending artery group with elevated diagnostic values of 80 percent of the left main coronary artery disease. The aim of my study is to determine the frequency of left main coronary artery disease in patient with acute coronary syndrome with ST elevation in lead avR. If result of my study shows high frequency of left main coronary artery disease, then recommendation will be to manage the patient earlier so that we can reduce morbidity and mortality.

**MATERIALS AND METHODS**

Two hundred and forty six consecutive patients from Department of cardiology, Liaquat National hospital, Karachi from March 2019 to September 2019 were enrolled in study after fulfilling the inclusion criteria. Risks, benefits and procedure of research were explained to the patient and informed consent was taken by the investigator. Demographic data like name, age, gender, chest pain, co-morbidities and left main disease were recorded on the attached performa. Identity was kept confidential. No fatal risk was present in the study. All patients had ST-segment elevation in lead avR were underwent coronary angiography (which is the gold standard to diagnose coronary artery disease) to diagnose left main coronary artery disease.

**Sample Selection**

**Inclusion Criteria:**
- Both genders. Age above 40 and below 75.
- Patients presenting with acute coronary syndrome having ST-elevation in lead avR > 0.5 mm on electrocardiogram.

**Exclusion Criteria:**
- Patients with chronic kidney disease who were on dialysis (GFR<15ml/min/1.73m2).
- Patients having severe anemia (Hb< 7g/dl).
- Patients with dextro-cardia defined by heart on the right side on chest x-ray.
- Patients who underwent circulatory collapse requiring cardiopulmonary resuscitation or any major complication during angioplasty like cardiogenic shock, renal failure or unconsciousness. (confirmed by patient history)
- Patients having ejection fraction less than 20%.
- Patients having previous history of coronary artery bypass graft.

**Data Analysis:** Confounding variable and biasness were controlled strictly by following inclusion and exclusion criteria. Data were analyzed using SPSS Version 21 quantitative data like age, duration of chest pain were presented as mean and standard deviation. Qualitative data like gender, diabetes mellitus, hypertension, smoking, obesity and left main coronary artery disease were presented on frequency tables and percentages. Data were stratified for age, duration of chest pain, gender, diabetes mellitus, hypertension, smoking and obesity. Post stratification Chi-Square test was used. P value < 0.05 was taken as significant.

**RESULTS**

In this analysis, a total of 246 patients of either sex over 40 years of age and below 75 years of age with acute coronary syndrome with ST-elevation on electrocardiogram in lead avR > 0.5 mm were included to evaluate the left main stem condition. After stratification Chi square test was applied to observe the effect of modifiers on the result. It was found that P-value 0.05 was relevant.

The findings showed 174 patients were male and 72 were female. The distribution of frequencies is set out. The median age of subjects at study was 54.42±9.35 years. The detailed descriptive age statistics are presented. For two classes age has been stratified. The lifespan of 155 patients was around 55 years and > 55 years was the lifespan of 91 patients. It provides detailed systematic estimates of age by age group.

The mean duration of chest pain was 45.01±14.40 minutes. The duration of chest pain was stratified in two groups. Duration of 130 patients was ≤45 minutes and duration of 116 patients was >45 years. The detailed descriptive statistics of duration of chest pain according to groups are presented.

The findings were reported individually on the history of associated diseases. Tests revealed that 42.3 per cent of patients had diabetes. Patients were 58.9 per cent hypertensive, 37.8 per cent smokers, and 42.3 per cent obese. The results showed that among total patients, STEMI was observed in 56.5% patients, NSTEMI was observed in 26.8% patients, and unstable angina was observed in 16.7% patients. Final outcome i.e. left main stem disease was observed in 201(81.7%) patients.

Stratification with regard to sex, age, period of chest pain, diabetes mellitus, hypertension, smoking, and obesity was performed to determine the impact on outcome of these modifiers. Chi square post stratification check was used and P-value 0.05 was found to be relevant. The results showed that smoking (p=0.017) and obesity (p=0.003) were significantly associated with left main stem disease. No significant association of left main stem disease was found with gender (p=0.764), age (p=0.825), duration of chest pain (p=0.163), diabetes (p=0.321), and hypertension (p=0.873). Detail description is given in tables no. 1, 2 and 3 and in graphs 1 and 2.

**Table No.1: Descriptive statistics of age, duration of chest pain**

<table>
<thead>
<tr>
<th>Statistics</th>
<th>Age (Years)</th>
<th>Duration of chest pain (minutes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimum</td>
<td>41</td>
<td>25</td>
</tr>
<tr>
<td>Maximum</td>
<td>72</td>
<td>70</td>
</tr>
<tr>
<td>Mean</td>
<td>54.42</td>
<td>45.01</td>
</tr>
<tr>
<td>Std. Deviation</td>
<td>9.35</td>
<td>14.40</td>
</tr>
</tbody>
</table>
Table No. 2: Frequency distribution of gender, Diabetes mellitus, hypertension, smoking status, Provisional diagnosis(n=246)

<table>
<thead>
<tr>
<th></th>
<th>Frequency (n)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>174</td>
<td>70.7%</td>
</tr>
<tr>
<td>Female</td>
<td>72</td>
<td>29.3%</td>
</tr>
<tr>
<td>Total</td>
<td>246</td>
<td>100%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Frequency (n)</td>
<td>Percentage (%)</td>
</tr>
<tr>
<td>Yes</td>
<td>104</td>
<td>42.3%</td>
</tr>
<tr>
<td>No</td>
<td>142</td>
<td>57.7%</td>
</tr>
<tr>
<td>Total</td>
<td>246</td>
<td>100%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Frequency (n)</td>
<td>Percentage (%)</td>
</tr>
<tr>
<td>YES</td>
<td>145</td>
<td>58.9%</td>
</tr>
<tr>
<td>NO</td>
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<td>41.1%</td>
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<tr>
<td>Total</td>
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<td>100%</td>
</tr>
<tr>
<td>Smoking status</td>
<td>Frequency (n)</td>
<td>Percentage (%)</td>
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<tr>
<td>NO</td>
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<td>62.2%</td>
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<td>Total</td>
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<td>100%</td>
</tr>
<tr>
<td>Obesity</td>
<td>Frequency (n)</td>
<td>Percentage (%)</td>
</tr>
<tr>
<td>YES</td>
<td>104</td>
<td>42.3%</td>
</tr>
<tr>
<td>NO</td>
<td>142</td>
<td>57.7%</td>
</tr>
<tr>
<td>Total</td>
<td>246</td>
<td>100%</td>
</tr>
<tr>
<td>Provisional diagnosis</td>
<td>Frequency (n)</td>
<td>Percentage (%)</td>
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<tr>
<td>STEMI</td>
<td>139</td>
<td>56.5%</td>
</tr>
<tr>
<td>NSTEMI</td>
<td>66</td>
<td>26.8%</td>
</tr>
<tr>
<td>UA</td>
<td>41</td>
<td>16.7%</td>
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<tr>
<td>TOTAL</td>
<td>246</td>
<td>100%</td>
</tr>
<tr>
<td>Left main disease</td>
<td>Frequency (n)</td>
<td>Percentage (%)</td>
</tr>
<tr>
<td>YES</td>
<td>201</td>
<td>81.7%</td>
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<tr>
<td>NO</td>
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<tr>
<td>TOTAL</td>
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<td>100%</td>
</tr>
</tbody>
</table>

Graph No.1: Histogram presenting distribution of age (years) (n=246)

Table No. 3: Frequency and association of left main stem disease according to gender(n=246)

<table>
<thead>
<tr>
<th>Left Main Stem Disease</th>
<th>Yes (n=201)</th>
<th>No (n=45)</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (n=174)</td>
<td>143</td>
<td>31</td>
<td>174</td>
<td>0.764**</td>
</tr>
<tr>
<td>Female (n=72)</td>
<td>58</td>
<td>14</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td>201</td>
<td>45</td>
<td>246</td>
<td></td>
</tr>
</tbody>
</table>

| ≤ 55 years (n=155) | 126 | 29 | 155 | 0.825** |
| > 55 years (n=91)  | 75  | 16 | 91  |         |
| TOTAL               | 201 | 45 | 246 |         |

Graph No.2: Histogram presenting distribution of duration of chest pain (minutes) (n=246)

Graph No.3: Frequency and association of left main stem disease according to gender(n=246)
DISCUSSION

The most daunting lesion in people with acute coronary syndromes is left main coronary artery stenosis. Although the amount of myocardium at risk is very high, the patient is always in a cardiogenic shock, with a high risk of death and much more so in a left dominant coronary system. Total left main thrombosis typically leads to abrupt cardiac arrest and patients who are affected will end up dying before they arrive at hospital. In example, patients with subtotal left main occlusion may have an acute coronary syndrome with a generalized electrocardiographic pattern of ST depression in the anterior with inferior leads. In the case of acute coronary syndromes, STE-aVR (1 mm) with diffuse ST weakness in other leads is generally a symptom of extreme left main disease; it is often associated with poor results...Ionescu et al16 stated that the electrocardiographic findings of thrombosis of the left principal coronary artery could be unspecific. STE-aVR will, however, raise fears of serious left principal disease. Furthermore, Taglieri et al17 reported that STE-aVR and reciprocal ST depression in other leads are highly predictive of serious left main disease in the context of non-STE acute coronary syndrome. The mechanism of STE-aVR is not completely understood. Lead aVR is electrically opposed to leads D1, D2, aVL, and V3–V6, and therefore a ST depression in these leads induces reciprocal STEaVR.19 However, lead aVR directly represents the electrical activity of the right upper part of the heart, including the basal portion of the interventricular septum and, subsequently, a transmural infarction. Accordingly, STE-aVR is thought to arise from one of the following two mechanisms: diffuse antero-lateral subendocardial ischemia with reciprocal improvement in aVR or basal portion of the heart transmural infarction. However, an anatomical version of the Purkinje fibers was evoked to clarify the absence of STE in anterior leads in some cases, following anterior transmural infarction. The upper right portion of the heart is the outflow path of the right ventricle and the basal portion of the interventricular septum, is supplied by the main stem of the left coronary artery and/or branches of the proximal sections of the left anterior descending artery; thus, lesions in these coronary segments induce elevations of the ST-segment in lead aVR due to the dominance of the basal ventricular mass, this should lead to produce elevation in lead aVR, as the ST-segment vector in the frontal plane points in a superior direction. In most studies, Lead aVR showed ST-segment elevation in occlusion of left main stem. In one study there was 88% (14/16) of patients showed ST segment-elevation in Lead aVR in the occlusion of left main stem group, whereas ST-segment elevation was found in 43% (20/46) of patients in the left anterior descending artery group and only 8% (2/24) of patients in the right coronary artery group. Kosuge et al conducted a comparable study to find, in patients with acute coronary syndrome, an early, clear and non-invasive indicator of left main stem or 3-vessel disease. He conducted a retrospective ECG study of 310 patients diagnosed with acute myocardial infarction in the ST-segment elevation, which was subsequently coronary angiography. Multivariate ECG findings review determined ST-segment elevation greater than 0.5 mm in lead aVR as the best indicator of left main stem or 3-vessel disease, higher than ST-segment depression in other leads. The AVR on a 12-lead ECG gives useful information of heart upper right side of heart. This is typically not used in clinical settings, however, and is usually used and interpreted as reciprocal information from the left lateral leads, or to detect changes in endocardial electrography. During the 1980s, it was noted that ST elevation in lead aVR was correlated with LM occlusion. But up until the late 1990s, ECG interpreters still ignored the aVR. Reports have shown over the past couple of years that ST elevation in lead aVR was not only associated with an occlusion of LM but also demonstrated an anterior wall infarction. As was mentioned earlier, and as proven in our data, ST elevation in lead aVR strongly suggests a significant LM lesion. Furthermore, if followed by ST elevation in lead V1, the specificity of an LM lesion which acts as the vessel of the guilty increases. Given that both leads aVR and V1 have ST elevations, a greater magnitude of ST in lead aVR relative to lead V1 is very similar to LM occlusion. In 2016, Morris et al studied a total of 12 best evidence papers chosen from 141 publications and found that "In patients with acute coronary syndrome, STE in lead aVR can reliably identify acute myocardial infarction caused by lesion with LMCA" and found that it has only a limited diagnostic benefit to identify patients with LMCA stenosis. Lead aVR reports a mirror-like image of lead V5. Therefore, if the lateral precordial leads contain depression in the ST-segment, lead aVR will almost exclusively display elevation in the ST-segment. Additionally, lead aVR has a special location by "looking" from the right shoulder into the left ventricular cavity, thereby indicating ischemia of the left ventricular wall’s internal layers. In most studies, Lead aVR showed ST-segment elevation in occlusion of left main stem. In one study there was 88% (14/16) of patients showed ST segment-elevation in Lead aVR in the occlusion of left main stem group, whereas ST-segment elevation was found in 43% (20/46) of patients in the left anterior descending artery group and only 8% (2/24) of patients in the right coronary artery group.
Upon multivariate evaluation, elevation of the ST segment in lead aVR was the only variable from the initial ECG that was closely correlated with repeated ischemic events and heart failure in hospitals, and was maintained as an independent predictor of death. Accordingly, Barrages concluded that the worse results in these cases would motivate doctors to try an early invasive method in treating patients with such alarming electrocardiographic findings.19,20

In our study left main stem disease was found in 201(81.1%) patients who had ST segment elevation on aVR lead. The significant association was observed with smoking and obesity. No association was observed with sex, age, duration of chest pain, diabetes, hypertension, and smoking. These results are comparable with the above stated studies and literature.

**CONCLUSION**

STE-aVR in the context of acute coronary syndrome is often associated with left main coronary severe disease and clinicians need to be alerted of this critical condition. For patients with acute coronary syndrome the elevation of the ST section for lead aVR distinguishes patients with serious coronary artery disease on angiography. In the global evaluation of patients with acute coronary syndrome, the study of electrocardiographic anomalies in lead aVR of widely available standard ECGs is critical.

In conclusion, the result of this study found that ST-segment elevation on lead aVR was an important predictor of occurrence of left main stem disease and found that ST-segment elevation in lead aVR was associated with increase risk factors like smoking and obesity.

**Author’s Contribution:**

Concept & Design of Study: Naveen Roy  
Drafting: Faisal Ahmed, Muhammad Ali Shakir  
Data Analysis: Sarfraz Ali Mangi, Imran Khan Sandeelo, Nouman Kakepoto  
Revisiting Critically: Naveen Roy, Faisal Ahmed  
Final Approval of version: Naveen Roy

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

**REFERENCES**

Comparative Study of Fine Needle Aspiration Cytology (F.N.A.C) Vs Tissue Biopsy in Thyroid Glands: Following Bethesda System

Nadeem Reyaz¹, Muhammad Bahadur Baloch², Muhammad Ejaz Butt³, Shaukat Siddique¹, Sadia Hussain Malik⁴ and Javeria Noor²

ABSTRACT

Objective: To appraise the diagnostic role of fine needle aspiration cytology (F.N.A.C) as preoperative tool in patients with enlarged thyroid glands to avoid unnecessary surgery.

Study Design: Descriptive study

Place and Duration of Study: Department of Histopathology, Gulab Devi Hospital Lahore during period of three years i.e. January 2012 to December 2015.

Materials and Methods: A total of 185 patients were recruited for study of fine needle aspiration. Smears were made with the aspirated material and were stained with Hematoxylin-Eosin stain.

Results: There were 138 (74.59%) females and 47 (25.41%) male patients. Smears from 32 (23.19%) female patients were classified as malignant-Bethesda VI, 84 (60.87%) as benign-Bethesda II, 4 (2.9%) as suspicious for follicular neoplasia-Bethesda IV, 2 (1.45 %) as suspicious for malignancy-Bethesda VI, 3 (2.17%) as atypical-Bethesda-III and 13 (9.42%) as unsatisfactory-Bethesda I. In case of 47 male patients, smears from 3 (6.38%) were classified as malignant-Bethesda VI, 38 (80.85%) as benign and 6 (12.77%) were considered as unsatisfactory-Bethesda I.

Conclusion: F.N.A.C is a safe, rapid, reliable and a simple test for discriminating between malignant and malignant lesions in nodules of the thyroid. It is currently practiced worldwide and proves to be the most cost-effective and dependable diagnostic procedure.

Key Words: Thyroid gland, Fine Needle Aspiration Cytology, Nodule, Bethesda Classification System

INTRODUCTION

Fine needle aspiration cytology (F.N.A.C) has now become a widely accepted and invaluable diagnostic tool in the overall management of patients¹. The thyroid enlargement is relatively common finding in clinical practice and one of the major problems in our country². The thyroid is influenced by a various pathologic lesions following inflammation, neoplasia, dietary iodine deficiency and iatrogenic causes that are manifested by varied morphologies³.

Despite the large number of lesions, it is convenient to consider them as categorized into two major types one who reveal a diffuse pattern and those that produce nodules. Diffuse thyroid lesions are those that are related with conditions affecting the whole gland such as thyroiditis and hyperplasia. Nodular lesion consists of non-neoplastic hyperplasia like in toxic multinodular goitre, benign tumors e.g. toxic adenoma, malignant tumors like papillary, medullary, follicular carcinomas, and anaplastic carcinoma⁴.

F.N.A.C is one of the accepted methods due to its simple, a-traumatic and cost effective qualities. Its specificity is >80 % in benign and >90% in malignant pathology giving it high precision rate⁵. Its diagnostic assessment has been found to be superior to ultrasonography and CT-scan⁶. Nowadays, F.N.A.C is recommended for the all patients before going for invasive procedures and treatment⁷. The diagnostic accuracy of this simple out-patient procedure is best when an experienced cytopathologist or a fully trained aspirator performs the aspiration, smearing and preservation⁸. To overcome deficiency and discrepancy of diagnosis, Bethesda System for reporting thyroid cytopathology is currently practiced. This system was established in 2008 to ensure strict
diagnostic criteria for thyroid F.N.A.C samples. This classification system facilitated effective communication among cytopathologists, surgeons, endocrinologists, radiologists and other health care providers correlating with thyroid diseases. The study was therefore designed to evaluate the efficiency of Bethesda system in cytological diagnosis of thyroid lesion and to correlate it with histologic findings.

MATERIALS AND METHODS

A total of 185 patients including 138 females and 47 males, who presented with clinically suspicious thyroid enlargement and subjected for excision biopsy, during January 2012 to December 2015, at the Department of Histopathology, Gulab Devi Hospital, Lahore, Pakistan were accrued into this study. After taking written informed consent, a detailed history and physical examination, they were selected for fine needle aspiration cytology before going for surgical biopsy of the thyroid gland. This study is approved from institutional review board for Ethical clearance. The study was therefore designed to evaluate the efficiency of Bethesda system in cytological diagnosis of thyroid lesion and to correlate it with histologic findings.

| Bethesda I | No diagnostic / Unsatisfactory |
| Bethesda II | Benign |
| Bethesda III | Atypia of undetermined significance or follicular lesion of undetermined significance |
| Bethesda IV | Follicular neoplasm or suspicious for follicular neoplasm |
| Bethesda V | Suspicious for malignancy |
| Bethesda VI | Malignant |

For histopathological assessment, 4-6µm thick sections of paraffin embedded tissue blocks were cut and stained with H&E stain. The histologic findings were recorded. Definite diagnosis was established under two categories:

1. Benign
2. Malignant

Surgical biopsies of all 185 patients underwent histopathological assessment.

RESULTS

A total of 185 fine needle thyroid gland aspirations were performed in the period between January 2012 to December 2015 at the Department of Histopathology, Gulab Devi Hospital, Lahore. These include 138(74.59%) female and 47(25.41%) male patients. Table-1 shows the results of gender distribution in palpable enlarged thyroid gland aspirations performed on 185 patients.

In 115 (62.16%) cases on which biopsy was executed, the lesion was a solitary nodule; in 48 (25.94%) cases, several nodules were present, and cytology was executed on the nodule which was dominant. In 22 (11.89%) cases, there was diffuse non-nodular enlargement of the thyroid gland. Lesion on which F.N.A.C was performed included 135 (72.97%) solid lesions, 26 (14.05%) partially cystic and partially solid lesions and 8 (4.32 %) cystic lesions (Figure-1). Data regarding consistency in 16 cases (8.64 %), was not available amongst the 22 cases of diffuse enlargement.

Sample Adequacy: Out of 185 fine needle aspiration cases, 179 (96.76%) of the cytology specimens were taken as sufficient for cytological diagnosis.

Female Thyroid Lesions: Malignancy-Bethesda daVI comprised 32 cases (23.19%) out of 138 aspirates performed on the thyroid gland. Benign lesion-BethesdaII accounted for 84 cases (60.87%), most of them consisting of uniform looking follicular arranged cells and colloid background. 3 (2.17) cases showed atypia-Bethesda III with slight pleomorphism and disturbed uniformity. A total of 4 (2.9%) cases were found to be suspicious for neoplasia-Bethesda-IV, 2 (1.45 %) cases were suspected for malignancy-Bethesda IV, 13 (9.42%) were considered as unsatisfactory-Bethesda I and were characterized by poor cellularity and hemorrhage. Majority of benign cases fall in age group of 10-19 years where as malignant are in 50-59 years age group (Table-2)

Male Thyroid Lesions: This group included 47 cases (25.41%), these comprised 3 (6.38%) as malignant-Bethesda IV with majority in 60-69 years age group, 38 (80.85%) as benign-Bethesda II in 10-19 years age group and 6 (12.77%) were considered as unsatisfactory cases-Bethesda I. There was no false-positive diagnosis of malignant neoplasm of the thyroid gland. The fine needle aspiration cytology findings were accordant with the histologic findings of the tissue biopsy (Table-3& 4).

The specificity, sensitivity and precision of fine needle aspiration cytology in the distinction of non-neoplastic (benign) from neoplastic (malignant) lesions of the thyroid gland in patients with an ample cytology smear were 83.56%, 100% and 87.03% respectively. The positive predictive value is 100 % while the negative predictive value is 61.9 % (Table-4).

Applying Fisher Exact test, no significant association (p =0.05) was seen between clinical variables and cytological as well as histological findings.
Table No.1: Cytological Diagnosis & Sex Distribution in 185 Cases of Thyroid Lesions

<table>
<thead>
<tr>
<th>Cytologic diagnosis</th>
<th>Bethesda classification</th>
<th>Gender</th>
<th>Total</th>
<th>Overall percentages</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Male</td>
<td>Female</td>
<td></td>
</tr>
<tr>
<td>Unsatisfactory</td>
<td>Bethesda-i</td>
<td>06</td>
<td>13</td>
<td>19</td>
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<tr>
<td>Benign</td>
<td>Bethesda-ii</td>
<td>38</td>
<td>84</td>
<td>122</td>
</tr>
<tr>
<td>Atypical</td>
<td>Bethesda-iii</td>
<td>Nil</td>
<td>03</td>
<td>03</td>
</tr>
<tr>
<td>Suspicious for</td>
<td>Bethesda-IV</td>
<td>Nil</td>
<td>04</td>
<td>04</td>
</tr>
<tr>
<td>Follicular Neoplasia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Suspicious for</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignancy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignant</td>
<td>Bethesda-VI</td>
<td>03</td>
<td>32</td>
<td>35</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>47</td>
<td>138</td>
<td>185</td>
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</table>

Table No.2: Correlation between cytological diagnosis, age group and gender

<table>
<thead>
<tr>
<th>Age Group (yrs)</th>
<th>Total No. of Patients</th>
<th>Gender Distribution</th>
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</thead>
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<tr>
<td></td>
<td></td>
<td>Male</td>
</tr>
<tr>
<td>0-9</td>
<td>02</td>
<td>B-I 1</td>
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<tr>
<td></td>
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<td>B-II 0</td>
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<td></td>
<td></td>
<td>B-III 0</td>
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<tr>
<td>10-19</td>
<td>92</td>
<td>B-I 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B-II 17</td>
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<tr>
<td></td>
<td></td>
<td>B-III 0</td>
</tr>
<tr>
<td>20-29</td>
<td>16</td>
<td>B-I 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B-II 5</td>
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<tr>
<td></td>
<td></td>
<td>B-III 0</td>
</tr>
<tr>
<td>30-39</td>
<td>24</td>
<td>B-I 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B-II 8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B-III 0</td>
</tr>
<tr>
<td>40-49</td>
<td>16</td>
<td>B-I 0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B-II 4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B-III 0</td>
</tr>
<tr>
<td>50-59</td>
<td>22</td>
<td>B-I 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B-II 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B-III 0</td>
</tr>
<tr>
<td>60-69</td>
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<td></td>
<td>B-II 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B-III 0</td>
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</table>

Table No.3: Histological Diagnosis of the Thyroid Lesions

<table>
<thead>
<tr>
<th>Histological Diagnosis</th>
<th>Number of Cases</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Malignant</td>
<td>35</td>
<td>18.91%</td>
</tr>
<tr>
<td>Papillary Carcinoma</td>
<td>14</td>
<td>40%</td>
</tr>
<tr>
<td>Follicular carcinoma</td>
<td>12</td>
<td>34.29%</td>
</tr>
<tr>
<td>Medullary carcinoma</td>
<td>04</td>
<td>11.43%</td>
</tr>
<tr>
<td>Hurtle cell tumor</td>
<td>02</td>
<td>5.71%</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>02</td>
<td>5.71%</td>
</tr>
<tr>
<td>Anaplastic carcinoma</td>
<td>01</td>
<td>2.86%</td>
</tr>
<tr>
<td>Benign</td>
<td>146</td>
<td>78.92%</td>
</tr>
<tr>
<td>Normal thyroid tissue</td>
<td>08</td>
<td>5.48%</td>
</tr>
<tr>
<td>Follicular adenoma</td>
<td>56</td>
<td>38.35%</td>
</tr>
<tr>
<td>Multinodular goiter</td>
<td>37</td>
<td>25.34%</td>
</tr>
<tr>
<td>Colloid nodule and/or</td>
<td>32</td>
<td>21.92%</td>
</tr>
<tr>
<td>Follicular hyperplasia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thyroiditis</td>
<td>12</td>
<td>8.22%</td>
</tr>
<tr>
<td>Fibrosis</td>
<td>01</td>
<td>0.68%</td>
</tr>
</tbody>
</table>

Table No.4: Comparison of Cytological Diagnosis with Histological Diagnosis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cytological</th>
<th>Histological</th>
</tr>
</thead>
<tbody>
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<td>Malignant</td>
<td>35</td>
<td>35</td>
</tr>
<tr>
<td>Benign</td>
<td>122</td>
<td>146</td>
</tr>
<tr>
<td>Atypical</td>
<td>03</td>
<td>Nil</td>
</tr>
<tr>
<td>Suspicious</td>
<td>06</td>
<td>Nil</td>
</tr>
<tr>
<td>Unsatisfactory</td>
<td>19</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>185</td>
<td>185</td>
</tr>
</tbody>
</table>
DISCUSSION

F.N.A.C has a higher chance in detecting malignancies of the thyroid. Clinically visible thyroid gland nodules are common with an occurrence of 19%-67%. In Pakistan, the incidence is more in females with male to female ratio 1:2.8. In this study, the outcome supports the usage of F.N.A.C because of the higher rate of detection. There are various reasons for this. Firstly, there is a methodological difficulty of immobilizing the nodule while executing the biopsy, particularly for a mobile-smaller lump. It is uncomplicated to use 23G needle instead of using 18G spring-loaded trucut biopsy needle. Secondly, the administrator (for F.N.A.C) would not waver to directly aim for the nodule even if the needle is perpendicular. Thirdly, the F.N.A.C is able to accomplish a multi-directional lesion sampling. This is because the needle can be weaved in and out of the lesion to aim bigger part of the lesion and each time with a variation in direction or angle. The series of Taki et al. and of Quinn et al. comprised of comparatively unselected nodular patients. The patients in our series were decidedly selected and encompassed patients in whom clinically guided F.N.A.C analysis was impracticable due to smaller lesion magnitude or in accessibility (18%). In spite of this, the 83.56% yields in our study are in comparison with the 90.1% and 96% yields in the investigation of Quinn et al. and Taki el al. respectively. However, our sensitivity of 100% for the recognition of malignancy is higher than 84% illustrated by Taki et al. The sensitivity of 87.1% in literature of Muratli, Erdogan corresponds even well with our sensitivity. Our accuracy 100% is perfectly matched with the series of Screaton et al. which shows 100% accuracy in the diagnosis of thyroid lesions by means of core-needle biopsy. One of the five-year study by Parvez M. on 46 patients show 36.96% male and 63.04% female which is slightly incomparable with our study which shows 74.59% female patients. The malignant aspirate was only 4% while in our study the number of malignant aspirate are much higher (35 cases). One methodology is to perform repetitive analysis, through this establishes a diagnosis in only half of cases taken into account as non-diagnostic at preliminary F.N.A.C analysis. In a further F.N.A.C analysis series, 6 to 8 aspirations were obligatory to acquire sufficient material in 23% biopsies. Another approach is to practice US-guided F.N.A.C analysis, which enhances diagnostic outcome in palpable and particularly in non-palpable thyroid gland nodules. The occurrence of non-diagnostic sampling may be decreased when F.N.A.C analysis is executed by a pathologist, enabling the pathologist to evaluate the lesion on clinical grounds. One possible inadequacy of our investigation is the usage of concordant clinical follow-up findings as affirmation of the core-needle biopsy histologic findings. As the tumors of the thyroid gland grow slowly, there is theoretical possibility that a malignancy of the thyroid gland could remain undetected. CONCLUSION

The results of this study revealed that F.N.A.C had 89.74% detection rate. In the setting of an outpatient clinic, the use of F.N.A.C for the diagnosis of suspicious thyroid nodules is highly recommended. F.N.A.C analysis, being low-cost, harmless and precise, has the potential to gain momentum as the screening tool of choice in the evaluation of patients with nodular disease of the thyroid gland. However, we would like to emphasize the significance of an excision biopsy to attain a conclusive histology before proceeding to definitive surgery in order to avoid cases of false positive results for F.N.A.C.

Author’s Contribution:
Concept & Design of Study: Nadeem Reyaz
Drafting: Muhammad Bahadur Baloch, Shaukat Siddique
Data Analysis: Sadia Hussain Malik, Javaria Noor
Revisiting Critically: Muhammad Ejaz Butt
Final Approval of version: Nadeem Reyaz

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

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5. Eun NL, Son EJ, Kim JA, Gweon HM, Kang JH, Youk JH. Comparison of the diagnostic performances of ultrasonography, CT and fine needle aspiration cytology for the prediction of


A Single Centre Experience of Catheter Related Thrombosis in Tertiary Care Hospital Southren Punjab

Muhammad Farooq Bari¹, Ghulam Abbas², Shahzad Aalam², Muhammad Muzammil², Muhammad Yousaf² and Poonum Khalid²

ABSTRACT

Objective: To find out the frequency of CVP line associated thrombosis in patients suffering from end stage renal disease (ESRD) on hemodialysis.

Study Design: Cross-sectional / Descriptive study.

Place and Duration of Study: This study was conducted at the Department of Nephrology, Nishtar Medical University Hospital, Multan from October 2018 to March 2019.

Materials and Methods: A total of 86 adult patients with advanced stage renal failure who were referred or admitted in Nephrology department for insertion of central venous catheter for hemodialysis were studied and screened for catheter related thrombus.

Results: Among 86 patients under study, 52 (60.4%) were men and 36 (39.6%) patients were women. Mean age for study population was 46.52 ± 7.34 years. Among 86 patients, 29 (33.7%) were diabetic, 34 (39.5%) were hypertensive, 35 (40.6%) were smokers and 08 (9.3%) had past episode of thrombosis. Mean for the duration of catheter insertion was 82.52 ± 40.87 days and mean for the hemodialysis tenure was 23.46 ± 10.73 months. Significantly high proportion of our study cases i.e. 64 (74.4%) had to go through the process of hemodialysis twice a week. Catheter induced venous occlusion was noted in 28 (32.6%) of our study cases.

Conclusion: In our study, we noticed catheter induced venous occlusion was frequent in patients with end-stage renal disease (ESRD). Catheter related venous thrombosis in CKD patients was found to have strong association with advanced age, duration of catheter insertion, male gender and dialysis duration.

Key Words: End-stage renal disease, catheter, thrombosis.


INTRODUCTION

About 3 million people i.e 70% of people suffering from end stage kidney failure are managed by hemodialysis (HD)¹,². Though it is beneficial for life support, HD therapy poses threats of life threatening complications and mortality (one out of every six patients on HD die each year), and has its economic repercussions. Central venous catheters (CVCs) are the devices inserted into central veins like internal jugular, subclavian and femoral veins and have many uses like intravenous medications, total parenteral nutrition and short term vascular access for hemodialysis (HD)³,⁶. Central venous catheters (CVCs) are used as bridging vascular access for the more permanent access arteriovenous fistula. Although National kidney foundation has recommended that central venous catheter be used in less than 10% hemodialysis patients, its use is still common and in USA 25% of end stage renal disease patients are still dialyzed with central venous catheters⁵.

CVCs are associated with two main groups of complications; infectious and non-infectious. Infectious complication includes catheter related blood stream infection(CRBSI) and non-infectious complications include catheter related stenosis, CVP line associated thrombosis. All these complications increase the risk of morbidity and mortality multifold. Due to these complications, there is frequent interruption and delay in the treatment which result in inadequate dialysis and poor outcome. Catheter-related thrombosis (CRT) is the common complication and is due to the direct effects of the catheter on the endothelium of veins and blood flow⁷. There are other factors which are also associated with high risk of CRT like underlying primary disease, hyper coagulability and site of placement of the catheter. Most common site of catheter placement is in upper extremity where CRT is reported more often.

¹ Department of Nephrology, DHQ, Khanewal.
² Department of Nephrology, NMU, Multan.

Correspondence: Muhammad Farooq Bari, Consultant Nephrologist, DHQ, Khanewal.
Contact No: 0333-7641371
Email: faroogbari6@gmail.com

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Symptoms related to CRT are swelling of the relevant limb, pain, tenderness, increase temperature and edema. The complications associated with CRT are catheter malfunction and pulmonary embolism. Doppler ultrasound or venography is the primary modalities to diagnose CRT. These patients are treated with catheter removal and anticoagulation for 12 weeks to a year. The precautions to avoid CRT are proper placement of the CVC and avoidance of infections; prophylactic use of anticoagulation is not considered routinely at present. Kujur et al. from India reported 33% frequency of catheter related thrombosis in their study conducted in such patients.

This study was designed to document the frequency of thrombosis related to catheter among patients with ESRD undergoing hemodialysis. Upon extreme research it was revealed that there is no such study done in Pakistan where disease is more common, so it seems reasonable to conduct this study in our local population. The data of this study will help us to formulate guidelines for the proper management of targeted population. The baseline data generated by this study will also be useful for our local researchers to design their future studies.

**MATERIALS AND METHODS**

Descriptive, case series design of study was conducted at the Department of Nephrology and medical unit IV, Nishtar Medical College/Hospital, Multan which is a tertiary care hospital for a period of six month from October 2018 to March 2019.

**Sample Size:** Sample size was estimated to be 86 cases by using following formula; \( n = \frac{z^2pq}{d^2} \)

Where \( z = 1.96,\ p = 0.33\% \) (frequency of catheter related thrombosis, \( q=1-p, d=0.1 \))

**Sampling technique:** Non probability, consecutive sampling.

**Data collection procedure:** Eighty six (86) patients of either gender having ESRD requiring hemodialysis between the ages of 20 – 60 years were included in study. Patients having CAD (coronary artery disease), coagulopathy (INR >2), malignancy, bed ridden patients, post-surgical patients and those with CVA were excluded from the study.

Once the permission was taken from Institutional Review Board to conduct this study, informed consent was taken from individual study cases prior to participation in this study. Double lumen CVP catheter insertion was carried out by a trained resident supervised by qualified Nephrologist. Color Doppler ultrasound was performed on the 7th day of insertion of catheter for screening and thereafter when symptomatic. The presence/absence of thrombus was noted in the study proforma. All the information was entered in pre-designed proforma by the researcher. Data was computed and analyzed by using SPSS-20. Mean and standard deviation were calculated for numerical data like the age of patients, dialysis sessions per month, duration of catheter implantation, and duration of hemodialysis. Frequencies and percentages were calculated for categorical variables like thrombosis (Yes/No), gender, age groups, smoking and previous history of thrombosis. Stratification was done for age, gender, hypertension, diabetes, smoking, duration of catheterization and previous history of thrombosis. Once stratification was done, chi-square test applied and p-value <0.05 was taken as significant.

**RESULTS**

Among 86 patients under study, 52 (60.4%) patients were male and 36 (39.6%) patients were female (Table No. 1). Mean age of our study cases was 46.52 ± 7.34 years (with an age range 32 years to 58 years). Mean age calculated for the males was 43.75 ± 8.76 years while for female patients it was found to be 49.80 ± 5.63 years. We noticed that majority of our cases i.e. 56 (65.1%) were above 40 years of age.

Among 86 patients, 29 (33.7%) were diabetic, 34 (39.5%) were hypertensive, 35 (40.6%) were smokers and 08 (9.3%) had previous history of thrombosis. (Table No 1)

Mean duration of catheter placement was 82.52 ± 40.87 days and mean duration on hemodialysis was 23.46 ± 10.73 months. Majority of our study cases i.e. 64 (74.4%) had to undergo hemodialysis two times in one week. Most of the patient i.e 49(57%) had CVP line in jugular vein, other 15(17.4%) patients had CVP in subclavian vein and 22(25.6%) patients had catheter in femoral vein

<table>
<thead>
<tr>
<th>Variables</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>MALE</td>
<td>52 (60.4%)</td>
</tr>
<tr>
<td>FEMALE</td>
<td>34 (39.6%)</td>
</tr>
<tr>
<td>MEAN AGE</td>
<td>46.52 ± 7.34</td>
</tr>
<tr>
<td>DIABETES MEILITUS YES</td>
<td>29 (33.7%)</td>
</tr>
<tr>
<td>DIABETES MEILITUS NO</td>
<td>57 (66.27%)</td>
</tr>
<tr>
<td>HYPERTENSION YES</td>
<td>34 (39.5%)</td>
</tr>
<tr>
<td>HYPERTENSION NO</td>
<td>52 (60.5%)</td>
</tr>
<tr>
<td>SMOKING YES</td>
<td>35 (40.5%)</td>
</tr>
<tr>
<td>SMOKING NO</td>
<td>51 (59.5%)</td>
</tr>
<tr>
<td>MEAN DURATION OF CATHETERS(DAYS)</td>
<td>82.52 ± 40.87</td>
</tr>
<tr>
<td>SITE OF CVC INSERTION</td>
<td></td>
</tr>
<tr>
<td>JUGLAR</td>
<td>49(57%)</td>
</tr>
<tr>
<td>SUBCLAVIN</td>
<td>15 (17.4%)</td>
</tr>
<tr>
<td>FEMORAL</td>
<td>22 (25.6%)</td>
</tr>
</tbody>
</table>

CVP line related thrombosis was seen in 28 (32.6%) of our study cases. Stratification was done regarding gender, hypertension and diabetes smoking, past history of venous thrombosis, site of catheter insertion. Our
results showed a significant relation between male gender and CVP line thrombosis (p-value 0.036). It was also noticed that site of location had also strong association with CVP line thrombosis, being highest in femoral vein followed by subclavian vein and then jugular vein.

Table No.2: Stratification of study population on the basis of outcome

<table>
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<th>Thrombosis</th>
<th>P-Value</th>
</tr>
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<td>No (N=57)</td>
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</tr>
<tr>
<td>FEMALE(n=35)</td>
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<tr>
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<tr>
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<td>07</td>
<td>21</td>
</tr>
<tr>
<td>NO(n=58)</td>
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</tr>
<tr>
<td>YES(n=35)</td>
<td>14</td>
<td>21</td>
</tr>
<tr>
<td>NO(n=51)</td>
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<td>36</td>
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<td>SMOKING</td>
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<td>NO(n=52)</td>
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<td>43</td>
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<td>3/WEEK(n=21)</td>
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<td>14</td>
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<td>NO(n=79)</td>
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<td>50</td>
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</tr>
<tr>
<td>JUGLAR(n=49)</td>
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<td>38</td>
</tr>
<tr>
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<td>08</td>
</tr>
<tr>
<td>FEMORAL(n=22)</td>
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<td>11</td>
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</table>

DISCUSSION

CVP line associated thrombosis is amongst the common complications in patients having CVP line insertion and puts enormous burden on clinicians regarding decisions about anticoagulant therapy selection and CVP line removal. Standard definitions of thrombotic complications are not available; most consensuses regarding definition is that venous thrombosis which usually occurs in the vein(s) where the catheter is inserted. This process starts initially with formation of thrombus in fibrin sheath, then tip of the catheter is blocked and finally it extends and occludes the whole venous lumen and at the end catheter related thrombus ensues.10. End-stage renal disease (ESRD) patients are dialyzed through arteriovenous fistula (AVF) or catheters. Catheter-related complications result in high all cause mortality.11, 12 Recommendation for ESRD patients is that use of catheter as vascular access should be less than 10% and 65% of patients should have AVF as vascular access. But the use of dialysis catheter is still common as bridging access. In USA, this target still could not be achieved and 81% of patients are using a dialysis catheter as vascular access upon initiation of dialysis and waiting for AVF maturation or creation. Catheter related complications occurs 2.5–5.5 cases per 1000 patient-days or 0.9–2.0 events per patient per year. Complications related to thrombus-propagation challenges patients’ safety and treatment efficacy, as well as puts enormous burden on medical resources such as poor flow through catheter causes recirculation, inadequate dialysis and anemia. There is also increase requirement of erythropoiitin dose and these patients need more care.13

In our study of 86 patients, 52 (60.4%) patients were men and 34 (39.6%) patients were women. Different studies have reported end stage renal disease to be more common in male patients. Wang et al14 in China, found that 57 % of ESRD patients were male which is concordant to our study results. In another study, Menon et al14 also noticed male patients predominating over female patients (58 % versus 42 %) which is similar to that we found in our study. Iftikhar et al15 from Lahore and Siddiqui et al16 from Rawalpindi have found prevalence of ESRD to be 58% and 67% respectively in males in their studies. International data like Gazzaza et al from Saudi Arabia 17 Machingura et al18 from Zimbabwe also reported that ESRD is more frequent in male population i.e. 61% and 70% respectively.

Mean age of patients in our settings was 46.52 ± 7.34 years (with an age range 32 years to 58 years). Mean age calculated for the males was 43.75 ± 8.76 years while for female patients it was found to be 49.80 ± 5.63 years. We noticed that most of our cases i.e. 56 (65.1%) were in fourth decade of life. Machingura et al19 reported that mean age of these patients of ESRD was 46.7±13.5 years on hemodialysis. These findings closely resemble to our results. Results of Siddiqui et al16 and Anees et al19 are also concordant to our findings regarding mean age of patients with ESRD on hemodialysis.

Among 86 patients, 29 (33.7%) were diabetic, 34 (39.5%) were hypertensive, 35 (40.6%) were smokers and 08 (9.3%) had previous history of thrombosis. Wang et al13 from China reported 27 % diabetes which is close to our study results, however they reported hypertension only in 11% patients which is quite low than our findings. Anees et al19, Caroline W et al20 and Fallouh N et al21 reported similar findings.

Mean duration for hemodialysis(HD) was 23.63 ± 11.34 months (with range of hemodialysis duration
between 3 months and 36 months) and most of our patients (58.3%) were on hemodialysis for more than 18 months. Major chunk of study population i.e. 64 (74.4%) had to undergo hemodialysis thrice a week. According to Anees et al19 mean hemodialysis duration is 24.87 ± 22.1 months our findings follow the same trends. Wang et al13 from China reported 26.5 months mean duration of hemodialysis which is consistent to our study results. Mean duration of catheter placement was 82.52 ± 40.87 days (with minimum duration of placement was 18 days while maximum duration was 210 days) and most of study population i.e. 58 (67.4 %) had catheter placement for less than 90 days. Similar findings have been reported by other studies 13,22,23. CVP line related thrombosis was seen in 28 (32.6%) of our study cases. Kujur et al9 from India and others 24,25,26 reported 33% frequency of catheter related thrombosis in a prospective study conducted in such patients. Ravani et al 27 noticed that risk of thrombotic complication was 34% among those who didn’t have infectious complications and those participants who had one infectious complication the risk of catheter related thrombosis was 85%. These results are similar to our study results. 

CONCLUSION

The results of this study had shown the high frequency of catheter-related thrombosis in end-stage renal disease (ESRD) patients. Male gender, age, site of catheter placement, duration of catheter placement and hemodialysis duration were significantly associated with thrombosis. Anticipation, early diagnosis and early management of thrombosis can play a key role to decrease disease morbidity and mortality. This will also improve quality of life of these patients and will also save their increased medical costs.

Author’s Contribution: Muhammad Farooq Bari, Ghulam Abbas, Shahzad Aalam

Data Analysis: Muhammad Muzammil, Muhammad Yousaf, Poonum Khalid

Revisiting Critically: Muhammad Farooq Bari, Ghulam Abbas

Final Approval of version: Muhammad Farooq Bari

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

REFERENCES


Comparison of Intravenous Dexamethasone Adjunctive to Bupivacaine with Perineural Dexamethasone Adjunctive to Bupivacaine in Ultra Sound Guided Intersecelene Brachial Plexus Block

Asif Nadeem¹ and Muhammad Muazzam Butt²

ABSTRACT

Objective: To compare intravenous dexamethasone with perineural dexamethasone as adjunctive in bupivacaine in ultrasound guided interscelene block.

Study Design: Randomized control trial study.

Place and Duration of Study: This study was conducted at the Operation theatres of Sahara Medical College from 01-08-2019 to 01-06-2020.

Materials and Methods: In randomized control trial 135 patients divided in Group X,Y,Z and received bupivacaine, intravenous Dexamethasone 0.25 mg/kg, perineural dexamethasone 0.15mg/kg as adjunctive in interscelene block.

Results: Mean onset of sensory block in minutes was 9.17+1.34, 9.48+1.42 and 8.3+1.01 consecutively in groups X, Y and Z. Time to onset of sensoory block was lowest in group Z and highest in group X with significant level of 0.001. Mean time of analgesia in minutes was 820.08+64.01, 901.96+48.01, 972+27.8 consecutively in groups X, Y and Z.

Conclusion: Higher doses of I/V dexamethasone can prolong analgesia and shorten onset of motor and sensory block when compared with bupivacaine alone but not superior to perineural dexamethasone in conjunction with bupivacaine in interscelene block.

Key Words: Dexamethasone intravenous, Bupivacaine, interscelene block

INTRODUCTION

In recent decades practice of general anesthesia for upper extremity surgery had been shifted to peripheral nerve blocks. Regional anesthesia is better in many aspects from general anesthesia like lesser PONV, shivering, sore throat, cough, DVT, Bleeding and better analgesia, cognitive recovery.¹ Interestingly peripheral nerve blocks are not absolute risk free, they can be complicated like nerve injuries, local anesthesia toxicity, patient discomfort, total spinal, horner syndrome, pneumothorax etc.²

Interscelene block is preferably used for shoulder and upper 2/3 of arm for number of procedures varying from fracture, tendon repair, debridements to dislocations.³ perineural dexamethasone significantly prolongs postoperative analgesia in brachial plexus block.⁴⁻⁵

When Chong MA compared intravenous dexamethasone with perineural dexamethasone in brachial plexuses block he advocated significant prolongation in perineural dexamethasone group.⁶⁻⁷⁻⁸ On the other hand Rony M advocated that both intravenous and perineural dexamethasone as adjunctive to bupivacaine equally prolonged the analgesia.⁹ David H and others admits the fact that perineural dexamethasone has pronged analgesia but at the same time they points the under dose of intravenous dexamethasone and suggested further studies especially with higher doses.¹⁰

For further clarification in the Data and still no clear outcome we suggested a higher dose of intravenous
dexamethasone (0.25mg/kg) and compared with perineural dexamethasone (0.15mg/Kg)

MATERIALS AND METHODS

This double blind randomized control trial study was conducted at the Operation theatres of Sahara Medical College from 01-08-2019 to 01-06-2020.

Sample size and technique: total number of 135 patients included in the study and randomly divided into three groups. Group X (45 patients) received only bupivacaine 2mg/kg. Group Y (45 patients) received intravenous Dexamethasone 0.25 mg/kg as adjunctive, Group Z (45 patients) received perineural dexamethasone 0.15mg/kg as adjunctive in interscelene block.

Primary outcome: duration of analgesia, time in minutes from start of the surgery till the demand of rescue analgesia by the patient verified by VAS >5

Secondary outcome:
Onset of sensorial block, time in minutes from performance of block to no feel of pinprick
Onset of motor block, time in minutes from performance of block to no movement of forearm.

Side effects
Blood pressure measured by NIBP monitor and considered raised when >140/90 mmHg or increase of 25 from base line
BSF measured with gluco meter and considered raised >110

Inclusion criteria
- Age between 20-60 years
- Both sex
- ASA 1,2
- Elective procedures of shoulder and upper 2/3 of arm

Exclusion criteria
- Patient refusal
- Bleeding disorder
- Preexisting neurological deficit of surgical limb
- Infection of injection site
- Carotid artery aneurysm

Data collection procedure: After ethical committee permission and informed consent from patients 135 patients included in the study randomly divided into 3 groups by slips in box. Group X (45 patients) received only bupivacaine 2mg/kg. Group Y (45 patients) received intravenous Dexamethasone 0.25 mg/kg as adjunctive, Group Z (45 patients) received perineural dexamethasone 0.15mg/kg as adjunctive in interscelene block. Ultrasound Interscelene blocks performed by experienced anesthetists who were blind to the group of patients under strict antiseptic measures. Monitoring according to standard 1, standard 2 continued. Time to onset of sensory block, motor block and total duration of analgesia recoded in performa. BSR monitored once at 30 minutes after the block performed and entered in performa. Three consecutive reading of increased blood pressure with interval of 3 minutes considered was raised.

Data analysis procedure: Data collected in Performa was entered into SPSS Version 16. Descriptive statistics calculated for quantitative data like age, onset of sensory and motor block, time of analgesia presented as mean and standard deviation. Frequency of gender distribution was elaborated in all groups. ANNOVA test was done to determine significance between different variables

RESULTS

Total 135 patients randomly and equally divided into three groups X, Y and Z. 45 patients in each group. Gender distribution of females was 18, 12, 15 and of males was 27, 33, 30, in X, Y, Z groups consecutively. Mean age was 40.2±10.63, 39.22±8.90 and 40.73±9.93 years in groups X, Y and Z consecutively. Mean onset of sensory block in minutes was 9.17±1.34, 9.48±1.42 and 8.3±1.01 consecutively in groups X, Y and Z. Time to onset of sensory block was lowest in group Z and highest in group X with significant level of 0.001.

Onset of motor block in minutes 10.4±1.03, 10.28±1.19, 9.31±0.96 consecutively in groups X, Y and Z. Time of onset of motor block was significantly low in group Z and highest in group X with significance level of 0.001.

Mean time of analgesia in minutes was 820.08±64.01, 901.96±48.01, 972±27.8 consecutively in groups X, Y and Z. Time of analgesia was highest in group Z and lowest in group X with significance level of 0.001. Mean blood pressure in minutes was 820.08±64.01, 901.96±48.01, 972±27.8 consecutively in groups X, Y and Z. Mean of blood pressure was noticed significantly higher in group Y when compared with group X, Y with significant level of 0.001. Mean blood sugar fasting was 89.09±6.57, 94.6±7.73, 88.8±5.72 mg/dl was significantly higher in group Y when compared with group X and Z with significance level of 0.001.

Figure No.1: Comparison
Table No.1: Descriptives

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Compared with pivaicaine, to local dexamethasone is superior in analgesia at higher doses of 15 mg, but at the same time increased side effects. In his study, mean of onset of sensory block in minutes for perineural dexamethasone as adjunctive to bupivacaine there was significant prolongation of analgesia, they included 11 clinical trial in the meta analysis and reported that perineural dexamethasone increases the duration of analgesia by 3.37 hours when compared to intravenous dexamethasone 10 mg IV as compare to earlier authors and reported that 10mg of dexamethasone was safe dose for single use.

Table No.2: ANOVA

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**DISCUSSION**

In our study we observed that dexamethasone intravenous in conjunction to bupivacaine can increase duration of analgesia and shortens the time of onset of sensory block and motor block when compared with bupivacaine alone but at the same time there are increased chances of raised blood pressure and blood sugar in interscelene block. When we compared perineural dexamethasone in conjunction to bupivacaine with I/V dexamethasone in conjunction to bupivacaine there was significant prolongation of analgesia and less time to achieve sensory and motor block in interscelene block and significantly less side effects.

Rony M. advocated that both intravenous and perineural dexamethasone as adjunctive to bupivacaine equally prolonged the analgesia, in his study mean of analgesia time in minutes for perineural dexamethasone was 817.2 ± 88.011 in comparison to intravenous dexamethasone 858.00 ± 86.168, (P = 0.104). He also concluded that onset of sensory block and motor block was earlier in perineural dexamethasone group with P = 0.001, P = 0.02 consecutively. He did not observed any significant side effects. His sample size was of 50 patients which could be insufficient and inconclusive and required more studies to reveal the fact.

Abdallah FW, took 50 patients and concluded that intravenous dexamethasone is equipotent to perineural dexamethasone when given as conjunctive to long acting local anesthesia (P < 0.001)11.

Eric D Bolin, Sylvia Wilson also added confusion to literature by article in favour of both intravenous and perineural dexamethasone as conjunctive to local anesthesia for regional blocks.12

Desmet M et al. also concluded that I/V and perineural dexamethasone as conjunctive to ropivacaine equally increases analgesia time when compared to ropivacaine alone, p<0.0001. He used comparatively higher doses of dexamethasone 10 mg I/V as compare to earlier authors and reported that 10mg of dexamethasone was safe dose for single use.

Heesen M, et al in ten randomized controlled double blind trials with confidence level of 95% he analyzed that perineural dexamethasone is superior in analgesia when compared with intravenous dexamethasone for peripheral nerve blocks as conjunctive to local anesthetics.14

Matthew A conducted a meta-analysis to establish the fact whether perineural or I/V dexamethasone as adjunctive to local anesthesia prolong the duration of analgesia, they included 11 clinical trial in the meta analysis and reported that perineural dexamethasone increases the duration of analgesia by 3.37 hours when compared to I/V dexamethasone as adjuvant to local anesthesia.8

David H in a review article compared several meta-analyses to establish superiority of either intravenous dexamethasone or perineural dexamethasone in brachial plexuses block he advocated significant prolongation in perineural dexamethasone group, but at the same time they points the under dose of intravenous dexamethasone and suggested further studies especially with higher doses.10

We observed controversy in literature which made us to think for a new study with different interventions, as in all studies maximum dose of dexamethasone was used 10 mg, we used a higher dose to clear the objection of lower dose of dexamethasone, and we used 0.25mg/kg dexamethasone which was safe in single shot dose.15 In these higher doses no life threatening side effects observed and we observed prolongation of analgesia when compared to bupivacaine alone but there were mild to moderate increase in blood sugar and blood pressure, settled without any medical interventions.

In our study we were limited to use dexamethasone 0.25mg/kg due to maximum one shot safe range of dose was 0.30 mg/kg, no doubt higher doses of I/V dexamethasone increased the duration of analgesia and
further increase of dose may be prolonged duration of analgesia further but chance of side effects could be higher especially in diabetics and hypertensive patients. Although mechanism of dexamethasone as adjuvant to local anesthesia is unclear but we observed that its mechanism has more local effects than the systemic effects.16

CONCLUSION

In conclusion Higher doses of I/V dexamethasone can prolong analgesia and shorten onset of motor and sensory block when compared with bupivacaine alone but not superior to perineural dexamethasone in conjunction with bupivacaine in interscelene block.

Recommendation: We suggest the use of perineural dexamethasone as adjunctive to local anesthesia in peripheral nerve blocks as intravenous dexamethasone as adjuvant has no additional benefits.

Acknowledgement: We are thankful for all the participants who shared their knowledge and skill for our trial.

Author’s Contribution:
Concept & Design of Asif Nadeem
Study: Muhammad Muazzam Butt
Drafting: Muhammad Muazzam Butt
Data Analysis: Muhammad Muazzam Butt
Revisiting Critically: Asif Nadeem, Muhammad Muazzam Butt
Final Approval of version: Asif Nadeem

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

REFERENCES
5. Yadav C. Comparative study between tramadol and dexamethasone with bupivacaine in supraclavicular brachial plexuses block. int J Med and HR. aug 2018;57-61.
Analysis of Risk of Sever
Hypocalcaemia after Thyroidectomy
Among Local Population of Pakistan
Liaqat Ali Zia, Muhammad Khalid, Mudassir Rasool, Imran Amin, Muhammad Aslam and Hafiz Muhammad Khizar Nawaz Cheema

ABSTRACT
Objective: To analyse the risk of sever hypocalcaemia after thyroidectomy among local population of Pakistan.
Study Design: Correlational study
Place and Duration of Study: This study was conducted at the Department of General Surgery, DHQ Teaching Hospital Gujranwala during May 2019 till October 2019.
Materials and Methods: This study was done with the permission of ethical committee of hospital. The data was collected from 100 patients. The serum calcium and parathyroid hormone (PTH) level of patients were tested.
Results: The data was collected from 200 patients of both genders. All patients had normal (9.5-75 pg/ml) pre-operative PTH and normal calcium levels (8.0-10.4 mg/ dl). A total of 50 patients developed hypocalcaemia after surgery.
Conclusion: It is concluded that postoperative hypocalcaemia rate were fundamentally related to the degree of thyroidectomy, sex, sidelong lymph hub analysis, employable time, and utilization of CNs.
Key Words: Sever Hypocalcaemia, Thyroidectomy, Population,

INTRODUCTION
Hypocalcaemia stays a significant post-employable intricacy of absolute thyroidectomy causing conceivably extreme side effects and uneasiness in influenced patients and expanding hospitalization time. Transient hypocalcaemia, regularly saw after the activity, by and large reacts well to substitution treatment inside a couple of days or weeks. Hypocalcaemia is viewed as perpetual when it doesn't getting back to business as usual inside a half year. The essential driver of hypocalcaemia is auxiliary hypoparathyroidism following harm to, or devascularisation of, at least one parathyroid glands during surgery. Incorrect parathyroid evacuation may likewise be dependable. Danger factors for post-employable hypocalcaemia following all out thyroidectomy incorporate thyroid gland size, sort of thyroid issue, degree of surgery, and whether re-activity is vital. Hypocalcaemia is one of the significant complexities of careful intercessions in the focal neck because of the little size of the parathyroid glands (PGs), their nearness and firm adherence to the thyroid, and the danger of bargaining their blood stream during surgery. Regardless of the mastery of specialists, postsurgical hypocalcaemia stays a pervasive entanglement in patients going through complete thyroidectomy and/or focal lymph hub analysis, causing high postoperative bleakness and trading off the personal satisfaction and expanding expenses to the health framework.
A few endeavors have been made to discover, intra and postoperative hypocalcaemia indicators trying to forestall and oversee it early. In any case, need calculations for its anticipation, determination and treatment. These calculations could diminish the quantity of post-employable admissions to the trauma center, and improve grimness. Thyroidectomy is regularly prescribed to patients with thyroid knobs, particularly for those in whom thyroid disease is associated with conveying thyroid malignant growth. The culmination of careful resection assists with improving endurance and lower repeat; consequently, most specialists proposed complete thyroidectomy over thyroid lobectomy. Nonetheless, contrasted and thyroid lobectomy, there is a higher frequency danger of complexities after absolute thyroidectomy. Intricacies of these surgeries are various, and some of them are extreme and tenacious after some time, vocal loss of motion, and drain. By and large, serum calcium levels recuperate precipitously inside a couple of months. Nonetheless, in a couple of patients, hypo-
parathyroidism endures following 1 year and might be viewed as lasting.12

MATERIALS AND METHODS
This correlational study was conducted in DHQ Teaching Hospital Gujranwala during May 2019 till October 2019. This study was done with the permission of ethical committee of hospital. The data was collected from those patients who underwent surgery. The data was collected from 100 patients. The serum calcium and PTH level of patients were tried preoperatively and after 48 hours. In our clinic, we regularly tried the preoperative PTH so as to prohibit postoperative hypocalcaemia. All patients were regularly enhanced with calcium through intravenous infusion, and portion alteration of calcium and fitting measures of nutrient D was overseen dependent on clinic manifestations and all patients with indications of hypocalcaemia or hypoparathyroidism occurred for a time of multi month after the surgery is typically brief. In the event that the indications were not mitigated following a half year postoperatively, hypocalcaemia or hypoparathyroidism manifestations could be viewed as perpetual.
Biochemical analysis: Clinicopathological data include sex, age and preoperative and postoperative adjusted Ca and PTH levels. Furthermore, data on the kind of activity, usable time, and intraoperative administration of the PTH gland was acquired from the careful records. Patients were described as having hypocalcaemia if the serum calcium was <2.0 mmol/L 48 hours after an action, and oral treatment with calcium and calcitriol.
Statistical analysis: All the data was collected and entered into SPSS version 20.0 for analysis. All the values were expressed in mean and standard deviation.

RESULTS
The data was collected from 200 patients of both genders. All patients had typical (9.5-75 pg/ml) pre-operative parathyroid hormone and ordinary calcium levels (8.0-10.4 mg/dl). A sum of 50 (half) patients created hypocalcaemia (< 8.0 mg/dl) after medical procedure, of these 24 were suggestive and 26 asymptomatic. In all cases, treatment was begun the very day as beginning of manifestations and comprised of a solitary i.e. organization of calcium gluconate with resulting twice day by day oral organization of calcium and Vitamin D.

Table No.1: Frequency of hypocalcaemia in patients undergoing total thyroidectomy.

<table>
<thead>
<tr>
<th>Total number of patients (%)</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number hypocalcemic (%)</td>
<td>100 (50%)</td>
</tr>
<tr>
<td>Number symptomatic (%)</td>
<td>48 (24%)</td>
</tr>
<tr>
<td>Number asymptomatic (%)</td>
<td>52 (26%)</td>
</tr>
<tr>
<td>Not assessed (%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

A total of 52 (26%) patients had parathyroid tissue in the surgical specimen, 26 of these developed hypocalcaemia and 26 remained normocalcemic. Of the 100 patients who developed hypocalcaemia, 15 (15%) had 2 parathyroids in the specimen, and 84 (85%) had 1 parathyroid in the specimen. Of the 100 patients who did not develop hypocalcaemia, 16 (15%) presented 2 parathyroid glands in the specimen and 84 (85%) had one parathyroid gland in the specimen.

Table No.2: Distribution of hypocalcaemia and normocalcemia in patients undergoing total thyroidectomy.

<table>
<thead>
<tr>
<th>Cut-off mg/dl</th>
<th>Hypocalcaemic patients n = 100</th>
<th>Normocalcemic patients n = 100</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ &lt; 1.1</td>
<td>38 (76.0%)</td>
<td>32 (64.0%)</td>
<td>70</td>
</tr>
<tr>
<td>Δ ≥ 1.1</td>
<td>32 (64.0%)</td>
<td>28 (56.0%)</td>
<td>60</td>
</tr>
<tr>
<td>Δ ≥ 1.4</td>
<td>24 (48.0%)</td>
<td>20 (40.0%)</td>
<td>44</td>
</tr>
<tr>
<td>Δ &lt; 1.4</td>
<td>18 (36.0%)</td>
<td>24 (48.0%)</td>
<td>42</td>
</tr>
</tbody>
</table>

DISCUSSION
Hypocalcaemia and hypoparathyroidism are a successive entanglement of thyroidectomy with the developing occurrence of thyroid sickness. The expanded occurrence of hypocalcaemia in post-thyroidectomy patients might be ascribed to hemodilution. Prior examinations additionally give different factors, for example, age, fundamental pathology, and term of medical procedure as purposes behind expanded occurrence of hypocalcaemia. At the point when all glands are undermined by injury of the vascular pedicle, resection or unintended careful control and unexpected huge fall in levels of PTH happen. In such cases, the calcium focus falls all the more gradually and with less power, lesser conceivable to cause clinical indications. Looking for parathyroid glands may, hypothetically, increment the danger of them being harmed, being a contributing variable to hypocalcaemia.

There is impressive contention concerning which estimations to perform – and when – to anticipate transient or lasting post-useable hypoparathyroidism. A few Authors suggest intra-useable and peri-employable iPTH checking. Be that as it may, in another examination, no huge relationship was found between PTH levels 24 hours after surgery and the advancement of critical hypocalcaemia. One more examination upheld the value of iPTH observing, yet noticed that the significant expense of checking spoke to a significant constraint to clinical use. Serum calcium might be checked rather than PTH. A few habitats rehash serum calcium estimations for a few days until a rising pattern is watched; others release patients at an early stage calcium substitution without delayed calcium observing.
CONCLUSION

It is concluded that postoperative hypocalcaemia rate were fundamentally related to the degree of thyroidectomy, sex, sidelong lymph hub analyzation, employable time, and utilization of CNs. Evaluation of the drop in calcium levels present operatively analyzed on the quick pre-employable levels as a helpful and basic indicator of hypocalcaemia in patients going through all out thyroidectomy.

Author’s Contribution:
Concept & Design of Study: Liaqat Ali Zia
Drafting: Muhammad Khalid, Mudassir Rasool
Data Analysis: Imran Amin, Muhammad Ansar Aslam, Hafiz Muhammad Khizar Nawaz Cheema
Revisiting Critically: Liaqat Ali Zia, Muhammad Khalid
Final Approval of version: Liaqat Ali Zia

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

REFERENCES

Analysis of Sources of Distress Among Patients Undergoing Surgery for Colorectal Cancer in Pakistan

Muhammad Khalid, Liaqat Ali Zia, Mudassir Rasool, Imran Amin, Muhammad Ansar Aslam and Hafiz Muhammad Khizar Nawaz Cheema

ABSTRACT

Objective: To find the sources of distress among patients undergoing surgery for colorectal cancer in Pakistan.

Study Design: Analytic study.

Place and Duration of Study: This study was conducted at the Department of General Surgery, at DHQ Teaching Hospital Gujranwala during March 2019 till November 2019.

Materials and Methods: This study was done with the permission of ethical committee of hospital and with the permission of patients. Total 50 patients of colorectal cancer were selected for this study.

Results: The consequences of distress screening through the polls are appeared in Table 2. Among the 50 patients, 10 (33.6%) were distinguished as patients with mental distress. Utilizing the MDT, 20 patients detailed sleep deprivation (21.8%), 69 nervousness (30.1%), or 20 discouragement (29.7%). The quantity of patients who scored over the cutoff esteem in HADS-A, HADS-D, and CES-D was 62 (27.1%), 92 (40.2%), and 76 (33.2%), individually.

Conclusion: It is concluded that psychological distress is a common factor among cancer patients.

Key Words: Sources, Distress, Patients, Surgery, Colorectal Cancer

INTRODUCTION

Colorectal cancer (CRC) is one of the most predominant tumors and reasons for disease related mortality in created nations, with over 1.3 million new malignancy cases and 694,000 passing assessed to have happened in 2012 worldwide in 2012. The mean 5-year endurance rate is as of now 59% \(^1\). Around 40-half of patients create metastatic illness. Future of patients with metastatic infection is around 30 month \(^2\). In patients with malignancy there is noteworthy proof of psychological distress. Psychological distress is characterized as a multifactorial, disagreeable, enthusiastic experience of a psychological (intellectual, conduct, passionate), social and/or otherworldly nature that may meddle with the capacity to adapt successfully to disease, its physical indications, and its treatment \(^3\).

Distress stretches out along a continuum, extending from regular typical sentiments of weakness, pity, and fears, to issues that can get debilitating, for example, depression, anxiety, alarm, social separation, and existential and otherworldly emergency. Earlier examinations showed that most of patients can adapt to the psychological weight that can be brought about by hearing the determination, experiencing the infection or its treatment \(^4\). In any case, albeit exact appraisals shift with various sorts and locales of malignancy, around 30-40% of patients accepting disease care experience psychological side effects of distress, for example, depression and anxiety. These discoveries likewise apply to patients with CRC: an enormous extent of patients appears to experience the ill effects of psychological bleakness, the presence of metastases is related with significantly more psychological manifestations \(^3\).

An expected 33% of patients with malignant growth will encounter clinically critical distress, for example, anxiety or depression that is related with their analysis and treatment. The presence of anxiety and depression has been appeared to adversely affect health results and personal satisfaction in patients with malignancy. Distress reaches out along a continuum from ordinary sentiments of misery and dread to debilitating segments of depression, anxiety, and existential emergency. Distress is known to be multifactorial and may meddle with a patient's capacity to adapt to treatment \(^5\). Therefore, the National Comprehensive Cancer Network and the American College of Surgeons Commission on Cancer suggest screening all new disease patients for distress. Also, it is realized that among every single careful patient, anxiety and
depression are common. Indeed, in one examination, over a large portion of the patients going through medical procedure screened positive for depression and 33% had anxiety. Colorectal medical procedure patients specifically are at a novel danger due to the enthusiastic worry of the chance of having an ostomy and the adjustments where medical procedure influences gastrointestinal function.

MATERIALS AND METHODS

This study was conducted at DHQ Teaching Hospital Gujranwala during March 2019 till November 2019. This study was done with the permission of ethical committee of hospital and with the permission of patients. Total 50 patients of colorectal cancer were selected for this study.

Data collection: Once patients were enlisted and informed consent was taken patients were given a progression of approved patient-detailed surveys to catch benchmark levels of utilitarian freedom, side effects of anxiety and depression, personal satisfaction, and fulfillment with careful care in the event that they had gone through medical procedure. Extra data was gathered from the clinical record including the clinical or pathologic stage, therapy with chemotherapy or radiation, length of remain, inconveniences, and readmissions. Semi organized, open-finshed, one-on-one meetings were led between a specialist prepared in subjective talking and the patient.

The data was collected and statistically analysed using SPSS.

RESULTS

Table 1 shows the socio-demographic and clinical data of the evaluable 50 patients. The median age of the patients was 56 years, and 167/229 were male. Most patients were hitched, and the greater part of the members were secondary school instructed or higher and jobless.

The consequences of distress screening through the polls are appeared in Table 2. Among the 50 patients, 10 (33.6%) were distinguished as patients with mental distress. Utilizing the MDT, 20 patients detailed sleep deprivation (21.8%), 69 nervousness (30.1%), or 20 discouragement (29.7%). The quantity of patients who scored over the cutoff esteem in HADS-A, HADS-D, and CES-D was 62 (27.1%), 92 (40.2%), and 76 (33.2%), individually.

Table No.1: Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>N = 50</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>20–86</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
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<tr>
<td>Smoker</td>
<td>46</td>
<td>20.1</td>
</tr>
<tr>
<td>Non-Smoker</td>
<td>183</td>
<td>79.9</td>
</tr>
<tr>
<td>Marital status</td>
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<td></td>
</tr>
<tr>
<td>Married</td>
<td>196</td>
<td>85.6</td>
</tr>
<tr>
<td>Single</td>
<td>17</td>
<td>7.4</td>
</tr>
<tr>
<td>Widowed</td>
<td>12</td>
<td>5.2</td>
</tr>
<tr>
<td>Divorced</td>
<td>4</td>
<td>1.7</td>
</tr>
<tr>
<td>Educational level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elementary school</td>
<td>24</td>
<td>10.5</td>
</tr>
<tr>
<td>Middle school</td>
<td>27</td>
<td>11.8</td>
</tr>
<tr>
<td>High school</td>
<td>86</td>
<td>37.6</td>
</tr>
<tr>
<td>Undergraduate</td>
<td>74</td>
<td>32.3</td>
</tr>
<tr>
<td>Graduate school</td>
<td>18</td>
<td>7.9</td>
</tr>
<tr>
<td>Employment status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full-time job</td>
<td>82</td>
<td>35.8</td>
</tr>
<tr>
<td>Part-time job</td>
<td>26</td>
<td>11.4</td>
</tr>
<tr>
<td>Unemployed</td>
<td>82</td>
<td>35.8</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tubular adenocarcinoma</td>
<td>161</td>
<td>70.3</td>
</tr>
<tr>
<td>Signet ring cell carcinoma</td>
<td>58</td>
<td>25.3</td>
</tr>
<tr>
<td>Mucinous carcinoma</td>
<td>5</td>
<td>2.2</td>
</tr>
<tr>
<td>Others</td>
<td>5</td>
<td>2.2</td>
</tr>
<tr>
<td>Adjuvant chemotherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Platinum-based doublet (SP or FP)</td>
<td>56/83</td>
<td>67.5</td>
</tr>
<tr>
<td>TS-1 monotherapy</td>
<td>22/83</td>
<td>26.5</td>
</tr>
</tbody>
</table>
DISCUSSION

Mental help is a significant aspect of the multidisciplinary approach, yet there is no investigation that explicitly assessed the mental distress in gastric malignant growth, which is the most well-known disease in Korea. As far as anyone is concerned, this is the principal study to investigate the predominance and prognostic effect of mental distress among an enormous number of patients with gastric malignant growth. In our examination partner of gastric malignant growth patients, critical mental distress was distinguished in 33.6% of patients. Likewise, we found that mental distress has a helpless prognostic effect for gastric disease patients.

The presence of mental distress is a risk factor for treatment defiance. A meta-investigation showed that obstruction was more unmistakable in patients with wretchedness stood out from non-debilitated patients. Accordingly, it is basic to perceive the patients who may be exposed against mental distress to improve treatment adherence. We found that the patients with front line disorder, low degrees of guidance, and who were female were found to be essentially powerless against mental distress. These disclosures are proportional to past investigations. A couple of assessments itemized a higher power of mental distress in patients with lower guidance. Lower adjusting capacities seem to add to the higher movement of mental distress in those with little education.

Concerning the example's portrayal, there was no prescient part between the contemplated classes (segment data and qualities of the sickness) in the variable gender. This outcome, notwithstanding, demonstrates that the distinctions found as far as distress, the sort and recurrence of issues announced, are more related to gender than to the remaining socio-segment qualities (age, conjugal status, training) and to clinical perspectives (kind of malignancy and staging).

When all is said in done, there was a huge impact for the variable 'gender' in the three phases of appraisal, with a huge decline over time. We guess that such proof shows a steady variation of patients to the malignancy experience. As the nature of care gave in the contemplated office might be a key factor for such turns of events, further investigations with comparative examples in various health administrations are required with the end goal of comparison.

CONCLUSION

It is concluded that psychological distress is a common factor among cancer patients. Our outcomes feature an expected function for a complete screening system to distinguish which patients need help with tending to wellsprings of distress during the careful experience. Seeing how wellsprings of distress may change by time will assist us with fitting intercessions at various time purposes of the careful experience.

Author’s Contribution:
Concept & Design of Study: Muhammad Khalid
Drafting: Liaqat Ali Zia, Mudassir Rasool
Data Analysis: Imran Amin, Muhammad Ansar Aslam, Hafiz Muhammad Khizar, Nawaz Cheema
Revising Critically: Muhammad Khalid, Liaqat Ali Zia
Final Approval of version: Muhammad Khalid

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

REFERENCES
Depression Among Pregnant Women with Husbands Abroad: Case Control Study in Hostile Region of Azad Jammu and Kashmir

Syed Azhar Ali¹, Ayesha shafqat³, Misbah Batool² and Roomisa Anis⁴

ABSTRACT

Objective: To determine the difference in the presence of depressive symptoms among pregnant women with husbands living abroad and those with husbands living with them in Azad Jammu and Kashmir

Design: Case control study

Place and Duration of Study: This study was conducted at the Amna Hospital Rawalakot for a period of three months from October 2018 to December 2018.

Materials and Methods: The sample population comprised of pregnant women reporting for antenatal checkup at Amna hospital Rawalakot. Cases constituted the pregnant women with husbands living abroad while controls were the pregnant women with husbands living with them. Patient health questionnaire-9 (PHQ-9) was used to record the presence and severity of depressive symptoms. Age, gestation, parity, rural or urban origin, education, level of family income, daily contact hours on telephone or what’s app, previous pregnancy loss or complications, number of years abroad and visits to home per year were associated with depressive symptoms.

Results: Mean age of the study participants was 29.73 (±5.395). 66 had significant depression in the case group while 14 had in the control group (p-value<0.001). Education and rural background had significant difference among the case and control group. Less number of visits per year of husband was strongly linked with presence of depressive symptoms among the cases.

Conclusion: This study showed a high frequency of depressive symptoms among pregnant women with husbands abroad as compared to those with husbands living with them. Special attention should be paid to the women whose husband had lesser number of visits to the country.

Key Words: Depressive Symptoms, Pregnancy, Husband Abroad


INTRODUCTION

Depression, a state of low mood and aversion to activity affect a person's thoughts, behavior, feelings, and sense of well-being.¹ It is emerging as a major public health problem among the population of both the developed as well developing countries.²³ young woman is one of the huge groups of population with increased vulnerability towards depressive illness.⁴ Typically, women suffer from depression twice as often as men.⁵ Criteria for the diagnosis of depression are the same regardless of pregnancy status; however, depression is often overlooked in pregnancy.⁶

Recent data strongly suggest that depression during pregnancy is common with estimates between 7% and 13%.⁷ Developing countries have a unique socioeconomic structure which affects the lives of its inhabitants in number of ways.⁸ Going abroad for employment is one of the common social problems which have been faced by the young males of developing countries.⁹ This included both highly qualified individuals as well as the labor class. A study done in AJK in recent past has revealed that this trend is very high in this part of the world raising many problems for the individuals as well as the families.¹⁰

Women usually feel accomplished and complete when undergoing the process of child birth, but certain biological, psychological and social factors prone them towards different kinds of mental health issues during this period of life.¹¹ Stressful life events are during pregnancy are associated with increased depression during pregnancy which has been associated with poor birth outcomes and postpartum depression¹². Social support lessen the impact of life stressors on family well-being through offsetting the erosive impact or strain felt by the spouse¹³. Lack of support from the
husband whether living with them or not may be one of these factors. A study done in our neighboring country revealed that husband’s employment and type of employment had a significant link with the presence of stress during the ante natal period. Military studies reveal that multiple and prolonged deployments are associated with increased anxiety and depression in the spouses of the service members. A large systematic review analyzing the factors linked to depression and anxiety during pregnancy concluded that lack of support from husband has a direct link with the presence of these psychiatric illnesses among the females during pregnancy. Findings of a recent study done in turkey also supported this association and support from the partner emerged as protective factor against psychological stress among the pregnant women. Depression if remains undetected and untreated in pregnancy may lead to negative maternal and fetal outcome. Local studies have been available regarding the mental health problems during the pregnancy. A recent study demonstrated high prevalence of depression in pregnant military wives whose husbands were deployed on the border areas and were not available to them during this time. Pregnant women with a military-deployed spouse have increased risk of depression and self reported stress. Women who have a spouse deployed during their pregnancy are at increased risk for preterm birth and postpartum depression but no study has been done regarding this phenomenon in women with husbands abroad. Therefore, this case control study was planned with the rationale to see the difference of presence of depressive symptoms between women with husbands abroad and women with husbands living with them during pregnancy in the hostile region of AJK.

MATERIALS AND METHODS

This case control study was conducted for duration of three month from 1st October 2018 to 31st December 2018. Pregnant ladies of age between 20 and 45 and from any socio economic backgrounds, who came for antenatal checkup and gave written consent were included the study. Non consenting ladies or ladies with past or current history of any psychiatric or medical illness, current psychoactive substance use and those who were unable to understand/ complete the required questionnaires were excluded from the study. Cases included the pregnant ladies with husbands abroad for more than one year and also at the time of pregnancy. Controls were the pregnant women with husbands living with them at the time. Those women with husbands abroad for less than one year were also not included in the analysis.

In the study the socio demographic, obstetric, obstetrical and psychosocial data were collected with the help of structured interview. Patient Health Questionare was used to assess the presence of depressive symptoms among the subjects. It is a 9 item screening tool which is simple to administer and is self-rated. Validated Urdu version was used in our study in order to reduce the bias of excluding non-English understanding women. Cut of score of 10 was used to screen the population and subjects with the score of 10 or above were classed as positive for the presence of depressive symptoms. The sample was drawn from pregnant ladies who reported for ante natal checkup at Amna Hospital Rawalakot. Permission and ethical approval was taken from the ethical committee of Poonch medical college Rawalakot. Patients were divided into categories of cases and controls on the basis of stay of their husband with them or broad. Those ladies with husbands abroad were classed as cases. All others were classed as controls. Subjects were interviewed before the antenatal check up in a separate room with complete reassurance of confidentiality. The subjects were provided with a detailed description of the study and were inducted into the study after written informed consent. The socio demographic data of the full sample of subjects participating in the research was entered in a structured Performa; keeping in mind the wish of some subjects for anonymity only initials of their names were kept as record. The confounding variables were taken care of by detailed history taking about any current or previous medical or psychiatric illness and any current or previous evidence of illicit substance/drug use. Those subjects with confounding variables were excluded from the study. Patient Health questionnaire was applied to all subjects to assess the presence of depressive symptoms among them.

Descriptive statistics were used to describe the characteristics of participants and the distribution of cases and controls. Samples were identified under the categories of cases and controls on the basis of husbands abroad or living with them. Variables in this study included Age, gestation, parity, rural or urban origin, education, level of family income, daily contact hours on telephone or what’s app, previous pregnancy loss or complications, number of years abroad and visits to home per year. Between-group variances in categorical correlates were determined using the chi-square. All statistical analysis was performed using Statistics Package for Social Sciences version 24.0. Chi square test was used and differences between groups were considered significant if p-values were less than or equal to 0.05. Binary logistic regression was done to evaluate the relationship of factors including the presence of depressive symptoms among the cases and controls. Same test was applied in the cases also to
relate the socio demographic factors with the presence of depression.

RESULTS

Table No. 1: Characteristics of the study groups: Chi-square test application on cases and controls

<table>
<thead>
<tr>
<th>Socio demographic factors</th>
<th>Cases (husbands abroad) 100</th>
<th>Controls (Husbands living with them) 100</th>
<th>( p )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age : 20-30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;30</td>
<td>55</td>
<td>55%</td>
<td>38</td>
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<tr>
<td></td>
<td>45</td>
<td>45%</td>
<td>62</td>
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<td></td>
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<td>Education</td>
<td></td>
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<tr>
<td>Matriculate or more</td>
<td>24</td>
<td>24%</td>
<td>58</td>
</tr>
<tr>
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<td>76</td>
<td>76%</td>
<td>42</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
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<tr>
<td>Gestation</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>1st trimester</td>
<td>38</td>
<td>38%</td>
<td>37</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>37%</td>
</tr>
<tr>
<td>2nd or 3rd trimester</td>
<td>62</td>
<td>62%</td>
<td>63</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>63%</td>
</tr>
<tr>
<td>Parity: 1</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>&gt;1</td>
<td>44</td>
<td>44%</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>56</td>
<td>56%</td>
<td>68</td>
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<td></td>
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<tr>
<td>Family income</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;Outgoings</td>
<td>62</td>
<td>62%</td>
<td>57</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>57%</td>
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<tr>
<td>&gt;Outgoings</td>
<td>38</td>
<td>38%</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>43%</td>
</tr>
<tr>
<td>Presence of depressive symptoms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>34</td>
<td>34%</td>
<td>86</td>
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<tr>
<td></td>
<td>66</td>
<td>66%</td>
<td>86%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Yes</td>
<td>86</td>
<td>86%</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>66</td>
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<td>14%</td>
</tr>
<tr>
<td>Origin: Rural</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>88</td>
<td>88%</td>
<td>71</td>
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<td>71%</td>
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<td>66</td>
<td>66%</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>29%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.003</td>
</tr>
<tr>
<td>Previous loss or complication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>70</td>
<td>70%</td>
<td>74</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>30%</td>
<td>26</td>
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<td></td>
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<tr>
<td></td>
<td>74</td>
<td>74%</td>
<td>26</td>
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<td>26%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.529</td>
</tr>
</tbody>
</table>

Table No.2: The correlated factors relating to the presence or absence of husband in the country: the binary logistic regression

<table>
<thead>
<tr>
<th></th>
<th>B</th>
<th>( p )-value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(ref. is &gt;30 years)</td>
<td>0.730</td>
<td>0.061</td>
<td>2.075 (0.968 – 4.449)</td>
</tr>
<tr>
<td>Gestation(ref. is early pregnancy)</td>
<td>-0.086</td>
<td>0.836</td>
<td>0.917 (0.404 – 2.080)</td>
</tr>
<tr>
<td>Parity(ref. is Multiparous)</td>
<td>0.731</td>
<td>0.089</td>
<td>2.076 (0.895 – 4.818)</td>
</tr>
<tr>
<td>Depressive symptoms(ref. is no depressive symptoms)</td>
<td>2.591</td>
<td>0.000</td>
<td>13.338 (6.052 – 29.398)</td>
</tr>
<tr>
<td>Origin (ref. is urban origin)</td>
<td>0.997</td>
<td>0.053</td>
<td>2.709 (0.988 – 7.427)</td>
</tr>
<tr>
<td>Family income(ref. is more than outgoings)</td>
<td>0.411</td>
<td>0.275</td>
<td>1.508 (0.721 – 3.153)</td>
</tr>
<tr>
<td>Previous loss or complication (reference is no complication)</td>
<td>0.092</td>
<td>0.834</td>
<td>1.096 (0.465 – 2.585)</td>
</tr>
<tr>
<td>Education (ref. is above matriculation)</td>
<td>1.370</td>
<td>0.000</td>
<td>3.935 (1.858 – 8.333)</td>
</tr>
</tbody>
</table>

DISCUSSION

Marriage is usually a contract between two people involving emotional component in addition to the legal binding therefore two persons who sign this contract are believed to stay with each other during all the phases of their lives. It holds especially true for the couples of eastern origin.24 For the past several decades, empirical studies have concluded that the married report better mental health than the unmarried.25 Supportive behaviors of one spouse may lessen symptoms of illness in their partner.26 Socioeconomic strain may affect this source of support and compel the husband to go abroad to earn the

After the application of inclusion and exclusion criteria 100 cases and controls were included in the study. Mean age of the study participants was 29.73 (±5.395). Table I shows that 66 women had depression in the case group while 14 had in the control group (\( p \)-value <0.001). Education and rural origin were also significantly different among both the groups (Table 1 & 2). Lesser number of visits per year to the country was strongly related to the presence of depressive symptoms among the case group when binary logistic regression was done (Table 3).
livelihood. Managing economic changes, filling the role of both mother and father, isolation, and fears of abandonment result in mental stress and profound sadness among the women.\textsuperscript{20} This trend is quite common in the developing countries including the hostile area of AJK.\textsuperscript{10} AJK is a disputed territory for more than seventy years now with constant stress of hostile political environment and limited employment opportunities. Women may adjust to this living away from husband and cope with the routine stressors but may face psychiatric morbidity during the special phases of life. Pregnancy has always been considered a unique phase in the life of a women. Few perceive it as a happy and satisfying time of life; others may feel fearful, stressed or even depressed.\textsuperscript{17,19} Both the cases and controls in our study showed the presence of depressive symptoms but the number was far high in the case group i-e among those with husbands abroad for the sake of employment. Similar results have been reported in the past as well in the studies done on this phenomenon.\textsuperscript{27,28}

Regression analysis revealed that week of pregnancy, site of recruitment, years of education, income, marital status, employment, and number of miscarriages and stillbirths were significant predictors of total BDI score.\textsuperscript{21} An interesting finding was the significant difference in education status of the cases and control. Pregnant women with husband abroad had significantly lower education status as compared to the women with husbands living with them. Previously women disadvantaged by poverty and lower education has been a consistent correlate with depressive symptoms in pregnant sample.\textsuperscript{29,31} Reason of this finding in our study may be overall low education status in the social framework of the population from which sample has been drawn. This low education might also have compelled husbands to go abroad for employment due to fewer opportunities for people with less education in our part of the world. Qualitative studies involving the partners may clear this association in future studies.

Most of the cases were from rural background while most of the controls were from the urban background. This was an incidental finding as this parameter was not matched deliberately in the study design. Difference was statistically significant and has also been reported in the previous studies.\textsuperscript{19,30} Rawalakot is a small city with number of villages in the surroundings. City provides certain job opportunities to the people but in villages these are rare. Usually they can grow crops and that too can’t be done in winters. Hostile environment with constrained relationship with India add to the uncertainty and compel the inhabitants especially those with less education to seek employment abroad.

Among the cases when binary logistic regression analysis was applied the only factor which had a significant relationship with presence of depressive symptoms among pregnant ladies with husbands abroad was the number of visits per year. Though with advancement in technology the social media and other ways of communication has made this world a global village and one can remain in touch with his family and loved ones all the time despite being abroad but still physical presence has its own importance. These finding correlate with the findings done in past that physical presence of husband with the spouse has a link with better mental health.\textsuperscript{27,28} Therefore if this parameter has some association in other studies as well, this can be advised in the antenatal visits that partner should increase the frequency of visits to the home if possible in order to protect the wife from psychological issues during this vulnerable time.

To the best of our knowledge, this is the first study in AJK to examine the difference in prevalence of depressive symptoms among pregnant women with husbands abroad and living with them. However, several important limitations should be noted. This study lacked clinical validation of the PHQ, and is therefore subject to error that arises from false positives and negatives inherent when using screening tools. Another interesting factor which was not scope of this study that women with husbands living with them but physically abusing them may show greater rate of depression as compared those with husbands abroad. This comparison might change the results of our study. Therefore, results of our analysis could not be generalized. Sample was from a private hospital. Inclusion of sample from government hospitals of AJK may also alter the results.

Given the high prevalence of antenatal depressive symptoms among the women with husbands abroad, early intervention may have important child health implications. Therefore, routine screening of psychological problems among the pregnant women with husbands abroad may affect the maternal and child outcome positively.

**CONCLUSION**

A large number of young males have been working abroad from the area of AJK and this study showed a high frequency of depressive symptoms among pregnant women with husbands abroad as compared to those with husbands living with them. Special attention should be paid to the women whose husband had lesser number of visits to the country.

**Author’s Contribution:**
- Concept & Design of Study: Syed Azhar Ali
- Drafting: Ayesha Shaqfaght
- Data Analysis: Misbah Batool, Roomisa Anis
- Revisiting Critically: Syed Azhar Ali, Ayesha Shaqfaght
- Final Approval of version: Syed Azhar Ali
Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES


Time Lapse from Appearance of First Symptoms to the Patients First Contact to Hospital in Laryngeal Carcinoma

Muhammad Saeed Razi¹, Javed Riaz Qureshi⁵, Anum Adnan², Kamran Hamid³, and M Sabir⁴

ABSTRACT

Objective: To study the Time Lapse from appearance of first symptoms to the patients first contact to hospital in laryngeal carcinoma.

Study Design: Experimental and Observational study.

Place and Duration of Study: This study was conducted at the Idris Teaching Hospital Sialkot Medical College Sialkot from Jan 2016 to Jan 2019.

Materials and Methods: Sixty patients were included in this study and Time Lapse from Appearance of first symptoms to the patients first contact to hospital in laryngeal carcinoma were recorded. The demographic data was also noted down on the designed perfsoma. The written informed consent was taken before the start of study. The permission of Ethical Committee was considered before collection of data and publishing in medical journal. The data was analyzed on SPSS version 10.

Results: The duration, time lapse from appearance of first symptoms first contact to hospital in case in 1 month, the number of patients were 03(5%), in 2 months the patients were 01(1.66%), in 3 months the number of patients were 08(13.33%), in 5 months the number of patients were 02(3.33%), in 6 months the number of patients were 12(20%), in 7 months the number of patients were 046.66%), in 9 months the number of patients were 04(6.66%), in 12 months the number of patients were 06(10%), in 18 months the number of patients were 06(10%), in 24 months the number of patients were 10(16.66%), in 30 months the number of patients were 04(6.66%) were detected. At age 35-40 years, there were 15(44.16%) Male and 13(50%) female, at age 41-55 years there were 10(29.41%) Male and 07(26.92%) Female, at age 56-66 years there were 07(20.58%) Male and 05(19.23%) Female, at age above 67 years there were 02(5.88%) Male and 01(3.84%) Female patients.

Conclusion: It was concluded that the time lapse from appearance of first symptoms to the patients first contact to hospital in laryngeal carcinoma was variable in different patients

Key Words: laryngeal carcinoma, time elapse, first symptom, hospital contact

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INTRODUCTION

Head and neck tumor (HNC) includes many tumors that derived in the nasal cavity, glands that discharge a fluid secretion and especially saliva into the mouth cavity, sinuses in nasal cavity, the membrane-lined cavity behind the nose and mouth, oral cavity and the hollow muscular organ forming an air passage to the lungs¹.

¹ Department of ENT / Medical Officer² / Surgery³ / Anatomy⁴, Sialkot Medical College Sialkot.
⁵ Department of ENT, Khawaja Muhammad Safdar Medical College Sialkot.

Correspondence: Mohammad Saeed Razi, Assistant Professor of ENT, Sialkot Medical College Sialkot.
Contact No: 0300-4949520
Email: hrd@smcs.edu.pk

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Printed: September, 2020

Approximately forty two/four hundred forty new HNC cases were diagnosed and eight thousand three hundred ninety HNC-related deaths were observed in the United States in two thousand fourteen. relating to larynx. Tumors description for thirty three point nine percent of all Head & Neck cancers⁵, relating to larynx tumor usually affects middle-aged male, & common form of skin cancer typically ninety percent of relating to larynx tumor. New occurrence is common in relating to larynx tumor. New occurrence rate in sick person with T1 stage relating to larynx tumor change from five to thirty percent and with T2 stage cancer, it change from twenty five to thirty percent⁶. As for sick persons with T3 and T4 stage disease, the New occurrence rate is thirty to fifty percent⁶. According to the cancer place, relating to larynx tumor can be grouped as above the glottis tumor, relating to the tongue tumors or below the glottis tumors. Primary carcinomas in the below the glottis area are comparatively less common, and only taken for one to two percent of all relating to larynx tumor⁷. The mostly of under the glottis tumors are
found late in the path of the sickness, at which point surgery is difficult. In addition to, the cancer cells break away from the original tumor rate of group of nodes found on the anterior part of the neck and along the trachea lymph nodes is high, which give to a poorer prognostication and a higher post-operative New occurrence rate. The majority of the treatment failures in cases of above the glottis relating to larynx tumor are due to difficulty in the elimination of restricted to a localized region sickness. Specially, regional disease in the lymph node of neck. New occurrence most usually occurs in the hollow muscular organ forming an air passage to the lungs, including the various parts surrounding the mouth of invertebrates area, followed by the regional lymph nodes and the less commonly affected distant sites.

The treatment choice for New occurrence relating to larynx tumor are as follows: i) Occurring again several times X-Ray treatment with or without medical treatment, ii) saving something surgery, iii) caring treatment or iv) treatment that relieves suffering medical treatment. The better than another method for the therapeutic treatment of New occurrence of larynx carcinoma after failure of non-surgical (X-Ray treatment or medical & X-Ray treatment) treatment failure is surgery. Prevention of wasteful use of a resource surgery is likely in approximately one-third of these New occurrence of carcinoma. Endoscopic surgery using a CO2 laser or open partial laryngeal surgery (partial vertical, supracricoid or supraglottic laryngeal surgeries) can also be used. A past work showed that, compared with total laryngeal surgery, An operation to remove the cancer and some normal tissue around it, but not the breast itself has a better prognostication, but it is possible that these results were caused by the bias introduced by the selection, as more advanced sick persons had to receive a total laryngeal surgery. As for sick person who have undergone surgery, a 2nd or 3rd surgery can also be the first preference as that aims at the complete cure of a disease. New occurrence advanced-stage tumors and those with below the glottis extension should generally be treated by total laryngeal surgery. The use of Treatment that is given in addition to the primary (initial) treatment depends on the dangerous factors. X-ray treatment with concurrent systemic treatment is advised when the new occurrence sites are non-surgical or when the sick person has not previously undergone X-ray treatment, providing the sick persons general condition allows it. If a sick person with tumor new occurrence is neither eligible for surgery nor eligible for X-ray treatment, then the treatment approach is the same as that for sick persons with produced by metastasis disease. The overall five-year survival rate of sick persons with local new occurrence who undergo Palliative surgery varies greatly from twenty-two to sixty-six percent. One previous study has even shown the five-year survival rate in this sick person population to be as low as two percent.

MATERIALS AND METHODS

Sixty patients were included in this study and Time Lapse from Appearance of first symptoms to the patients first contact to hospital in laryngeal carcinoma were recorded. The demographic data was also noted down on the designed performa. The written informed consent was taken before the start of study. The permission of Ethical Committee was considered before collection of data and publishing in medical forum journal. The data was analyzed on SPSS version 10.

RESULTS

The duration, time lapse from appearance of first symptoms first contact to hospital in case in 1 month, the number of patients were 03(5%), in 2 months the patients were 01(1.66%), in 3 months the number of patients were 08(13.33%), in 5 months the number of patients were 02(3.33%), in 6 months the number of patients were 12(20%), in 7 months the number of patients were 04(6.66%), in 9 months the number of patients were 04(6.66%), in 12 months the number of patients were 06(10%), in 18 months the number of patients were 06(10%), in 24 months the number of patients were 10(16.66%), in 30 months the number of patients were 04(6.66%) were detected as shown in table no 1.

Table No.1: Time Lapse from Appearance of first symptoms to the patients first contact to hospital in laryngeal carcinoma

<table>
<thead>
<tr>
<th>Duration</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month</td>
<td>03</td>
<td>5%</td>
</tr>
<tr>
<td>2 month</td>
<td>01</td>
<td>1.66%</td>
</tr>
<tr>
<td>3 months</td>
<td>08</td>
<td>13.33%</td>
</tr>
<tr>
<td>5 months</td>
<td>02</td>
<td>3.33%</td>
</tr>
<tr>
<td>6 months</td>
<td>12</td>
<td>20%</td>
</tr>
<tr>
<td>07 months</td>
<td>04</td>
<td>6.66%</td>
</tr>
<tr>
<td>9 months</td>
<td>04</td>
<td>6.66%</td>
</tr>
<tr>
<td>12 months</td>
<td>06</td>
<td>10%</td>
</tr>
<tr>
<td>18 months</td>
<td>06</td>
<td>10%</td>
</tr>
<tr>
<td>24 months</td>
<td>10</td>
<td>16.66%</td>
</tr>
<tr>
<td>30 months</td>
<td>04</td>
<td>6.66%</td>
</tr>
<tr>
<td>Total</td>
<td>60</td>
<td>100%</td>
</tr>
</tbody>
</table>

At age 35–40 years, there were 15(44.16%) Male and 13(50%) female, at age 41–55 years there were 10(29.41%) Male and 07(26.92%) Female, at age 56–66 years there were 07(20.58%) Male and 05(19.23%) Female, at age above 67 years there were 02(5.88%) Male and 01(3.84%) Female patients (table 2).
The present study shows the significance of various serving to predict the likely course of a medical condition factors for primary and new occurrence laryngeal tumors, and the corresponding treatments. The three-five & ten-year survival rates of the entire sick person sample were approximate to be sixty-eight point nine, fifty-three point six & thirty-five point seven percent, respectively. The sick persons who developed local new occurrence had five-year survival rates of sixty-one point eight percent, which is better than the rate of fifty-two point one percent in the sick persons who developed regional recurrence and zero percent in the sick person who developed distant cancer cells break away from the original (primary) tumor. These figures are in accordance the results reported by Brenner et al, in which the two & five-year survival rates were approximated to be sixty-seven & fifty-six percent, respectively.

Due to the natural boundaries that stop the spread of tumor cells in the body and the relatively early symptoms associated with new occurrence, the possibility of successfully performing palliative surgery in sick persons with local new occurrence without damaging vital function is quite high\textsuperscript{18,39}. In the present work, palliative surgery resulted in a better prognosis in cases of local recurrence. Palliative surgery was performed in sixty-eight point three percent of the cases of local new occurrence and resulted in a five-year survival rate of seventy-three percent, which was much better than the thirty-two point three percent survival rate in local new occurrence cases in which palliative surgery was not performed. This is similar to the results of the above said work by Brenner et al\textsuperscript{9}, where sixty-nine percent of the local new occurrence cases received palliative surgery, with a five-year survival rate of seventy-six percent. However, Lacy and Piccirillo mentioned that for sixty-four point five percent of the sick persons with new occurrence who underwent palliative surgery, the two-year survival rate was only fifty-five percent. The reason that the present work had a better survival rate was possibly due to the fact that there were more initial early-stage sick persons (fifty-eight point six vs. fifty point eight percent). Moreover, in the work by Yuen et al\textsuperscript{2}, only twenty-one percent of the sick persons with local new occurrence underwent palliative surgery, and the five-year tumor-free survival rate was just forty-two percent.

The reason that so few sick persons were suitable for palliative surgery in this work was as ninety-seven point nine percent sick persons presented with initial T3 or T4 tumors and hundred percent sick persons underwent total laryngeal surgery prior to new occurrence. Sick persons with a disease-free interval of twelve months showed a seventy-four point one percent five-year survival rate, which was significantly better than those with an interval of less than twelve months. This was also in somewhat good resemblance with the figures reported by Lacy and Piccirillo, where the two-year OS rate for the group with a disease-free interval of twelve months, two years and less than two years was thirty-three, thirty-seven & fifty-three percent respectively, and Brenner et al, where the five-year OS rate for the group with a disease-free interval of fifty-six & less than six months was forty-four & seventy percent, respectively\textsuperscript{9}.

The present variable quantity analysis showed that the following factors are negatively correlated with the five year OS rate: Age less than sixty years, smoking index six hundred, poor tumor grade, above the glottis and below the glottis tumors, initial tumor T stages T3 and T4, initial tumor UICC stages III and IV, positive located at or near a node of the initial tumor, disease-free interval less than twelve months, distant produced by metastasis disease and non-eligibility of the new occurrence tumor for surgery. In addition, medical treatment & X-ray treatment for the initial tumor were found to be significant poor serving to predict the likely course of a medical condition factors. There could be several reasons for this association. Firstly, and most importantly, the effect of selection unfairness cannot be ruled out. Sick persons who initially had poor serving to predict the likely course of a medical condition factors (poorly-differentiated tumors and more advanced Universal Integrated Circuit Card stage) would be more likely to receive surgery plus X-Ray treatment or medical treatment with other treatment; new occurrence tumors in the case of such sick persons would have a poorer serving to predict the likely course of a medical condition. This probably also mention why sick persons who underwent surgery plus X-Ray treatment or medical treatment with other treatments had a poorer five-year OS rate than those who received surgery or X-Ray treatment alone. Similar results have been showed by Lacy and Piccirillo. The groups that received only surgery and X-Ray treatment for the initial tumor had a two-year OS rate of sixty & fifty-seven percent, respectively, while the group that received surgery plus X-Ray treatment had a two-year OS rate of only fifteen percent. Secondly, repeating the medical treatment protocol for new occurrence tumors cannot ensure effectiveness of the medical treatment, as certain cancer cells may have drug resistance. Thirdly, if X-Ray treatment was already used for the initial tumor, repeat

### Table No.2 : Age and Gender Distribution

<table>
<thead>
<tr>
<th>Serial no</th>
<th>Age(years)</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>35-40</td>
<td>15(44.16%)</td>
<td>13(50%)</td>
</tr>
<tr>
<td>2</td>
<td>41-55</td>
<td>10(29.41%)</td>
<td>07(26.92%)</td>
</tr>
<tr>
<td>3</td>
<td>56-66</td>
<td>07(20.58%)</td>
<td>05(19.23%)</td>
</tr>
<tr>
<td>4</td>
<td>67 and above</td>
<td>02(5.88%)</td>
<td>01(3.84%)</td>
</tr>
<tr>
<td>Total(60)</td>
<td></td>
<td>34(100%)</td>
<td>26(100%)</td>
</tr>
</tbody>
</table>
radiation for the new occurrence tumor is not feasible and at the same time, palliative surgery may also not be possible due to the acute side-effect of the radiation, particularly in sick persons who experienced a shorter disease-free interval.

The present work found that smoking years was not a significant serving to predict the likely course of a medical condition factor, which is similar to the result shown by Brenner et al. However, the present work found that smoking index was a significant serving to predict the likely course of a medical condition factor. This is different from the finding of Lacy and Piccirillo, according to which, smokers and non-smokers had a similar two-year OS rate of forty percent. A thorough search of other relevant literature did not show any more findings with regard to the association between smoking and new occurrence laryngeal tumors; however, a work on passive smoking and the prevalence of laryngeal tumors revealed that sick persons with advanced tumors were mostly in the environmental tobacco smoking exposure group. Therefore, the present work attempted to determine the association between smoking and initial T stage and tumor grade. It was observed that the group with a smoking index of less than six hundred had a higher proportion of T3 and T4 tumors than the group with smoking index of < less than six hundred; moreover, the former group also had a higher proportion of sick persons with poorly and moderately differentiated tumors than the latter. These values may explain why sick persons with new occurrence tumors who had a smoking index of less than six hundred had poor prognostic factors.

In total, one hundred & twenty-two (thirty-nine point nine percent) sick persons presented with well-differentiated tumors, one hundred thirty-eight (forty-four point seven percent) with moderately differentiated tumors and forty-nine (fifteen point nine percent) with moderately-differentiated tumors. The five-year of values were sixty-two point two, fifty-five point one & twenty-three point six percent, respectively. These were quite different from the values reported by Brenner et al, where the proportion of well-differentiated and moderately- and poorly-differentiated tumors was twenty-three point two& seventy-six point eight percent, respectively, with corresponding five-year of rates of sixty-one & sixty-five percent, respectively. These are different from the values reported by Lacy and Piccirillo too, in which the proportion of well differentiated, moderately-differentiated, and poorly-differentiated cancer was sixty-six point one, twenty-five point eight & seven point three percent, respectively, and the corresponding two-year of rates were forty-four, thirty-four & twenty-two percent, respectively.

Multivariate analysis showed that the five-year of rate was significantly associated with the initial T stage, grade, nodal status, disease-free interval and eligibility for surgery. This is in resemblance with the results of the works by Lacy and Piccirillo and Marshak et al. The work by Lacy and Piccirillo showed that initial treatment, initial TNM stage and extent of new occurrence were independent serving to predict the likely course of a medical condition factors for new occurrence in laryngeal tumor. The work by Brenner et al showed that the initial tumor site, the nodal status, the extent of new occurrence and its operability were the only factors that predicted survival.

The major limitation of retrospective studies is that the data collected are not originally designed for application in research. Therefore, certain factors responsible for the ultimate treatment outcome may be missing in the analysis and contribute to an unfairness. Thus, the conclusions from the present study should be validated in future prospective works.

In summary, the present work found five factors to be predictors of good survival in sick persons with new occurrence laryngeal tumor: Initial tumor T stages T1 and T2, a high differentiation rate, no cervical lymph node the spread of a disease-producing agency (such as cancer cells) from the initial or primary site of disease to another part of the body of the initial tumor, a disease-free interval of twelve months and eligibility for surgery.

**CONCLUSION**

It was concluded that the Time Lapse from Appearance of first symptoms to the patients first contact to hospital in laryngeal carcinoma was variable in different patients.

**Author’s Contribution:**

Concept & Design of Study: Muhammad Saeed Razi
Drafting: Javed Riaz Qureshi, Anum Adnan
Data Analysis: Kamran Hamid, M Sabir
Revisiting Critically: Muhammad Saeed Razi, Javed Riaz Qureshi
Final Approval of version: Muhammad Saeed Razi

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

**REFERENCES**

recurrent laryngeal cancer following initial nonsurgical therapy. Head & Neck 2012;34:727–735.
Trend of Sexual Offences in Pakistan

M Ijaz¹, M Asif², Azhar Masud Bhatti, Tanveer Hussain⁴ and Abdul Hamid³

ABSTRACT

Objective: To Study Trend of Sexual Offences in Pakistan.

Study Design: Retrospective Study

Place and Duration of Study: This study was conducted at the Departments of Forensic Medicine, FMC, Abbatabad, SMC, Sialkot, RMDC, Lahore and FJMU, Lahore from Feb 2018 to Jan 2020.

Materials and Methods: Two Hundred and sixty-three Victims of sexual offences were included in this study. The performa was designed to record demographic data. Injuries inflicted during sexual offence, Swab positive and negative were recorded. The history & examination was also recorded in the performa. The permission of Ethical Committee was also considered before collecting the data and get publish Medical Journal. The written informed consent was also taken before collecting the data. The results were analyzed by SPSS version 10.

Results: The incidence of sexual offences was maximum in age group 11-15 years 7(21.21%) and minimum in age group 51-70 years 1(3.03%) in male and in female incidence was maximum in age group 26-30 years 37(16.15%) and minimum in age group 71 & above years 09(3.93%). The incidence of sexual offences was maximum in Lower class population 135(51.33%) and minimum in high gentry 27(10.26%). The incidence of sexual offences was maximum in rural population 201(74.42%) as compared to urban population 62(23.57%) as most of the people live in rural area. There was 173(65.77%) victims who had swab positive and 90(34.22%) swab negative. There was maximum incidence of injuries of genital area & genital tract 76 (28.89%) and minimum incidence of injuries chest & abdomen 27(10.26%).

Conclusion: Women reaching the at risk age should be educated regarding the signal warning of danger for such a prevalence and how best to respond to such a situation. Survivors and the closely associated people should be educated to rep on such an incident immediately and get the victim examined so that proper evidence can take place and evidence collected. Facilities for seminal fluid grouping and Deoxy Ribo Nuclic Acid analysis should be developed to help in identifying the illegal. Finally,

Key Words: Trend, Sexual Offences, Demographic data, Informed consent, Ethical Committee & Pakistan


INTRODUCTION

Grown-up rape is a significant general wellbeing worry all through the globe¹ and is currently considered as a circumstance requiring crisis clinical therapy⁵. In the same way as other different nations of the world, grown-up sexual maltreatment is fundamentally confined inside the legitimate framework in Pakistan. The legal doctor is principally associated with the evidence of the discoveries and the assortment of proof.⁶

¹ Department of Forensic Medicine, FMC, Abbatabad.
² Department of Forensic Medicine, SMC, Sialkot.
³ Department of Forensic Medicine, RMDC, Lahore.
⁴ Department of Forensic Medicine, FJMU, Lahore.

Correspondence: Dr. M Ijaz Assistant Professor of Forensic Medicine Frontier Medical College, Abbatabad.
Contact No: 0300-5619525
Email: hrd@smc.com

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This division of the clinical reaction to assault into a legitimate and clinical part is an impediment to an ideal assistance for survivors.⁷ The clinical reaction to rape ought to incorporate treatment of the wounds and follow up advising notwithstanding the documentation and assortment of proof. In numerous nations, uncommon component has been set up which oblige all parts of the survivor related with sex maltreatment 1rom announcing and assessment to therapy and development.

In United States of America, six lakhs eighty three thousand women are assaulted every year.4 This is disregarding the way that rape is the least announced o1 the brutal violations with just sixteen to thirty nine percent being accounted for to the police.⁵⁶ Those among twelve to twenty-four years old are generally inclined to related with sex brutality in United States of America.6 However no age is resistant, with cases being accounted for in the age scopes of three months to eighty-six years in Lisbon, Portugal.⁷ The likelihood of evidence of wounds and assortment of positive proof abatements as the time stretch among
the ambush and clinical assessment increases.8 disregarding this between twenty to thirty-eight point five percent of the casualties announced following twenty-four hours o1 the occasion and countless casualties revealed over seventy-two hours after the attack at the National Institute of Legal Medicine in Portugal.7

The Culprit o1 the ambush was typically somebody known to the casualty in concentrates in Nairobi, Denmark and Canada9-11 and the quantity o1 attackers was more than one out of countless cases in Ohio, USA.12

Most of legal proof for a situation of rape is seen on the garments and sheet.8 the body of the casualty may have bodily discoveries characteristic of power or savagery not with manding nearby wound or wound to the private parts zone. These wounds might be characteristic o1 whether the demonstration was involving consent or was against assent, something that is probably going to have wide legitimate meanings. The wounds can be featured by the utilization o1 toluidine blue to the influenced parts.13

The nearness of seminal fluid in the swabs taken Irom the body o1 the casually is a significant authenticating proof. This increases further significance of seminal fluid gathering or Deoxy Ribo Nuclic Acid composing of the original stains should be possible. The evidence can be additionally TortiTied by detachment of women Deoxy Ribo Nuclic Acid (having a place with the person in question) from penile swabs taken from the suspected attacker.14

This examination was directed to know the components o1 this significant general wellbeing concern. This would help us in creating techniques to forestall such rates by teaching women in the powerless gathering.

MATERIALS AND METHODS

This study was conducted at the Departments of Forensic Medicine, FMC, Abbatabad, SMC, Sialkot, RMDC, Lahore and FJMU, Lahore. Two Hundred and sixty-three victims of sexual offences were included in this study. The Performa was designed to record demographic data, Injuries inflicted during sexual offence, Swab positive and negative were recorded. The history & examination was also recorded in the perform. The permission of Ethical Committee was also considered before collecting the data and get publish Medical Journal. The written informed consent was also taken before collecting the data. The results were analyzed by SPSS version 10.

RESULTS

The incidence of sexual offences was maximum in age group 11-15years 7(21.21%) and minimum in age group 51-70years 1(3.03%) in male and in female incidence was maximum in age group 26-30years 37(16.15%) and minimum in age group 71 & above years 09(3.93%) as shown in table 1.

Table No 1: Age and gender distribution

<table>
<thead>
<tr>
<th>Serial No</th>
<th>Age (years)</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5—10</td>
<td>515.15%</td>
<td>15.65%</td>
</tr>
<tr>
<td>2</td>
<td>11—15</td>
<td>7 21.21%</td>
<td>25.10.91%</td>
</tr>
<tr>
<td>3</td>
<td>16—20</td>
<td>3 9.09%</td>
<td>27.11.79%</td>
</tr>
<tr>
<td>4</td>
<td>21—25</td>
<td>4 12.12%</td>
<td>30.13.10%</td>
</tr>
<tr>
<td>5</td>
<td>26—30</td>
<td>5 15.15%</td>
<td>37.16.15%</td>
</tr>
<tr>
<td>6</td>
<td>31—40</td>
<td>3 9.09%</td>
<td>34.14.84%</td>
</tr>
<tr>
<td>7</td>
<td>41—50</td>
<td>2 6.06%</td>
<td>25.10.91%</td>
</tr>
<tr>
<td>8</td>
<td>51—60</td>
<td>1 3.03%</td>
<td>14.6.11%</td>
</tr>
<tr>
<td>9</td>
<td>61—70</td>
<td>1 3.03%</td>
<td>13.5.67%</td>
</tr>
<tr>
<td>10</td>
<td>71 &amp; Above</td>
<td>2 6.06%</td>
<td>09.3.93%</td>
</tr>
</tbody>
</table>

Total 33 (100%) 229 (100%)

The incidence of sexual offences was maximum in Lower class of population 135(51.33%) and minimum in high gentry 27(10.26%) as shown in table 2.

Table No. 2: Socio economic status distribution

<table>
<thead>
<tr>
<th>Serial No</th>
<th>Socio economic status</th>
<th>No of Victims (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Low</td>
<td>135 51.33%</td>
</tr>
<tr>
<td>2</td>
<td>Middle</td>
<td>101 38.40%</td>
</tr>
<tr>
<td>3</td>
<td>High</td>
<td>27 10.26%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>263 (100%)</td>
</tr>
</tbody>
</table>

The incidence of sexual offences as maximum in rural population 201(74.42%) as compare to urban population 62(23.57%) as most of the people live in rural area as shown in table 3.

Table No. 3: Area distribution

<table>
<thead>
<tr>
<th>Serial No</th>
<th>Area</th>
<th>No of Victims</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Rural</td>
<td>201 (74.42%)</td>
</tr>
<tr>
<td>2</td>
<td>Urban</td>
<td>62 (23.57%)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>263 (100%)</td>
</tr>
</tbody>
</table>

There was173(65.77%) victims who had swab positive and 90(34.22%) swab negative as shown in table 4.

Table No. 4: Swab positive or negative distribution

<table>
<thead>
<tr>
<th>Serial No</th>
<th>Swab</th>
<th>No of Victims</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Positive</td>
<td>173 (65.77%)</td>
</tr>
<tr>
<td>2</td>
<td>Negative</td>
<td>90 (34.22%)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>263 (100%)</td>
</tr>
</tbody>
</table>

Table No 5: Injuries distribution on the body of victim

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Injuries</th>
<th>No of Victims</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Face</td>
<td>35 (13.30%)</td>
</tr>
<tr>
<td>2</td>
<td>Head &amp; Neck</td>
<td>37 (14.06%)</td>
</tr>
<tr>
<td>3</td>
<td>Chest &amp; Abdomen</td>
<td>27 10.26%</td>
</tr>
<tr>
<td>4</td>
<td>Back</td>
<td>57 21.67%</td>
</tr>
<tr>
<td>5</td>
<td>Upper &amp; Lower limbs</td>
<td>31 11.78%</td>
</tr>
<tr>
<td>6</td>
<td>Genital area &amp; Genital tract</td>
<td>76 28.89%</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>263 (100%)</td>
</tr>
</tbody>
</table>
There was maximum incidence of injuries of genital area & genital tract 76(28.89%) and minimum incidence of injuries chest & abdomen 27(10.26%) as shown in table 5.

DISCUSSION

In our examination, the age bunch generally inclined to a rape was age group 26-30years 37(16.15%) while the casualties went in age from six years to forty years old. This is in accordance with concentrates in Bangladesh \^{15}, and is like that detailed in some European countries.\^{2,4,6,16} However concentrates in Canada \^{11} and Nairobi \^{9} demonstrated nineteen-multiyear age section generally inclined to a rape. The previous time of inclination in our examination could be because of the way this is the age at which women in our general public are less mindful and obliviousness of the impulses of community. As they develop, they will in general be progressively defensive of outsiders and associates the same. It is a result of this reality that no lady more than forty years old was accounted for to have been attacked explicitly in our investigation. There is a need to instruct women arriving at pubescence. Social restrictions making moms or other old women in the background reluctant to talk about the way toward developing into mature ought to be disheartened. Women who need to go out autonomously or may some way or another experience such a circumstance ought to be made mindful of the alert signs characteristic of such an approaching circumstance and how they ought to react so as to ensure themselves.

The late detailing in this investigation is presumably because of the dynamic procedure in our general public. Such an episode is taken as a blow on the background respect. The grievous casually first sets aside some effort to talk about it with her mom or other senior women. Further hesitance and thought goes into the episode before it is brought to the notification of the male of the house and here again delay happens in dynamic as revealing the occurrence adds up to making it open and an affront to the background.

Clear rules ought to be created for casualty and background reaction to such a circumstance as early revealing improves the probability of acquiring clinical proof for sentencing the attacker. Moreover, components ought to be set up for assurance of the security/personality of the plaintiff and the background and undue exposure ought to be dodged. By and large it has been seen that clinical assessments are done after a postponement of days as well as weeks bringing about loss of significant proof. It has been accounted for that ninety percent cases with positive legal proof were seen inside twenty-four hours of their attack.\^{8} The casualty had changed garments worn at the hour of the episode and had washed before the clinical assessment in eighty-three percent of the cases, in this manner bringing about loss of significant proof. This is carefully about in the way that in just three out of one hundred twenty-three cases were fundamental stains found on the garments. This was normal in the conditions where about eighty-eight percent of the casualties revealed 1or clinical assessment following forty-eight hours of the episode. This is enhanced by discoveries in United States of America that of all the legal proof gathered, sixty-four percent was found on the garments and cloth. Following twenty-four hours practically all positive proof is recouped from the garments or sheet.\^{8}

Bodily wounds were available on the body in There was maximum incidence of injuries of genital area & genital tract 76(28.89%) and minimum incidence of injuries chest & abdomen 27(10.26%) cases. Indications of ongoing injury to the genital region were available in just 76(28.89%) cases. This was not out of the ordinary as the greater part of the cases introduced for assessment after over seventy-two hours. The discoveries of wounds on the body and the genitalia are reliable with discoveries in Dhaka where thirteen point four eight percent of the casualties had proof of not related to private parts brutality and ten percent had indications of late injury to the private parts.\^{15} In concentrates from progressively created nations private parts wound is accounted for in a bigger extent (twenty two to fifty three percent) of the cases examined as is not related to private parts wound.\^{17,18} This could be clarified by the early detailing of the cases in these nations contrasted with Pakistan and Bangladesh.

An absorbent pad was taken for the nearness of seminal fluid in There was 173(65.77%) victims who had swab positive and 90(34.22%) swab negative cases. Semen was identified in 173(65.77%) cases, while it was negative in 90(34.22%) cases. This is a sudden finding as the likelihood of recognizing semen diminishes as the stretch between the ambush and clinical assessment increments and it is commonly acknowledged that recognition of complete sperms gets troublesome following twenty six hours and sperm heads after five days.\^{19} Chemical tests like corrosive phosphatase test and seminal fluid explicit glycoprotein (P30) might be certain for twenty four & forty eight hours respectively.\^{20} False constructive tests could bring about conviction of honest individuals. No seminal fluid gathering or Deoxy Ribo Nucleic Acid investigation was done as such offices were not accessible at that point. The unimportant discovery of seminal fluid is of little worth particularly in wedded women and even in unmarried casualties it is essential to build up a reason impact relationship by doing Deoxy Ribo Nucleic Acid investigation of the sperms and coordinating them with that of the suspects.

CONCLUSION

Women reaching the at risk age should be educated regarding the signal warning of danger for such a prevalence and how best to respond to such a situation.
Survivors and the closely associated people should be educated to report on such an incident immediately and get the victim examined so that proper evidence can take place and evidence collected. Facilities for seminal fluid grouping and Deoxy Ribonucleic Acid analysis should be developed to help in identifying the illegal. Finally, special centers should be developed where all needs of the survivors can be catered to. Staring from police reporting to medico-legal examination and continuing to medical and psychiatric treatment. This would prevent further causing injury the already injured survivors and the background; something that they have to undergo in taking help from the system in its current form.

**Author’s Contribution:**

- Concept & Design of Study: M Ijaz
- Drafting: M Asif, Tanveer Hussain
- Data Analysis: Azhar Masud Bhatti, Abdul Hamid
- Revisiting Critically: M Ijaz, Abdul Hamid, Azhar Masud Bhatti
- Final Approval of version: M Ijaz

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

**REFERENCES**

In-Hospital Outcomes and Angiographic Pattern in Primary Percutaneous Coronary Intervention (PCI) Among Patients of Acute Myocardial Infarction

Badar ul Ahad Gill1, Nisar Ahmed1, Muhammad Tahir Mohy-ud-Din1, Muhammad Zohaib Zahoor1, Muhammad Ikram Farid1 and Abubakr Ali Saad2

ABSTRACT

Objective: To find out the in-hospital outcomes and angiographic pattern of coronary artery disease in patients subjected to primary percutaneous coronary intervention (PCI) undergoing primary PCI for AMI.

Study Design: A descriptive cross-sectional study.

Place and Duration of Study: This study was conducted at the Department of cardiology, Chaudhry Pervaiz Elahi Institute of Cardiology, Multan January 2018 to September 2018.

Materials and Methods: Among these 135 study cases, 115 (85.1%) were having male gender, and 20 (14.88%) were having female gender. In our study cases, the mean age was 47.17 ± 6.89 years (The minimum age of included cases was 30 years, on the other hand the maximum age of study cases was 60 years). Among these 135 study cases, 30 (22.2%) were having diabetes mellitus and 45 (33.3%) were having a history of hypertension. History of cigarette smoking was present in 55 (40.7%) of our study case. Family history of coronary artery disease (CAD) was present in 15 (11.1%). A successful outcome was noted in 129 (95.6%) of our study cases. Single vessel involvement was present in 90 (66.6%) of study population, involvement of two vessels by coronary artery disease was found in 25 (18.5%) of patients and multi-vessel involvement in 20 (14.8%) of our study cases.

Results: A total of 135 patients fulfilling inclusion criteria of the study were recruited for study from Department of cardiology, Chaudhry Pervaiz Elahi Institute of Cardiology, Multan. Patients undergoing PCI were enrolled in the study to document in-hospital outcomes (success rate) and angiographic pattern. IBM SPSS version 18 was used to analyze the data.

Conclusion: The primary percutaneous intervention is seen to be a most effective, dependable and highly effective method of coronary revascularization in the setting of acute myocardial infarction. So our study results support employing primary PCI for high success rate and desired clinical outcomes among the patients who present with acute myocardial infarction, however, there are limitations to the applicability of this modality due to lack of resources.

Key Words: Primary Percutaneous Intervention, Outcome, Acute Myocardial Infarction

INTRODUCTION

Coronary artery disease (CAD) is one of the most prevalent reasons of hospital admission and death all around the world in all socioeconomic strata1,2.3. One of the presentations of coronary artery disease is acute myocardial infarction (MI). Acute MI is not only known to be a disease of the developed industrial world but its incidence is also quite high in the developing world and males are known to be affected more as compared to the females4. Over the last three to four decades, the research and advancements in the field of interventional cardiology showed Percutaneous coronary intervention (PCI) as considerable evidence-based invasive treatment of patients with IHD. Extensive research and advancements in drugs and hardware related to coronary interventions during the last decade resulted in an extensive use of primary PCI (PPCI) for management of patients who present to emergency departments with acute ST-segment elevation myocardial infarction (STEMI)5.

Primary PCI not only reduced the death rate associated with acute myocardial infarction but also decreases the
chances of re-infarction and neurological deficits due to intracranial bleeds associated with fibrinolysis and resulting stroke leaving some patients with permanent disability. It is the most beneficial therapy for acute STEMI, as rapid and more consistent reperfusion is achieved with a low complication rate when compared to fibrinolysis. Despite the beneficial effects of primary PCI, this modality of management for acute myocardial infarction has not been widely used in developing third-world countries, especially in the tertiary public health institutions and even university-level teaching hospitals where most of the patients expect a free treatment. The sole reason is the financial situation of these countries which led to low health budget hindering the availability of such procedures. This is the reason why a small amount of data is available from the countries of Subcontinent regarding the outcome of primary PCI. Up till now nothing surpasses Primary percutaneous intervention with regards to speed and accuracy in reperfusion of the affected myocardium. The side effects of treatment are minimal when the comparison is made using fibrinolytic therapy in acute myocardial infarction.

The rationale of this study was to ascertain in-hospital outcomes and angiographic pattern of patients undergoing primary PCI in our local population because little data is available on this topic. The availability and documentation of local experience will help other hospitals to start primary angioplasty program and to help in management of patients with acute myocardial infarction with the preferable and gold standard method of coronary revascularization.

**MATERIALS AND METHODS**

A descriptive cross-sectional study was carried out at the Department of Cardiology, Chaudhry Pervaiz Ellahi Institute of Cardiology (CPEIC), Multan from January 2018 to September 2018. The sampling method used in the study was Non-probability consecutive sampling. The inclusion criteria were patients of either gender within the age bracket of 30 to 60 years. The included patients initially presented in the emergency department, with chest pain where prompt ECG was done and focused history was obtained. The patients who were having chest pain less than 24 hours and elevation of ST segments more than one millimeter were considered for primary PCI and shifted to cardiac catheterization laboratory. The patients undergoing fibrinolytic treatment within twenty-four hours were not included in the study. Similarly, patients having non-ST elevation myocardial infarction were not included in the study. The patients having long-standing kidney disease with uraemia were also excluded. The patients were also evaluated for having an overt or covert hepatic disease and if found to be having hepatic cirrhosis were excluded from the study based on history, physical examination and previous laboratory reports including abdominal ultra-sonogram. The subjects who did not give written consent for the interventional procedure were not taken to cardiac catheterization laboratory and managed conservatively. During the study period, 135 patients were selected for intervention applying the above inclusion and exclusion criteria.

The study variables were registered on a dedicated proforma on the same day of procedure and patients were followed for three days in the hospital. Patients undergoing PCI were enrolled to document the angiographic pattern and in-hospital outcomes during current hospitalization. The in-hospital outcome was taken in terms of success rate, assessed on 3rd day of the procedure. The Successful procedures were taken as the attainment of TIMI III flow in the index vessel and the stenosis of less than thirty per cent in the stented segment. The patients were classified based on coronary angiograms to be having single-vessel coronary artery involvement if they were having equal to or greater than fifty per cent narrowing of the major epicardial coronary vessel. Two Vessel coronary involvement was labelled when a combination of left anterior descending and dominant left circumflex artery was found to be present or left anterior descending artery and dominant right coronary vessel were involved and were having equal to or greater than fifty percent narrowing of the major epicardial coronary vessel. Patients with left main stem involvement were also excluded from study. When all three coronary vessels were involved, the patients were labelled to be having three-vessel coronary artery disease or multi-vessel involvement. All the study data after registering in the study proforma was replicated in the data file created using IBM SPSS software version 18. Numerical quantitative data as Minimum, maximum, Mean and standard deviation for the age of the patients and Body mass index (BMI) were calculated. Categorical data were presented as frequencies and percentages. A separate table was created for coronary risk factors involvement. The major conventional risk factor as male sex, diabetes mellitus, increased blood pressure, tobacco/cigarette smoking, dyslipidaemias, and family history of ischemic heart disease, associated with coronary heart disease were recorded. The frequency and percentages for each risk factor were calculated. Tables were also created to record in hospital outcomes and pattern of disease as seen in coronary angiograms.

**RESULTS**

In our study population of 135 patients, the total number of patients having male gender was 115 (85.1%). On the other hand, the total number of female gender in study patients was only twenty, which constitutes 14.8 percent of the study patients. The mean age of all patients in our study population was 47.17 ± 6.89 years. The minimum and maximum age of our
study population were thirty and sixty years respectively. The mean age in the male gender group was 44.09 ± 5.79 years. In contrast to the male gender, the female gender group was having a mean age of 54.24 ± 2.94 years, with a p-value equal to 0.001 which is statistically significant. The results in the study population have shown that 65(48.1%) were having age greater than 45 years. The age group comprising of age 30 to 45 years was having a frequency of 70 in number, with a percentage of 51.8 in study population (Table 1). The frequency and percentage of different conventional major risk factors were as following. Out of total study population which comprise of 135 patients, 30 (22.2%) were having diabetes mellitus, and 45(33.3%) were having a history of high blood pressure. Cigarette smoking was found in 55 (40.7%) of our study patients. Positive Family history of coronary artery disease (CAD) was present in 15 (11.1%). (Table 2).

**Table No. 1: Age-wise distribution of study cases (n = 135)**

<table>
<thead>
<tr>
<th>Age Groups</th>
<th>No. of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 – 45 Years</td>
<td>70</td>
<td>51.8</td>
</tr>
<tr>
<td>More than 45 Years</td>
<td>65</td>
<td>48.1</td>
</tr>
<tr>
<td>Total</td>
<td>135</td>
<td>100</td>
</tr>
</tbody>
</table>

**Table No 2: Distribution of risk factors among study patients Total no.135**

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Yes(%)</th>
<th>No(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>55(40.7%)</td>
<td>80(59.3%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>45(33.3%)</td>
<td>90(66.7%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>35(25.9%)</td>
<td>100(74.1%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>30(22.2%)</td>
<td>105(77.8%)</td>
</tr>
<tr>
<td>Family history</td>
<td>15(11.1%)</td>
<td>120(88.9%)</td>
</tr>
</tbody>
</table>

**Table No. 3: Distribution of successful outcome among study cases (n = 135)**

<table>
<thead>
<tr>
<th>Success</th>
<th>No. of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>129</td>
<td>95.6</td>
</tr>
<tr>
<td>No</td>
<td>06</td>
<td>4.4</td>
</tr>
<tr>
<td>Total</td>
<td>135</td>
<td>100</td>
</tr>
</tbody>
</table>

**Table No. 4: Distribution of angiographic pattern among study cases (n = 135)**

<table>
<thead>
<tr>
<th>Angiographic pattern</th>
<th>No. of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single vessel disease</td>
<td>90</td>
<td>66.6</td>
</tr>
<tr>
<td>Double vessel disease</td>
<td>25</td>
<td>18.5</td>
</tr>
<tr>
<td>Multi-vessel disease</td>
<td>20</td>
<td>14.8</td>
</tr>
<tr>
<td>Total</td>
<td>135</td>
<td>100</td>
</tr>
</tbody>
</table>

A successful outcome was noted in 129 (95.6%) of our study population. Single vessel involvement was present in 90 (66.6%), two vessels were involved in 25 (18.5%) of patients. Three vessel involvement was seen in 20 (14.8%) of patients under study. (Table 3 and 4).

**DISCUSSION**

Interventional cardiology organizations and current extraordinary large volume trials emphasize timely intervention of acute STEMI by primary PCI. This leads to the initiatives in the developed world to provide the facility to the maximum number of people, with the least possible door to balloon time. If we consider as a model, coronary intervention capable hospitals in Canada are organized to deliver 24/7 facility of primary coronary intervention for acute myocardial infarction patients. To minimize the door to balloon time they have organized systems for the prompt delivery of patients to the hospitals for primary coronary intervention. Diagnosis of acute myocardial infarction before arriving in the hospital by the ambulance staff also facilitates the timely execution of primary percutaneous intervention in patients with acute myocardial infarction.

Fulfilling our inclusion criteria as described in material and methods section, this study of primary coronary intervention in acute myocardial infarction comprised of 135 patients. The total number of patients having male gender was 115 with a percentage of 85.1. on the other hand, the total number of female gender in study patients was only twenty, which constitutes 14.8 percent of the study patients.

Numerous studies have shown the similar trends of male majority in patients presenting with acute myocardial infarction. Malik et al also recognized 79.8 % with male gender. Jaffery et al from Jamshoro Medical College in Sindh province has shown that 77 % of their patients presenting with acute myocardial infarction were males. Shahzad et al also analysed that 67 % of their study population of acute myocardial infarction patients consisted of the male gender. Furthermore, Ahmed et al researchers from Quaid-e-Azam Medical College Bahawalpur documented a preponderance of male gender in patients with acute myocardial infarction. They reported 67% males in their research. All these results are in congruence with findings in the present study.

The mean age of all patients in our study population was 47.17 ± 6.89 years. The minimum and maximum age of our study population were thirty and sixty years respectively. The mean age in the male gender group was 44.09 ± 5.79 years. In contrast to the male gender, the female gender group was having a mean age of 54.24 ±2.94 years, with a p-value equal to 0.001. The results in the study population have shown that 65(48.1%) were having age greater than 45 years. The group comprising of age 30 to 45 years was 70 in number, with a percentage of 51.8 in the study population. This reflects the bias of selecting young patients for primary intervention. This also shows the
increased frequency of exclusion criteria in relatively older patients. (Table No. 1).

A study conducted by Atta et al reported 49.6±8.0 years mean age of the patients and Malik et al reported 54.99±11.25 years mean age of the patients with acute myocardial infarction. This depicts that our population is more prone to coronary artery disease as compared to the western population. Among 135 patients, we reported positive success outcome in 95.6% of our patients. This is in accordance with the success rate noted in multiple international and national studies. Pedrazzini et al from Switzerland also documented 89% successful recanalization outcome with primary PCI which is approximately same as seen in our findings. Farman et al reported procedural success in 98% of patients. A study was done in Karachi by Shaikh et al which also registered a 97% success among patients subjected to primary percutaneous intervention in acute myocardial infarction patients. These results are congruent to our observations.

Single vessel involvement was present in 90 (66.6%), two vessels were involved in 25 (18.5%) of patients. Three vessel involvement was seen in 20 (14.8%) of patients under study. (Table No 4). Farman et al reported single-vessel coronary artery disease in 64.6%, two-vessel CAD in 9.7% and multi-vessel CAD in 25.7%. These results comply with our study results.

CONCLUSION

The primary percutaneous intervention is seen to be a most effective, dependable and highly effective method of coronary revascularization in the setting of acute myocardial infarction. So our study results support employing primary PCI to attain high success rate and desired clinical outcomes among the patients who presented with acute myocardial infarction, however, there are limitations to the applicability of this modality due to lack of resources.

Author’s Contribution:
Concept & Design of Study: Badar Ul Ahad Gill
Drafting: Nisar Ahmed, Muhammad Tahir Mohyud-din
Data Analysis: Muhammad Zohaib, Zahoora, Muhammad Ikram Farid, Abubakr Ali Saad
Revisiting Critically: Badar Ul Ahad Gill, Nisar Ahmed
Final Approval of version: Badar Ul Ahad Gill

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

REFERENCES


Assessment of the Effect of Evening Primrose Oil Therapy in the Management of Breast Fibroadenoma

Shamaila Ayub¹, Yabinda Sahrish², Omer Bin Khalid Jamil¹, Aafia Maqsood³, Summaya Saeed³ and Aun Ali Khowaja¹

ABSTRACT

Objective: To assess the effect of evening primrose oil usage on reduction in size of breast fibroadenoma in Pakistani female population.

Study Design: Experimental study.

Place and Duration of Study: This study was conducted at the Quasi experimental study conducted at Creek General Hospital Karachi during February 2018 to March 2020.

Materials and Methods: One hundred and eighty females with fibroadenoma as in breasts were administered evening primrose oil daily for 6 months. Pre therapy and post therapy size of the fibroadenoma was compared via ultrasound. The finding of ultrasound and lab investigation and demographic record was entered in design Performa. Written informed consent was taken before history and examination. The permission of Ethical Committee was taken before start of study and get publishing in Medical Journal. The data was analyzed for results by SPSS version 27.

Results: A total of 180 patients were able to complete the trial. There was no decrease in the size of fibroadenoma after therapy.

Conclusion: Evening primrose oil has no established role in management of breast fibroadenoma.

Key Words: Evening primrose oil, Fibroadenoma, Breast neoplasms.

INTRODUCTION

Evening primrose oil is herbal medication extracted from seeds of a medicinal plant Oenothera biennis¹. Evening primrose oil contains linoleic acid, γ-linoleic acid, stearic acid, oleic acid, palmitic acid, and steroids campesterol and β-sitosterol. The basic indications of evening primrose oil described in literature are mastalgia²,³ and atopic dermatitis⁴. Evening primrose oil is rich in essential fatty acids which decreases the effect of estrogen on breast tissue and therefore help alleviating the mastalgia associated with menstrual cycle⁵.

Fibroadenoma is a fairly common disorder of the breast with a reported incidence of 25% in asymptomatic women⁶. A local study showed that 45% of women presenting to clinic with history of breast lump had fibroadenoma⁷. Being a benign pathology most fibroadenomas are left alone without treatment, surgical resection is the most common intervention carried out if lump become enlarged, suspicious or if patient desires⁸. Other treatment modalities include cryoablation⁹, and high intensity focused ultrasound¹⁰. Fibroadenomas are found to have estrogen receptors and may lead to periodic growth of these swellings¹¹. Evening primrose oil may have a beneficial role in this context on fibroadenoma and hence preventing its further growth or even reduction in size. Our study evaluates the same hypothesis after administration of oral evening primrose oil for 6 months in female patients with fibroadenomas.

MATERIALS AND METHODS

This research was conducted under full accordance with the declaration of Helsinki. All the patients were kept anonymous, and data utilized only after obtaining informed consent. This was a Quasi experimental study conducted at Creek General Hospital Karachi between February 2018 to March 2020. Approval from ethical review board was taken, and patients were enrolled in the trial only after obtaining informed consent. All females
presenting with breast fibroadenoma of size 5 cm or less (confirmed on ultrasound) were for non-surgical management were included in the study.

Inclusion criteria
All females between the age of 16 and 45 years presenting with breast fibroadenoma of size 5 cm or less (confirmed on ultrasound) who were selected for non-surgical management were included in the study.

Exclusion criteria
- Age less than 16 years or more than 45 years
- Multiple swellings in breasts or bilateral swellings
- Patients having menstrual irregularities
- Pregnancy and lactation
- Post-menopausal females with fibroadenoma
- Any comorbidities such as diabetes or hypertension
- Patients on oral contraceptives

All patients underwent ultrasound examination of breasts before commencing evening primrose oil therapy and size of the fibroadenoma was recorded. Patients were then prescribed evening primrose oil 4gm orally daily in divided dose for the period of 6 months. After the completion of therapy, a repeat ultrasound was carried out to assess the response of evening primrose oil. Paired t test was used to compare the significance of difference between the size reduction. The data was analyzed for results by SPSS version 27.

RESULTS

A total of 218 patients enrolled in the trial initially, however only 180 patients were available that were eligible for analysis. Out of the 38 dropped patients, 16 (42.10%) opted out for surgical excision, 8 (21.05%) patients had discontinued therapy on their own, 4 (10.52%) patients conceived pregnancy and the remaining 10 (26.31%) patients were lost to follow up. The average size as noted on ultrasound prior to administering evening primrose oil was 2.76 cm (see figure – I). All of the patients had noticed the swelling as an incidental finding in duration of 8 months or less. Most of these patients had no pain associated with the swelling. Thirty percent (30%) of the ladies reported that they have taken self-medication (mostly multivitamins) in the past (see Table – I).

Table No.1: Patient data and comparison of size of the swelling

<table>
<thead>
<tr>
<th>Patient Characteristic</th>
<th>Value (N = 180)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>26.33±7.9 years</td>
</tr>
<tr>
<td>Weight</td>
<td>69.0±8.70 kg</td>
</tr>
<tr>
<td>BMI</td>
<td>23.6 ± 3.2 kg/m²</td>
</tr>
<tr>
<td>Duration of swelling</td>
<td>11.12±7.09 weeks</td>
</tr>
<tr>
<td>Pre-therapy size cm</td>
<td>2.77±0.86</td>
</tr>
<tr>
<td>Post-therapy size cm</td>
<td>2.71±0.74</td>
</tr>
</tbody>
</table>

* = Paired t test

Figure No.1: Some history queries of the patients included in the study

No decrease in size of swelling was noted at the end of evening primrose oil therapy (P=0.531), in fact there were 21 (11.66%) cases where there was increase in size of the swelling and 3 (1.66%) case where a new swelling was noted in the same breast.

DISCUSSION

Fibroadenoma is the most common diagnosis in females presenting to surgical clinics with palpable breast masses. Although significant number of these females experience uncertainty and anxiety prior to the definitive diagnosis because of dread of having malignancy, most after diagnosis of benign disease opt for conservative management as they are also afraid of cosmetic disfigurement and scar formation. Although two thirds of fibroadenomas tend to resolve within five years without any sequelae, medical treatment have been tried to manage these swellings. Danazol has been used in treatment of fibroadenoma but with disappointing results. Evening primrose oil has been used in treatment of various disorders such as mastalgia, attention deficit hyperactivity disorder, osteoporosis, rheumatoid arthritis, hypertension, diabetic neuropathy and weight loss. Via animal trials evening primrose oil has also been found to be effective as an anticoagulant and antiplatelet agent. Evening primrose oil although found to reduce the effect of estrogen on breast tissue, in our study it showed no value in significant reduction in size or resolution of fibroadenoma. The reason why evening primrose oil was not able to reduce estrogen regulated growth of fibroadenoma is unclear and needs to be confirmed via conducting more scientific trials.

Our study was initially targeted for a study group that would be more than 500 patients but due to large number of drop outs and no ambiguity in the obtained results from study, we concluded our study early. Similar study has been done in international literature by Kollias J. et al. Their study had a prospective comparative design which is better than ours but their study inclusion and exclusion criteria were not well defined. No exclusion of patients on oral
contraceptives, any other hormonal therapy or any other comorbidities is mentioned. This may have affected the outcome of their study however their results also showed no benefit of evening primrose oil use for fibroadenoma.

CONCLUSION

Evening primrose oil although used frequently in cyclical mastalgia patients with good results, it has no role in medical management of breast fibroadenoma patients.

Author’s Contribution:
Concept & Design of Study: Shamaila Ayub
Drafting: Yabinda Sahrish, Omer bin Khalid Jamil
Data Analysis: Aafia Maqsood, Summaya Saeed, Aun Ali Khowaja
Revisiting Critically: Shamaila Ayub, Yabinda Sahrish
Final Approval of version: Shamaila Ayub

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

REFERENCES

Relationship Between Fiber in Diet and Acute Appendicitis

Fauzia Siraj¹, Muhammad Azam Qureshi¹, Mushtaq Ahmad¹, Owais Siddiqi² and Bilal Hassan¹

ABSTRACT

Objective: To determine the relationship of fiber in diet and other socio-demographic factors with acute appendicitis among adult population of Rawalpindi.

Study Design: Case control study

Place and Duration of Study: This study was conducted at the Department of Surgery & histopathology of Benazir Bhutto Hospital and Isra University Medical College Islamabad for two years from Jan 2018 to Jan 2020.

Materials and Methods: Two hundred patients operated for acute appendicitis and confirmed by histopathology report were included in the study along with equal number of age and gender matched controls from the community. Detailed dietary history was obtained with the help of structured questionnaires to calculate the amount of fiber in diet of both the cases and controls. Level of fiber in diet, Body mass index, family income and presence of co morbid diseases were compared among the cases and controls with chi-square. Mean dietary fiber in grams was also compared among the cases and controls by student-t test.

Results: Out of 200 confirmed cases with acute appendicitis, 123 (61.5%) showed the presence of low dietary fiber while 73 (38.5 %) had adequate or high dietary fiber. Among the healthy controls 91 (45.5%) showed the presence of low dietary fiber while 109 (54.5%) had adequate or high dietary fiber (N=400). Mean age of the cases was 30.5±2.15 years and of the controls was 30.3±3.311 years. After applying the chi-square, we found that amount of dietary fiber and family income had significant difference among the cases and controls (p-value<0.05). Mean dietary fiber in grams among the cases was 22.6±2.12 grams while for the controls was 32.7±2.91 grams (p-value <0.05).

Conclusion: Low dietary fiber emerged as predictor of acute appendicitis as it was significantly present in the cases confirmed with acute appendicitis as compared to controls. In addition to dietary fiber low family income also had a significant relationship with the presence of acute appendicitis among the cases.

Key Words: appendicitis; dietary fiber; relationship.

Citation of article: Siraj F, Qureshi MA, Ahmad M, Siddiqi O, Hassan B. Relationship between fiber in diet and acute appendicitis. Med Forum 2020;31(9):181-184.

INTRODUCTION

Appendicectomy has been one of the most common surgical procedures performed all over the world.¹ Surgical units around the globe have high indices of patients presenting with acute appendicitis.² Diagnosis is usually clinical, supported by the relevant investigations. Surgical management has been the treatment of choice in most of the patients.³

¹ Department of Anatomy, Al Nafees Medical College, Isra University Islamabad.
² Department of General Surgery, Benazir Bhutto Hospital, Rawalpindi.

If not intervened in time, this condition may have a high mortality and morbidity.⁴ Recently researches have been done to look for the factors which may prevent this condition.⁵ Dietary fiber has been regarded as one of the essential component of a balanced diet which has been usually overlooked. Adequate amount of fiber in the diet not only responsible to maintain adequate gut functioning but also prevents a lot of clinical condition. Studies done in recent past emphasize high fiber diet for overall being and health of the individuals.⁶ Few studies have been done in western population regarding the role of dietary fiber in prevention of acute appendicitis among the adult and pediatric population. Naeedar et al. in 1998 raised this point and performed a study with the negative findings that dietary fiber may not be the important factor in acute appendicitis and other luminal and/or morphological factors may be predisposing factors.⁷ Nelson et al. studied this phenomenon long ago in 1984 and concluded that there were no statistically significant differences in the average daily intake of cereal in the cases and controls, giving limited support to reduced cereal fiber intake acting as a determinant of appendicitis. Low water
intake may also be a causative influence. There is some evidence that infection and a familial predisposition may increase susceptibility to the disease. Damanic et al. in 2016 performed a similar study on the pediatric population and revealed that there’s a significant correlation between low-fiber diet with appendicitis incidence (p=0.0001). From the 19 patients with low-fiber diet, 14 of them (73.7%) have acute appendicitis. Meanwhile only 2 of the patients (12.5%) with high-fiber diet have acute appendicitis. Adamidis et al. published a similar study in 2000 and concluded that Appendectomy performed in children had statistically significant lower mean daily intake of fiber (17.4 g versus 20.4 g, P < 0.001) including all fiber fractions: cellulose, uronic acid, pentose, expose and lignin. No statistical difference was found for energy, protein, carbohydrate and fat intake. Discriminate analysis proved that only cellulose and expose are independently correlated to appendicitis and lower fiber intake is thought to be the cause in 70% of the cases. Recurrent abdominal pain, chronic constipation and positive family history of appendectomy were more frequent in appendectomy performed in children (P < 0.001). This study gives evidence that low fiber intake could play an important role in the pathogenesis of appendicitis.

Limited data has been available in this regard. A very interesting study done in Gilgit population which is north of Pakistan analyzed the general food intake pattern of patients with appendicitis and concluded that females (67.4%) were more prone to appendicitis as compared to male (36.8%). More than (55.2%) young adults between the ages of 18-30 years were suffering from appendicitis as compared to other life stage groups. All the appendicitis suffered volunteers had less servings of fruits and vegetables while the servings of fast/junk food was much higher given in Food Guide Pyramid as recommended by WHO. Nutritional health status emerged as a leading factor responsible for appendicitis in Gilgit city of Pakistan. We planned this study with the objective to determine the relationship of fiber in diet and other socio-demographic factors with acute appendicitis among adult population of Rawalpindi.

MATERIALS AND METHODS

This case control study was conducted at the department of Surgery and histopathology, Benazir Bhutto Hospital. Study duration was two years (Jan 2018 to Jan 2020). Ethical approval (IRB letter number: F, 2/IUIC-ANMC/EC-127/2016) was granted by the ethical committee of ISRA university. WHO sample size calculator was used to calculate the sample size for this study with population prevalence proportion of 54.3%. Non probability consecutive sampling was done to collect the cases and controls were recruited from the community after that by matching the age and gender of the cases. All the patients between the age of 18 and 60 years presenting with symptoms of acute appendicitis and operated with histopathology proven diagnosis were included in the study. Exclusion criteria were the patients more than 60 years of age or those who did not consent to or those with a past or current history of any eating disorder or any other diagnosed nutritional deficiency. Patients with non-inflamed appendix at gross appearance or negative histopathology report were also excluded from the study.

Normal dietary fiber was regarded as between 25 and 35 grams of fiber in diet per day. Low fiber diet was regarded as less than 25 grams of fiber each day. After formal consent from the patients and controls after providing them all the information regarding the study and mentioning them their right to withdraw at any time from the study if they don’t feel comfortable being the part of study. Controls were age and gender matched people living in the community without having any symptoms of acute appendicitis and never operated from acute appendicitis in life. Family income was categorized into equal to or more than outgoing or less than outgoings with the help of a recent economic survey done in Pakistan. A Performa was designed in collaboration with the dietician to assess the usual intake of whole-grain breads and cereals, fruits, vegetables, legumes, nuts, and seeds. For each food group, cases and controls were given a standard serving size, and each food group was also weighted according to its relative mean crude fiber content as determined from standard food tables. Daily total fiber and whole-grain bread and cereal intake scores were calculated for each subject. Descriptive statistics were used in the study to describe the variables of the study. Qualitative variables like BMI, patients with low or high fiber diet, patients with low or high income and presence of comorbid illness were expressed by frequency and percentage. Mean and standard deviation for age was calculated for both the cases and controls. Chi-square was the statistical test applied initially to establish any correlation between the variables among the cases and controls. Student t-test was applied to look for the difference of mean values of dietary fiber in both the cases and controls. SPSS-23.0 was the software used to process all the data and perform the analysis. Differences between groups were considered significant if p-values were less than or equal to 0.05.

RESULTS

A total of 200 cases and 200 control were included in the final analysis. Out of these cases confirmed with acute appendicitis, 123 (61.5%) showed the presence of low dietary fiber while 73 (38.5%) had adequate or high dietary fiber. Among the healthy controls 91 (45.5%) showed the presence of low dietary fiber while 109 (54.5%) had adequate or high dietary fiber. Mean
age of the cases was 30.5±2.15 years and of the controls was 30.3±3.31 years.

Table 1 shows that after applying the chi-square, we found that amount of dietary fiber and family income had significant difference among the cases and controls (p-value<0.05) while BMI and presence of co morbid conditions has no such significant relationship (p-value>0.05).

Table II showed Mean dietary fiber in grams among the cases was 22.6±2.12 grams while for the controls was 32.7±2.91 grams (p-value <0.001 when student t-test was applied).

### Table No.1: Characteristics of the patients and controls: Chi-square test

<table>
<thead>
<tr>
<th>Factors</th>
<th>Patients</th>
<th>Controls</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Mass Index</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>111 (55.5%)</td>
<td>106 (53%)</td>
<td>0.616</td>
</tr>
<tr>
<td>Overweight or obese</td>
<td>89 (44.5%)</td>
<td>94 (47%)</td>
<td></td>
</tr>
<tr>
<td>Dietary Fiber</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low fiber</td>
<td>77 (38.5%)</td>
<td>91 (45.5%)</td>
<td>0.001</td>
</tr>
<tr>
<td>High fiber</td>
<td>123 (61.5%)</td>
<td>109 (54.5%)</td>
<td></td>
</tr>
<tr>
<td>Presence of co morbid illness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>125 (62.5%)</td>
<td>137 (68.5%)</td>
<td>0.207</td>
</tr>
<tr>
<td>Yes</td>
<td>75 (37.5%)</td>
<td>63 (31.5%)</td>
<td></td>
</tr>
<tr>
<td>Family income</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>More than outgoing</td>
<td>132 (66%)</td>
<td>153 (71.5%)</td>
<td>0.020</td>
</tr>
<tr>
<td>Less than outgoing</td>
<td>68 (34%)</td>
<td>47 (28.5%)</td>
<td></td>
</tr>
</tbody>
</table>

### Table No.2: Comparison of mean dietary fiber in grams among the patients and controls

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients</th>
<th>Controls</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean dietary fiber in grams</td>
<td>22.6±2.12</td>
<td>32.7±2.91</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

### DISCUSSION

This study is instrumental in understanding the relationship of underlying dietary deficiency with an acute surgical condition. Acute appendicitis has not been an uncommon condition all over the world. Situation is not different in our part of the world and all age groups get affected by this condition but young population is usually more at risk. It would be of utmost importance if clinicians and researchers would find any dietary modifications to prevent this condition which pose a lot of strain on health budget due to high incidence. Western clinicians, dietitians and researchers have been working on this phenomenon for years but limited work has been done in our part of the world. We therefore planned this study with the objective to determine the relationship of fiber in diet and other socio-demographic factors with acute appendicitis among adult population of Rawalpindi.

Arnbjörnsson published a paper more than thirty years ago in 1983 in which study design was similar to ours but sample size was small. He concluded that the average daily dietary fiber intake was 17.4 g in the group with appendicitis and 21.0 g in the control group. The difference was statistically significant. The results supported the hypothesis that diet, in particular a lack of fiber, may be an important factor in the pathogenesis of acute appendicitis. Our sample size was quite large as compared to his sample size but still results were quite similar and statistically significant difference was found among dietary fiber intake of the cases and controls.

Brender et al. in 1985 published similar paper but chose pediatric population as study sample. They concluded that estimated risk of appendicitis decreased as monthly intake of whole-grain foods increased. Children 7 to 18 years of age who had an intake of whole-grain foods in the upper fiftieth percentile were estimated to have a 50 per cent lower risk of appendicitis. This reduction in risk was not observed in the group of children less than 7 years of age. Though our design and target population was different but still high fiber diet emerged as protective factor for acute appendicitis as healthy population without appendicitis had significantly high fiber intake as compared to the cases with appendicitis (p-value<0.01).

Inam et al. published an interesting study in Pakistan Armed forces medical journal in 2012 with the objective to determine the association of socioeconomic strata with fecoliths in acute appendicitis. They came up with the findings that out of 80, 40 patients belonged to high social class and 40 patients belonged to low social class. Both the groups were comparable with respect to age (p = 0.435) and gender (p = 0.104) (Table-1 and 2). On naked eye examination fecoliths was present in 20 (50%) patients of high social class and 9 (22.5%) patients of low social class (p=0.011). Odds ratio calculated was 1.759. Though our objective was a bit different but still low monthly income emerged as predictor of acute appendicitis in our study. There could be multiple reasons for that as dietary patterns may be altogether different in different social classes. Though high fiber diets usually don’t lie in category of high-priced diets but still this phenomenon need exploration in future researches.

Our study had few limitations. Cases were enrolled from one hospital which was a public sector hospital which reduce the chances of high-income people to get enrolled in the study. Recall bias regarding the type of diet and amount of fiber calculation based on that information also weakens the possibility of generalization of the results. Future studies with use of more sophisticated methods and enrolling sample from multiple public and private sector hospitals may generate better results.
CONCLUSION

Low dietary fiber emerged as predictor of acute appendicitis as it was significantly present in the cases confirmed with acute appendicitis as compared to controls. In addition to dietary fiber low family income also had a significant relationship with the presence of acute appendicitis among the cases.

Author's Contribution:
Concept & Design of Study: Fauzia Siraj
Drafting: Muhammad Azam Qureshi, Mushtaq Ahmad
Data Analysis: Owais Siddiqi, Bilal Hassan
Revisiting Critically: Fauzia Siraj, Muhammad Azam Qureshi
Final Approval of version: Fauzia Siraj

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

REFERENCES

Protective Effects of Metformin on Doxorubicin-Induced Cardiotoxicity and its Early Detection
Khalida Ajmal¹, Saima Rafique¹, Ayesha Afzal¹, Abeera Sikandar¹ and Uzma Naeem²

ABSTRACT

Objective: To evaluate the protective effects of Metformin on Doxorubicin cardiac toxicity and to identify myocardial damage at early phase by quantitative estimation of serum Troponin I (cTnI).

Study Design: Randomized lab base study

Place and Duration of Study: This study was conducted at the Departments of Pharmacology, Army Medical College, Rawalpindi in collaboration with CREAM (Centre for Research in Experimental and Applied Medicine) and completed in four months from April to July 2015.

Materials and Methods: Eighteen healthy male adult rabbits randomly divided into three batches were used. Doxorubicin was administered in a group of rabbits to produce cardiotoxicity; while control group received normal saline. The third experimental group got pretreatment for ten days with Metformin before doxorubicin administration.

Results: Doxorubicin inflicted marked cardiac damage apparent by elevated serum biomarkers (LDH, CK-MB and cTnI) levels and necrosed cardiomyocytes on histological examination. Metformin pretreatment ensued in decreased serum levels of biomarkers and improved the histological grades of heart tissue.

Conclusion: The doxorubicin based chemotherapy can be made efficacious with the concomitant administration of Metformin. The quantitative assessment of serum cTnI for recognition of cardiotoxicity at early stage may direct to substantial financial bearing and improved quality of life in cancer survivors.

Key Words: Doxorubicin (Dox), Metformin, Cardiac Troponin I (cTnI), Lactate Dehydrogenase (LDH), Creatine kinase-MB (CK-MB). Adenosine monophosphate-activated protein kinase (AMPK), Endothelial Nitric Oxide Synthase (eNOS).

Citation of article: Ajmal K, Rafique S, Afzal A, Sikandar A, Naeem U. Protective Effects of Metformin on Doxorubicin-Induced Cardiotoxicity and its Early Detection Med Forum 2020;31(9):185-189.

INTRODUCTION

Doxorubicin (Dox), one of the anthracyclines, isolated from Streptomyces peucetius, is a potent anticancer agent. It is widely used for chemotherapy of several deadly solid and hematological cancers since half century however cardiac toxicity documented among 20% patients limits its use in full clinical doses¹,². Its main cytotoxic effects are exerted due to blockade of DNA topoisomerase IIβ & DNA interposing in cancer cells. The semiquinone centered unstable intermediate compounds of Dox generate highly reactive oxidized free radicals that are responsible for cardiotoxicity.

The cardiac cells have innate vulnerability to oxidative stress. These free radicals inflict nuclear DNA damage and impair mitochondrial functions³,⁴. These metabolites also lead to myofibrils structural proteins damage causing myocytes necrosis, resulting in release of the cardio-specific cardiac troponins I (cTnI) and cytosolic enzymes like creatine kinase MB (CK-MB) and lactate dehydrogenase (LDH) in blood.⁵,⁶ cTnI is myocardial contractile protein and does not normally circulate in the circulation. It is expressed only in myocardium and is more abundant than CK-MB. cTnl is probably less cardiac specific. cTnI is considered most specific and highly sensitive biomarker of cardiotoxicity. cTnI estimation reveals the existence of cardiotoxicity at an initial phase, considerably before compromised cardiac function can be diagnosed by any other procedure.⁵

The cardiotoxicity caused by Dox necessitates lifelong concerns and costly medical management. Cardiac monitoring is largely done by qualitative estimation of cTnI which is often unreliable. As significant number of cancer patients comes from countries with poor socio-economic conditions further imposing financial burden. The quantitative measurement of cTnI offers a promising alternate in effective monitoring of cancer survivors.⁷
Numerous pharmacological modulations for prevention of cardiotoxicity have been suggested and are currently in practice. Yet, protection imparted by these is often limited and is expensive as well. Metformin, a biguanide, is used all over the world in type 2 diabetes mellitus as it lowers basal and postprandial glucose level. It is also prescribed to treat prediabetes, gestational diabetes mellitus and has other off-label uses in polycystic ovarian syndrome, weight loss and cancer. It has been reported to prevent Dox induced cardiotoxicity. Metformin exerts its beneficial effects through various possible mechanisms. It decreases in oxidative stress and free radical generation by prevention of ferritin heavy chain expression in cardiomyocytes. The drug increases the glutathione level in heart tissue and restores mitochondrial bioenergetics. In experimental animal models, metformin has shown the increased tolerance of the myocardium to ischemia-reperfusion injury and decrease in occurrence of heart failure after infarction. Metformin is also said to enhance the efficacy of doxorubicin.

The aim of the study was the definite and early recognition of cardiac damage by estimation of cTnI and its probable amelioration by Metformin, ensuring better results with Dox based chemotherapeutic regimen.

**MATERIALS AND METHODS**

This experimental study was reviewed and approved by Ethical Committee of “Centre for Research in Experimental and Applied Medicine” (CREAM), and conducted in the Pharmacology Department, Army Medical College, Rawalpindi. Eighteen male healthy adult rabbits, each with average weight of 2.0 kg were divided randomly into groups. Control Group-1: (n=6) was daily administered 2 ml of normal saline solution orally for whole period of study. Experimental Group-2: (n=6) was given injection Doxorubicin 12 mg/kg body weight (BW) into marginal vein of rabbit’s ear on tenth day of experiment. Group-3: (n=6) received Metformin 250 mg/kg BW orally for eleven days consecutively and a single dose of Dox 12 mg/kg BW on the tenth day by intravenous route. The blood for biomarker study was drawn from rabbit’s ear in the beginning and on the last day of the study. After centrifugation of the blood, plasma was stored in serum storage vials at -20°C for analysis of biomarkers.

Doxorubicin HCL was purchased from Park-Davis Pak while Metformin from Merck. cTnI kit was procured from Pharmaceutical Manufacturers’ Association while CK-MB and LDH kits from Merck Pak Ltd. Measurement of cTnI and CK-MB is based on general principle that there is striking similarity between human and rabbit CK-MB sequences and cTnI antibodies. A cut-off value of 0.50 ng/ml cTnI was proposed by kit manufacturer for diagnosing myocardial damage. CK-MB estimation was carried out as per the principles of IFCC. All the rabbits were weighed and slaughtered to take out the heart. Cardiac tissue sections were prepared for histological study under electron microscope. Qualitative and quantitative assessment was done on all myocardial sections. Semiquantitative histological classification and scoring was done in accordance with Billingham technique.

Statistical analysis of serum results was computed on SPSS 22 and expressed as means ± standard error of means (SEM) calculated by using One Way ANOVAs. Chi square test was utilized for histopathological analysis. The p value <0.05 was considered significant to measure the difference between two observations.

**RESULTS**

Observation of individual parameters

**Changes in Body Weight:** The rabbits in control group-1 gained weight by 12.52±2.69%, however Goup-2 animals (receiving12 mg/kg of doxorubicin) showed fall of 26.88±2.03 %. The Gp-3 animals (receiving both doxorubicin and metformin) displayed less fall in weight of 5.55±7.78 percent as compare to Gp-2.

**Serum Cardiac troponin I (cTnI):** Cardiac troponin I levels measured in ng/l, were strikingly raised upto 10.00±0.00 among rabbits of Goup-2 while levels in Gp-1 remained normal. The rise in levels of cTnI in Gp-2 was much low as compared to Gp-2 although quite raised when matched with levels of group-1 with significant value of p (<0.05) (table-1& fig-1).

**Serum CK-MB:** Serum CK-MB (U/L) increased considerably among Goup-2 to 345 ±36 in comparison to 122±4. (Control Gp-1), with statistically significant p value. The Gp-3 rabbits receiving pretreatment with metformin exhibited less rise (180 U/L±10.00) in levels with significant value (p<0.05) when equated with group-2(table-1).

**Serum LDH:** Serum LDH (U/l) were elevated noticeably up to 1413±112 in Gp-2 in contrast to Gp-1.
and with significant p<0.005. In Gp-3, there was no increase (636±54 U/l) in LDH levels seen (table- 1).

**Histopathological Analysis:** Microscopic study of heart tissue sections among control Gp-1 revealed no damage to the cardiomyocytes. The gross disruption in cardiac cells histological texture was observed in Gp-2 (toxic group) with no obvious normality. The 85.0% heart sections of this group displayed necrosis of grade-3 and of grade- 2 only among 15.0%. The ventricular sections manifested interstitial edema, vacuolization and clumping of nuclear matter. In few slides, there was structural breaks of myofibrils. The mild necrosis of grade-1 was witnessed in 65.6 percent in heart sections of Gp-3 (treated with metformin and doxorubicin) and 16.7% percent of sections exhibited thorough inhibition while the equal number showed modest damage measured as necrosis (table and figure- 2).

<table>
<thead>
<tr>
<th>Table No.1: The values of estimated Serum biomarkers of rabbits in control Goup-1, doxorubicin Goup-2, Goup-3 receiving both metformin plus doxorubicin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum biomarkers</td>
</tr>
<tr>
<td>-----------------</td>
</tr>
<tr>
<td>Ctni (ng/l)</td>
</tr>
<tr>
<td>± sem</td>
</tr>
<tr>
<td>Ck-mb (u/l)</td>
</tr>
<tr>
<td>Ldh</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table No.2: Grades * Groups Cross tabulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Groups</td>
</tr>
<tr>
<td>--------</td>
</tr>
<tr>
<td>Normal</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Mild</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Moderate</td>
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<tr>
<td></td>
</tr>
<tr>
<td>Severe</td>
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<tr>
<td></td>
</tr>
<tr>
<td>Total</td>
</tr>
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</tbody>
</table>

Figure No.2: The (Hematoxyline & Eosin) stained micrographs (×300) from specimens of rabbit cardiomyocytes: (A) from (Gp-1)) with cardiac cell structure, (B) picture of Gp-2 showing extent of cardiac damage of toxic dose of Dox (C) and micrograph of rabbit heart cell from Gp-3 showing less derangement of myofibrils as compared to Gp-2.
DISCUSSION

The study was aimed to evaluate possible prevention of dox-induced cardiotoxicity with Metformin and its early, reliable detection by quantitative estimation of cTnI that might help to institute any interventional strategy.

In our study, group of animals exposed to toxic dose of doxorubicin showed considerably deranged serum biomarkers and grade-3 necrosis of heart tissue. There was increase of 58.32% in LDH, 147.39% increase in CK-MB and serum cTnI values with increase of 30110.53% all with significant difference in comparison with control group rabbits. Histologically, heart sections of Goup-2 expressed necrosis of grade-3 while picture from Gp-1 animals was completely normal. Similar changes both in morphology and biomarkers following the use of doxorubicin in rabbits were observed by many other researchers. Cardinale and colleagues in clinical study on cancer patients and Sawyer and his colleagues in both their in-vitro and in -vivo preclinical experiments recognized that doxorubicin in varying concentrations produced a substantial cardiac cells death and apoptosis within 1-2 days of its administration. It was depicted in our histological slides too and our results are fairly homogenous with these studies. 

Doxorubicin remains a preferred therapeutic agent for various solid and haematological malignancies. However, a noteworthy number (20%) of patients develop cardiotoxicity causing lifelong co-morbidities and this clinical impact is growing with increasing cancer survivors. In this experiment, the reason for inculcating measurement of LDH and CK-MB was their chronological worth and main emphasis remained on highly sensitive and specific biomarker cTnI. As recognized by The Food and Drug Administration and European Medicines Agency, it is considered the benchmark serum biomarker of cardiac damage in all species of mammals to detect the early anthracyclin-induced cardiotoxicity. cTnI is exclusively a myocardial biomarker, no evidence of cTnI presence in injured or healthy skeletal muscle and in other tissue has been found. Jaffe and others, in clinical study established that measuring cTnI levels perceives cardiotoxicity very early, positively before cardiac dysfunction can be discovered by any other diagnostic modalities. cTnI has also been integrated into the National Cancer Institute (NCI) for classifying anticancer therapy induced cardiotoxicity .

The subsequent part of experiment work was conducted to appraise the protection conferred by metformin. The Goup-3 rabbits pretreated with 250 mg/kg metformin for ten consecutive days prior to administration of doxorubicin revealed the value of cTnI depicting significant difference with 75.84% less ups urge, 42.93% less elevation in CK-MB and LDH with 57.42% less rise in Goup-3 in relation to Goup-2. Histopathological alterations were also analogous with significant difference (p<0.000). The morphological grading shifted from necrosis of grade 3 to 1 whereas one-quarter of the tissue slide exhibited fairly normal myofibrillar arrangement. The weight loss (4.57±2.48%) among the animals of this group was of lesser degree.

The cardioprotective actions of metformin are mediated by an AMPK-eNOS signaling pathway. Activation of adenosine monophosphate-activated protein kinase, increased formation of adenosine, and the prevention of the mitochondrial injury all contribute to cardioprotection by metformin. Metformin therapy attenuates post infarction cardiac remodeling. Moreover metformin has been explored to reduce radiation-induced cardiac toxicity risk in women with early-stage breast cancer being treated with doxorubicin containing regimen.

CONCLUSION

The promising results from this study supported that the quantitative evaluation of cTnI may be crucial for early detection of Doxorubicin inflicted cardiotoxicity. Subjects with negative troponin may be barred from costly and long term programs for cardiac monitoring. Similarly, pretreatment with metformin is beneficial as it has attenuated the doxorubicin induced cardiotoxicity.

Acknowledgements: The experiment was partly funded by National University of Sciences and Technology (NUST), Islamabad, Pakistan

Author’s Contribution:
Concept & Design of Study: Khalida Ajmal
Drafting: Abeera Sikandar
Data Analysis: Uzma Naem
Revisiting Critically: Ayesha Afzal, Rashada Farooqi
Final Approval of version: Saima Rafique

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

REFERENCES


Neuroendoscopic Biopsy of Brain Lesions; Accuracy and Complications
Syed Zahid Hussain Shah¹ and Shoaib Saleem Khan² and Muhammad Aamir¹

ABSTRACT

Objective: To assess the accuracy of neuroendoscopic biopsy of brain lesions and complications associated with it.

Study Design: Retrospective study.

Place and Duration of Study: This study was conducted at the Department of Neurosurgery, Nishtar Hospital Multan from January 2010 to March 2020.

Materials and Methods: There were 347 cases of neuroendoscopic processes performed in different patients during a period of almost 10 years. We selected 40 patients with intra-ventricular or periventricular lesions according to the database present and obtained the biopsy samples from these patients. Only life threatening complications were taken into account. Bleeding was considered as major complication that leads to execution of the procedure, requirement of unplanned EVD insertion or if detected postoperatively cause further surgery. All the data was subjected to statistical analysis with the help of computer software SPSS version 23. Frequency and percentages were calculated for categorical variables while mean and standard deviation was calculated for continuous variables.

Results: Total 33 (82.5%) samples were accurately diagnosed as 12 of these were reconfirmed by new sample. 13 patients’ diagnoses showed compatibility with the ongoing treatment, and diagnosis of 8 patients was compatible with the follow up. Total 5 (12.5%) samples were inaccurately diagnosed as new biopsy results varied in 3 patients, clinical course was nor aligned with the diagnosis in one patient and indecisive findings were observed in one patient. Of 40 biopsies, 38 samples were included in complete study because one patient died and one patient lost follow up.

Conclusion: The results of our study show that the use of the new method to assess the accuracy of endoscopic biopsy revealed high accuracy in diagnostic biopsy.

Key Words: Neuroendoscopic Biopsy, Brain, Lesions, Intraventricular, Periventricular, Hemorrhage, Endoscope.

Citation of article: Shah SZH, Khan SS Aamir M. Neuroendoscopic Biopsy of Brain Lesions; Accuracy and Complications. Med Forum 2020;31(9): 190-193.

INTRODUCTION

Endoscopic brain biopsy was a technique first established by Fukushima in 1973 with a flexible fiberoptic ventriculofiberscope¹. Later on after 5 years he reported that out of 21 endoscopic biopsies in patients with intraventricular tumors only 11 patients had correct histopathological diagnosis.² Now-a-days endoscopy is an important technique for management of intra- and periventricular tumors³⁴⁵. It is a highly acceptable by the clinicians and preferable technique by the clinicians for tissue sampling.

¹ Department of Neurosurgery, Nishtar Medical University, Multan.
² Department of Neurosurgery, Multan Medical and Dental College Multan.

Correspondence: Syed Zahid Hussain Shah, Assistant professor Neurosurgery, Nishtar Medical University, Multan.
Contact No: 03356151510
Email: zahidshah140@hotmail.com

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A variety of diagnostic outcomes for endoscopic procedures were reported in spite of its high acceptance⁶. Literature review on the technical aspects of the endoscopic biopsy of brain tumors showed its success rate and accuracy, as they relate to the diagnostic outcomes of the procedure.

Use of neuroendoscopic procedures has spread enormously due to latest developments in the optics and lens technologies. There are some reports on the use of neuroendoscopic biopsy in order to obtain tissue samples of brain⁶⁷⁸. On the other hand, there are a number of studies present already dealing with same issue but there is still no clarification regarding accuracy of this technique. In many reports there is no comparative study of endoscopy with any other technique or any other developed treatment and along with this, only cases of tumor were studied in almost all of the literature papers. As there is difference in the techniques and very few cases have been assessed in studies, the complication rate varies study to study. In our study aim was to evaluate the accuracy by comparison of neuroendoscopic biopsy with other biopsy techniques in previous studies and thereby evaluating the treatment evolution. The difficulties and other complications during the neuroendoscopic biopsy
procedure are presented and compared with those reported in other study present.

MATERIALS AND METHODS

In the Department of Neurosurgery in Nishtar Hospital Multan, there were 347 cases of neuroendoscopic processes performed in different patients during a period of almost 10 years from January 2010 through March 2020. We selected 40 patients with intraventricular or periventricular lesions according to the database present and obtained the biopsy samples from these patients. Sample size was calculated using the reference study by Giannetti et al.9 Non probability consecutive type of sampling technique was used to collect the sample. There was no age limitation for the patients in this study. Furthermore, patients having any pathology of walls of the supratentorial ventricular system (inside or outside the wall) and biopsy plans in spite of its success were a part of inclusion criteria for this study. Patients, in whom procedures like tumor resection such as for colloid cysts, cyst aspiration, or cyst removal were performed, were not included. After approval from the Ethics Committee of the Hospital for the research projects, patients were called for the follow-up after reviewing their charts and histopathology reports. In case of CSF flow obstruction, CSF diversion process was done along with biopsy using different techniques on the basis of site CSF flow obstruction. Tissues were stained by H and E staining, after embedded in the paraffin, while few were stained by immunohistochemical staining later on.

There was no suggested treatment approach in case of the benign and unrectable neoplasms or ependymitis resulting to cystercerosis. For measuring the accuracy and diagnostic confirmation of biopsy specimen comparison between, histopathological outcomes and specimen taken postoperatively (after open surgery), reaction to the treatment plan as medical treatment, chemotherapy, and/or radiotherapy and the clinical and radiographic findings was necessary. When histopathological diagnosis and sample obtained during craniotomy matched, there was consistency between the treatment and the diagnosis, the diagnosis and follow-up symptoms were well-matched then endoscopic biopsy was believed to be correct.

On the other hand, when each new sample taken during craniotomy required new diagnosis or changing in tumor rank leading to change in treatment strategy or prognosis and difference in treatment response in follow-up patients than expected response, endoscopic biopsy was considered inaccurate. Minor complications of endoscopic procedure were not considered in this type of retrospective study and were underestimated and only life threatening complications were taken into account.

Shunt related dysfunctions were also ignored because this study did not included patients with hydrocephalus.

Bleeding was considered as major complication that leads to execution of the procedure, requirement of unplanned EVD insertion or if detected postoperatively cause further surgery. The cause of these complications may relate directly to biopsy, or to the opening of the third ventricle, or to the endoscopic navigation. Other hemorrhagic conditions were excluded. CSF examination and positive culture were carried out for diagnosing bacterial meningitis or ventriculitis. In case of any complication reoperation was considered i.e. any second surgery, but EVD insertion was not regarded as second surgery (even not scheduled before). All the data was collected in the form of a predesigned proforma by the researcher himself. All the data was subjected to statistical analysis with the help of computer software SPSS version 23. Frequency and percentages were calculated for categorical variables while mean and standard deviation was calculated for continuous variables.

RESULTS

Successful biopsy was performed in 40 patients and histopathological diagnosis was made. Most common tumor was glioma grade II and it was present in 5 (12.5 %) of the patients. High grade glioma (III & IV) and Cysticercosis were diagnosed in 4 (10 %) patients each. Pilocytic astrocytoma, Pineoblastoma and Germinoma were diagnosed in 3 (7.5 %) patients each. Cryptococcosis, Epidermoid tumor, Craniopharyngioma, Leukoencephalopathy, Medulloblastoma (metastasis), Paracoccidioidomycosis and Toxoplasmosis, each was diagnosed in 2 (5.0 %) patients. Non-specific finding was observed in 3 (7.5 %) biopsy samples, while one (2.5 %) sample consisted of normal tissue. Table-1

Table No.1: Histopathological diagnosis of 40 biopsy samples

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glioma grade II</td>
<td>5</td>
<td>12.5%</td>
</tr>
<tr>
<td>High-grade glioma (III &amp; IV)</td>
<td>4</td>
<td>10.0%</td>
</tr>
<tr>
<td>Cysticercosis</td>
<td>4</td>
<td>10.0%</td>
</tr>
<tr>
<td>Pilocytic astrocytoma</td>
<td>3</td>
<td>7.5%</td>
</tr>
<tr>
<td>Pineoblastoma</td>
<td>3</td>
<td>7.5%</td>
</tr>
<tr>
<td>Germinoma</td>
<td>3</td>
<td>7.5%</td>
</tr>
<tr>
<td>Cryptococcosis</td>
<td>2</td>
<td>5.0%</td>
</tr>
<tr>
<td>Epidermoid tumor</td>
<td>2</td>
<td>5.0%</td>
</tr>
<tr>
<td>Craniopharyngioma</td>
<td>2</td>
<td>5.0%</td>
</tr>
<tr>
<td>Leukoencephalopathy</td>
<td>2</td>
<td>5.0%</td>
</tr>
<tr>
<td>Medulloblastoma (metastasis)</td>
<td>2</td>
<td>5.0%</td>
</tr>
<tr>
<td>Paracoccidioidomycosis</td>
<td>2</td>
<td>5.0%</td>
</tr>
<tr>
<td>Toxoplasmosis</td>
<td>2</td>
<td>5.0%</td>
</tr>
<tr>
<td>Non-specific</td>
<td>3</td>
<td>7.5%</td>
</tr>
<tr>
<td>Normal tissue</td>
<td>1</td>
<td>2.5%</td>
</tr>
</tbody>
</table>
Total 33 (82.5%) samples were accurately diagnosed as 12 of these were reconfirmed by new sample, 13 patients’ diagnoses showed compatibility with the ongoing treatment, and diagnosis of 8 patients was compatible with the follow-up. Total 5 (12.5%) samples were inaccurately diagnosed as new biopsy results varied in 3 patients, clinical course was not aligned with the diagnosis in one patient and indecisive findings were observed in one patient. Of 40 biopsies, 38 samples were included in complete study because one patient died and one patient lost follow-up. Table-2.

Table No.2: Accuracy of Neuroendoscopic biopsy results

<table>
<thead>
<tr>
<th>Results</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accurate</td>
<td></td>
</tr>
<tr>
<td>Diagnosis confirmed by new sample</td>
<td>12</td>
</tr>
<tr>
<td>Diagnosis compatible with treatment response</td>
<td>13</td>
</tr>
<tr>
<td>Diagnosis compatible with follow-up</td>
<td>8</td>
</tr>
<tr>
<td>Total accurate</td>
<td>33 (82.5%)</td>
</tr>
<tr>
<td>Inaccurate</td>
<td></td>
</tr>
<tr>
<td>New biopsy results varied</td>
<td>3</td>
</tr>
<tr>
<td>Clinical course not align with diagnosis</td>
<td>1</td>
</tr>
<tr>
<td>Indecisive finding</td>
<td>1</td>
</tr>
<tr>
<td>Total inaccurate</td>
<td>5 (12.5%)</td>
</tr>
<tr>
<td>Total included</td>
<td>38</td>
</tr>
<tr>
<td>Excluded</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>1</td>
</tr>
<tr>
<td>Lost follow up</td>
<td>1</td>
</tr>
<tr>
<td>Total excluded</td>
<td>2 (5.0%)</td>
</tr>
<tr>
<td>Total biopsies</td>
<td>40</td>
</tr>
</tbody>
</table>

DISCUSSION

Many studies related to use of endoscopic biopsy for managing intraventricular and periventricular lesions have been conducted in recent past years. There was a variation of diagnostic yield for this procedure ranging from 69.6% and 100% and these variations can be described by the methodological differences. The past studies covered topics of tumors only, and only tumors of specific single site e.g. pineal region and patients of specific age limit such as children were considered in these articles. Variation in types of endoscope used either rigid or flexible, in tumor forceps cups size, in the number of samples taken, and in surgeon’s experience were included in the factors related to the success rate of this technique. On the other hand, on literature review of past studies most significant factor was how authors define the accuracy of technique. Patients with unsuccessful biopsies were excluded by most of the authors in the past studies while some diagnosed even histopathological abnormalities. Non-specific histopathological outcomes of the biopsy were not considered positive in order to institute a possible treatment. According to a study pathological report was classified by Depreitere et al. into four levels: Level I, completely diagnostic with no uncertainties, Level II diagnostic but with few uncertainties along with strong arguments for the preferred diagnosis by the pathologist, Level III certainly showing abnormal or neoplastic tissues but with problematic in the specific diagnosis and Level IV neither show any tissue abnormality nor able to make any explanation.

In a recent study conducted by Constantini et al. over 293 cases from different countries, 27% of the patients (78 of them) underwent open surgery whose biopsy findings were believed to be informative. Two samples were compared, 82% had fully matching diagnosis while 6.4% with not matching but meaningful and 11.5% with mismatched and meaningful diagnosis. Our study was conducted to provide solution to methodological issues because our study included all types of patients (along with patients without neoplastic disease). But still it was in spite of fully correct diagnosis all of the patients were not going to show same response to the treatment strategies. Similarly, the patients not adherent to the treatment plans also had different nature of the disease as compared to those completed the treatment. Apart from this if such methodological issues were present these can affect the outcomes of our study.

Rates of morbidity and mortality were little with the use of endoscopic biopsy. Minor complications which can be underestimated were ignored and were not included in our retrospective study. Hemorrhage was the major complication and major concern while performing the endoscopic procedure. Although the hemorrhage is a subjective term but different authors define “important hemorrhage” differently. In different studies the hemorrhage was classified as mild, moderate, and severe type of complication. According to our definition of “important hemorrhage” it is the type of bleeding that lead to need of an EVD insertion, causes execution of the process and second surgery is required for sufficient management.

CONCLUSION

The results of our study show that the use of the new method to assess the accuracy of endoscopic biopsy revealed high accuracy in diagnostic biopsy. When compared to the previous studies this method of assessing the accuracy is safer and effective as well.

Author’s Contribution:

Concept & Design of Study: Syed Zahid Hussain Shah
Drafting: Shoaib Saleem Khan
Data Analysis: Shoaib Saleem Khan, Muhammad Aamir
Revisiting Critically: Syed Zahid Hussain Shah, Shoaib Saleem Khan
Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES


Serum Ferritin Status and Chelation Therapy of Children and Adolescents with Transfusion Dependent Thalassemia Major in Mirpur, AJK
Saba Haider Tarar¹, Waseem Ahmed Khan², Iftikhar Ahmed¹ and Shakil Asif³

ABSTRACT

Objective: To assess the serum Ferritin levels and chelation therapy in transfusion dependent Thalassemia major children and adolescents in Divisional Headquarters Teaching Hospital, Mirpur, AJK.

Study Design: Descriptive Observational Study

Place and Duration of Study: This study was conducted at the Thalassemia Center of Divisional Headquarters Teaching Hospital, Mirpur, AJK from Oct, 2019 to March, 2020.

Materials and Methods: After taking permission from hospital ethics committee, children with transfusion dependent Thalassemia aged up to 18 years were added in the study after informed written consent. Blood samples were sent for Serum Ferritin levels. Serum Ferritin measurement was done by indirect ELISA kit. Chelation therapy was assessed in terms of Deferasirox Tablets and Desferrioxamine injection. Data were analyzed on SPSS 20 and the correlation between age, gender, serum Ferritin level and chelation therapy were checked.

Results: A total of 100 children registered with Thalassemia center, Divisional Headquarters teaching hospital, Mirpur were included in this study. There were 55 (55%) males and 45 (45%) females. There were 18 (18%) children between 1-3 years, 20 (20%) in 4-5 years, 17 (17%) in age group 6-8 years, 30 (30%) in 9-15 years and 15 (15%) above 15 years of age. Serum Ferritin monitoring revealed 29 (29%) children having Serum Ferritin level between 500-2500ng/dl, 16 (16%) between 2501-3500ng/dl, 19 (19%) between3501-5000ng/dl, 26(26%) between 5001-9000ng/dl and 10 (10%) were having above 9000ng/dl. Maximum children (29%) were found in 500-2500ng/dl serum Ferritin. Majority (66%) was taking chelation as compared to 34% who were not taking any chelation. A strong association was present between Child’s age and serum Ferritin levels with P-value < 0.001. With increasing age, more number of children were taking chelation as compared to younger age (93.33%) at 15 years of age as compared to (45.00%) at 4-5 years of age. Comparing Gender versus chelation revealed that more females i.e. 33 (73.33%) out of 45 were taking chelation as compared to males (60%) taking chelation. It was observed that chelation percentage increased with increasing Ferritin level with P-value < 0.004.

Conclusion: The average serum Ferritin levels are significantly raised as compared to the normal permissible levels in these patients. This is further made worse by the fact that around one third of them are not receiving any kind of iron chelation therapy.

Key Words: Thalassemia, Ferritin, Chelation, AJK

Citation of article: Tarar SH, Khan WA, Ahmed I, Asif S. Serum Ferritin Status and Chelation Therapy of Children and Adolescents with Transfusion Dependent Thalassemia Major in Mirpur, AJK. Med Forum 2020;31(9):194-198.

INTRODUCTION

Thalassemia is one of the genetically acquired disorders of defective globin chain synthesis, resulting in imbalance between the alpha and beta globin chains present in Hemoglobin¹. Globally around 70,000 new children are born with different types of Thalassemia annually.² Thalassemic children who are transfusion dependent generally require monthly RCC (red Cell concentrate) transfusions resulting in excessive iron load on the body. Every single unit of packed RCC produces 200mg of free iron in human body.³ During normal condition, iron binds with a carrier protein Transferrin which transports iron in various tissues. However, if there is excessive iron in the body due to any cause, Transferrin becomes fully saturated leaving free iron in blood circulation. Free iron radicals

¹ Department of Pediatrics / Ophthalmology² / Psychiatry³, Divisional Headquarters Teaching hospital/ Mohtarma Benazir Bhutto Shaheed Medical College (MBBS, MC), Mirpur, AJK.

Correspondence: Saba Haider Tarar, Assistant Professor, Pediatrics, Divisional Headquarters Teaching hospital/MBBS, MC, Mirpur, AJK.

Contact No: 03015634943

Email: saba_tarar80@yahoo.com

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are highly toxic and generate reactive oxygen forms which can badly damage various organs. Vital organs damage like liver, heart and endocrine glands is the leading cause of complications, disability and even death of children in thalassemia. There are many investigations both invasive as well as non-invasive to check iron status of Thalassemia patients, however serum Ferritin is the readily available and cheap method. Iron Chelation therapy (ICT) is started in all patients generally after 1-2 years of RCC transfusions with a target to keep serum Ferritin < 1000 μg/l. Excessively high values of serum Ferritin crossing 2500 μg/l can lead to vital organ damage especially heart, liver and endocrine glands. Regular blood transfusions in Thalassemia patients demand continuous Iron Chelation Therapy (ICT) to avoid the excessive iron load which can lead to cardiomyopathy and decreased cardiac output. This can even decrease total life expectancy of these patients and may have high mortality. On the other hand, this ICT therapy is very expensive and time consuming as well and put another financial burden on these patients. Deferasirox, a novel oral chelator, although effective and easy to administer but it is quite expensive and poses a considerable financial risk as it has to be given daily and lifelong. Deferoxamine (DFE), the traditional ICT, being given parenterally is being used for more than 4 decades. It is found to be quite effective iron chelator but needs assistance as well as long time for administration. It is found that Thalassemia patients are still unable to attain the optimum levels of Serum Ferritin so mostly a combination of chelators is used to control serum Ferritin levels.

MATERIALS AND METHODS

In this study, we enrolled children suffering from Transfusion dependant Thalassemia aged less than 18 years registered with Thalassemia center of Divisional headquarters teaching hospital. A well-informed written consent was taken. Patients who were undergoing regular blood transfusions monthly for last 2 years were recruited in the study. Blood samples were sent for Serum Ferritin assays. Serum Ferritin levels were done by indirect ELISA kit. Chelation therapy was assessed in terms of Deferasirox Tablets as well as Deferoxamine injections. Data were analyzed on SPSS 20 and the association between age, gender, serum Ferritin level and whether taking chelation therapy or not were established.

RESULTS

A total of 100 children registered with Thalassemia center, Divisional Headquarters teaching hospital Mirpur were included in this study. There were 55 (55%) males and 45 (45%) females. Age was divided in further subgroups for analysis purpose. There were 18 (18%) children between 1-3 years, 20 (20%) in 4-5 years, 17 (17%) in age group 6-8 years, 30 (30%) in 9-15 years and 15 (15%) above 15 years of age.

All Thalassemia patients were having high serum Ferritin. Serum Ferritin monitoring revealed 29 (29%) children having Serum Ferritin level between 500-2500ng/dl, 16 (16%) between 2501-3500ng/dl, 19 (19%) between 3501-5000ng/dl, 26 (26%) between 5001-9000ng/dl and 10 (10%) were having above 9000ng/dl. Maximum children (29%) were found in 500-2500ng/dl serum Ferritin.

**Table No.1: Serum Ferritin Status:**

<table>
<thead>
<tr>
<th>Ferritin Level</th>
<th>Frequency</th>
<th>Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>500-2500</td>
<td>29</td>
<td>29.0</td>
<td>29.0</td>
</tr>
<tr>
<td>2501-3500</td>
<td>16</td>
<td>16.0</td>
<td>45.0</td>
</tr>
<tr>
<td>3501-5000</td>
<td>19</td>
<td>19.0</td>
<td>64.0</td>
</tr>
<tr>
<td>5001-9000</td>
<td>26</td>
<td>26.0</td>
<td>90.0</td>
</tr>
<tr>
<td>&gt;9000</td>
<td>10</td>
<td>10.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

**Figure No. 1: Ferritin Status with Frequency**

**Table No.2: Chelation status**

<table>
<thead>
<tr>
<th>Chelation Status</th>
<th>Frequency</th>
<th>Percent</th>
<th>Cumulative Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valid Yes</td>
<td>66</td>
<td>66.0</td>
<td>66.0</td>
</tr>
<tr>
<td>No</td>
<td>34</td>
<td>34.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

The statistical analysis revealed a strong association between Child’s age and serum Ferritin levels with P-value < 0.001.

**Table No.3: Child’s Age * Ferritin status Cross – tabulation**

<table>
<thead>
<tr>
<th>Ferritin Level</th>
<th>500-2500 ng/dl</th>
<th>2501-3500ng/dl</th>
<th>3501-5000ng/dl</th>
<th>5001-9000ng/dl</th>
<th>&gt;9000ng/dl</th>
<th>total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child’s Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-3yr</td>
<td>8</td>
<td>6</td>
<td>4</td>
<td>0</td>
<td>1</td>
<td>18</td>
</tr>
<tr>
<td>4-5Yr</td>
<td>10</td>
<td>3</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>20</td>
</tr>
<tr>
<td>6-8yr</td>
<td>3</td>
<td>2</td>
<td>4</td>
<td>5</td>
<td>3</td>
<td>17</td>
</tr>
<tr>
<td>9-15yr</td>
<td>5</td>
<td>4</td>
<td>4</td>
<td>15</td>
<td>2</td>
<td>30</td>
</tr>
<tr>
<td>15yr</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>4</td>
<td>15</td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
<td>16</td>
<td>19</td>
<td>26</td>
<td>10</td>
<td>100</td>
</tr>
</tbody>
</table>
As far as Chelation Status was concerned, Majority (66%) was reportedly taking chelation in the form of Deferasirox and Injection Desforaximine as compared to 34% who were not taking any chelation despite counseling.

Table No.4: Chi-Square Tests

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>DF</th>
<th>Asymp. Sig. (2-sided)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson Chi-Square</td>
<td>33.779</td>
<td>16</td>
<td>.006</td>
</tr>
<tr>
<td>Likelihood Ratio</td>
<td>37.284</td>
<td>16</td>
<td>.002</td>
</tr>
<tr>
<td>Linear-by-Linear Association</td>
<td>17.923</td>
<td>1</td>
<td>.000</td>
</tr>
<tr>
<td>N of Valid Cases</td>
<td>100</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- 19 cells (76.0%) have expected count less than 5. The minimum expected count is 1.50.

Figure No.2: Association of Gender with Ferritin level

Males were having high serum ferritin levels as compared to female children in our study.

Association of age of child with chelation:

Table No.5: Child’s Age * chelation status Cross Tabulation

<table>
<thead>
<tr>
<th>Child’s Age</th>
<th>Chelation status</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3yr</td>
<td>Yes</td>
<td>10</td>
</tr>
<tr>
<td>4-5yr</td>
<td>Yes</td>
<td>9</td>
</tr>
<tr>
<td>6-8yr</td>
<td>Yes</td>
<td>11</td>
</tr>
<tr>
<td>9-15yr</td>
<td>Yes</td>
<td>22</td>
</tr>
<tr>
<td>15yr</td>
<td>Yes</td>
<td>14</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>66</td>
</tr>
</tbody>
</table>

Table No.6: Ferritin status * chelation status Cross Tabulation

<table>
<thead>
<tr>
<th>Ferritin Status</th>
<th>Chelation Status</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>500-2500</td>
<td>Yes</td>
<td>14</td>
</tr>
<tr>
<td>2501-3500</td>
<td>Yes</td>
<td>11</td>
</tr>
<tr>
<td>3501-5000</td>
<td>Yes</td>
<td>15</td>
</tr>
<tr>
<td>5001-9000</td>
<td>Yes</td>
<td>18</td>
</tr>
<tr>
<td>&gt;9000</td>
<td>Yes</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>66</td>
</tr>
</tbody>
</table>

It was observed that with increasing age, more number of children were taking chelation as compared to younger age (93.33%) at 15 years of age as compared to (45.00%) at 4-5 years of age.

Cross-tabulating Gender versus chelation revealed that more females i.e. 33 (73.33%) out of 45 were taking chelation as compared to males (60%) taking chelation. It was observed that chelation percentage increased with increasing ferritin level with P-value < 0.004, however, there was one exception in 500-2500ng/dl ferritin level.

Figure No.3: Ferritin Status with Count

DISCUSSION

It is estimated that the patients suffering from Thalassemia Major receive approximately 20 times higher intake of free iron, so excessive iron load is already anticipated in them. Serum Ferritin assays are the most commonly used method for the estimation of iron overload in these patients as it is simple, cheap and readily available worldwide. A total of 100 children registered with Thalassemia center, Divisional headquarters teaching hospital Mirpur were included in our study. There were 55 (55%) males and 45 (45%) females. Age was divided in further subgroups for analysis purpose. There were 18 (18%) children between 1-3 years, 20 (20%) in 4-5 years, 17 (17%) in age group 6-8 years, 30(30%) in 9-15 years and 15 (15%) above 15 years of age.

All Thalassemia patients were having high serum Ferritin. Serum Ferritin monitoring revealed 29 (29%) children having Serum Ferritin level between 500-2500ng/dl, 16 (16%) between 2501-3500ng/dl, 19 (19%) between 3501-5000ng/dl, 26(26%) between 5001-9000ng/dl and 10 (10%) were having above 9000ng/dl. Maximum children (29%) were found in 500-2500ng/dl serum Ferritin and mean Ferritin was 3201ng/dl. These very high values depict ineffective and inadequate degree of chelation and put these children at a high risk of developing complications.
These results were similar to study done by Mishra et al. where 87.4% of the children had significantly higher Ferritin levels. The mean serum Ferritin level was also similar to our study i.e. 2767.52 ng/ml. In that study, around half of the patients had serum Ferritin between 1000 to 2500 ng/ml, while rest of the patients had values above 2500 ng/ml. Serum Ferritin levels were low in a study done in Sri Lanka where Mean serum Ferritin was 1778(± 1458) μg/l and one third of their patients had normal serum Ferritin. A considerably high mean serum Ferritin Value of 9542 ± 782 ng/ml is reported by Al-Zubaidietal which is much higher as compared to our study but no reason has been attributed as a cause of so high Ferritin levels. In our study, majority (66%) of patients were taking chelation in the form of tab. Deferasirox and Injection Desferoxamine as compared to 34% who were not taking any chelation despite counseling. Similar results were shown by Riazetal, in which 58.2% cases were taking chelation and 41.8% were not taking any chelation.

The statistical analysis revealed a strong association between Child’s age and serum Ferritin levels with P-value < 0.001. Males were having high serum Ferritin levels as compared to female children in our study but there was no significant statistical analysis. It was observed that with increasing age, more number of children were taking chelation as compared to younger age (93.33%) at 15 years of age as compared to (45.00%) at 4-5 years of age. This is in comparison with Riazetal, who showed that Age and chelation therapy have a significant correlation with Serum Ferritin measurements. This study demonstrated that age in years is directly proportional to the serum Ferritin levels.

Comparing Gender versus chelation revealed that more females i.e 33 (73.33%) out of 45 were taking chelation as compared to males (60%) taking chelation. It was observed that chelation percentage increased with increasing Ferritin level with P-value < 0.004. However, there was one exception in 500-2500ng/ml Ferritin level. Another study by Faruqietal showed similar results with the mean Ferritin value of 6062.61 + 3641.796 ng/ml. He showed that most of the patients were not receiving adequate ICT. And those patients with less optimal ICT were having high serum Ferritin values. This was also in comparison with a study done in Karachi where serum Ferritin levels were comparable to our study (3319.6 ± 1925.8) ng/ml in the chelation group as compared to non-chelation group (5514.8 ± 2383.0) ng/ml.

CONCLUSION

The high serum Ferritin levels in our study strongly supports the rationale of regular monitoring and follow up regarding adequate chelation to minimize iron overload and associated life-limiting complications. We need to create more knowledge and awareness in the Thalassemia patients about the value of monitoring regular serum Ferritin levels. They should be well aware of the consequences and complications of iron overload. Proper chelation of iron overload could improve the quality of life of these patients.

LIMITATIONS:

The dose of Deferasirox and Deferoxamine infusions is not ascertained which is a limitation in our study.

AUTHOR’S CONTRIBUTION:

Concept & Design of Study: Saba Haider Tarar
Drafting: Saba Haider Tarar
Data Analysis: Waseem Ahmed Khan
Revisiting Critically: Shakil Asif
Final Approval of version: Waseem Ahmed Khan

CONFLICT OF INTEREST: The study has no conflict of interest to declare by any author.

REFERENCES


Objective: To determine the accuracy of clinical examination versus magnetic resonance imaging (MRI) for meniscal injuries of knee joint taking arthroscopy as the gold standard.

Study Design: Cross sectional study

Place and Duration of the Study: This study was conducted at the Department of Orthopedic and Spine Surgery from January to June 2019.

Materials and Methods: A total of 178 patients with knee injury were enrolled who were candidates for arthroscopy. Prior to MR I and arthroscopy, a detailed physical examination of the affected knee was done following with preliminary diagnosis. Findings of arthroscopy were taken as the definitive diagnosis and findings of the physical examination and MRI were compared.

Results: The mean age of the patients was 25.94±7.16. Among all those cases 119(66.5%) were male while 59(33.5%) were female cases. Meniscal injury was detected by MRI in 111(65.3%) of cases while it was undetected in 59(34.7%) of cases. On other hand meniscal injury was detected by clinical examination in 115(64.1%) and not detected in 63(35.9%) of cases. All arthroscopy detected meniscal injury in 113(63%) of cases while it remains undetected in 62(37%) of cases. Clinical examination had a sensitivity of 77%, specificity of 54% and diagnostic accuracy of 78% while MRI had the sensitivity of 86%, specificity of 73% and diagnostic accuracy of 81%.

Conclusion: No significant difference was observed between the accuracy of clinical examination and MRI regarding the diagnosis of meniscal tears. MRI, other than specific circumstances, is an expensive and unnecessary diagnostic test in patients with suspected meniscal pathology.

Keywords: Meniscal tears, arthroscopy, magnetic resonance imaging, clinical examination.


INTRODUCTION

Soft tissue injuries of the knee including meniscal and cruciate injuries are frequently seen by orthopedic surgeons. The meniscus is a very important structure of the knee joint. It has key functions like load transmission, shock absorption and stress reduction. Treatment of meniscal and cruciate ligament injuries accurately is of prime importance not only for the normal function of knee but also to prevent complication like osteoarthritis. The overall incidence of meniscal injury in knee trauma is 76%. In the past, injuries of the soft tissues of the knee were evaluated clinically which had its own pitfalls. Invention of MRI and arthroscopy revolutionized the diagnosis and treatment of such injuries. Initially emphasis was placed in determining the diagnostic accuracy of MRI alone which was of course high and this lead to a false impression of requiring MRI in almost every case of suspected knee injury. Schurz et al. noted MRI to be more accurate in diagnosing medial and lateral meniscus injuries as compared to clinical examination (83% & 83% vs. 55% & 64% respectively) with better sensitivity (93% & 66% vs. 62% & 22% respectively) and specificity (65% & 90% vs. 45% & 78%). Similar results were achieved by Nikolau et al and Gupta et al. Reciprocal results were however achieved by Ryan et al. However the difference was only marginal in case of lateral meniscus and cruciate tears. Similar results were achieved by Siddiqui et al. in 2012. Doubt thus exists about the accuracy of clinical examination and MRI for diagnosing knee injuries.
Purpose of this study is therefore to confirm whether clinical examination is better or at least equally accurate in knee injuries as compared to MRI which if found true will provide a quick, cheap and effective way of patient assessment in future limiting the use of MRI only in difficult cases thus reducing economic burden on the society.

MATERIALS AND METHODS

This cross sectional study was conducted at “Department of Orthopedic and Spine Surgery, Sughr Shafi Medical Complex, Narowal” from January to June 2019. Approval from the Institution’s Review Board was sought. A total of 178 patients of both genders aged 18–45 years and presenting with history of sports or accidental knee injury were enrolled. Informed consent was sought from all study participants. All patients with history of previous knee surgery or arthroscopy, or those who had degenerative changes on X-rays of knee joint were excluded. All the patients had clinical as well as MRI evaluation prior to arthroscopy. Details were recorded regarding findings on clinical examination, MRI and arthroscopy. Clinical Examination included history and examination namely suggestive symptoms (including pain, swelling, limited motion, locking, and clicking) and clinical tests (Mc Murray Test).

All the data was entered into specially designed template. Findings of arthroscopy were taken as definitive diagnosis while observations of physical examination and MRI were compared subsequently. All the cases were managed by senior consultant of the unit to eliminate bias. All the collected data was analyzed using SPSS version 26.0. Numerical variables i-e age was presented by mean ±SD and range. Categorical variables i-e gender, meniscal and cruciate tear were presented as frequency and percentage. A 2x2 contingency table was generated to calculate sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of clinical examination & MRI in the detection of cruciate and meniscal injury by taking arthroscopy as gold standard.

RESULTS

In a total of 178 patients, mean age was 25.94±7.16 years. Among all these cases, 119 (66.5%) were male while 59(33.5%) were female. Meniscal injury was detected by MRI in 117 (65.3%) cases while it was undetected in 61(34.7%) of cases. On other hand, meniscal injury was detected by clinical examination in 115 (64.1%) cases and undetected in 63 (35.9%) cases. Arthroscopy detected meniscal injury in 113 (63%) cases while it remained undetected in 65 (37%) of cases.

It became clear by 2x2 contingency table that clinical examination has a sensitivity of 77%, specificity of 54% and diagnostic accuracy of 78% (Table No.1):

<table>
<thead>
<tr>
<th>Meniscal Injury on Clinical Examination</th>
<th>Meniscal Injury on Arthroscopy</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detected</td>
<td>85 (73.9%)</td>
<td>115 (100%)</td>
</tr>
<tr>
<td>Not Detected</td>
<td>28 (42.4%)</td>
<td>63 (100%)</td>
</tr>
<tr>
<td>Total</td>
<td>113 (62.9%)</td>
<td>178 (100%)</td>
</tr>
</tbody>
</table>

Sensitivity = 77% Specificity = 54% PPV = 74% NPV = 58% Accuracy = 78%

MRI had sensitivity of 86%, specificity of 69% and diagnostic accuracy of 81% (Table No.2).

<table>
<thead>
<tr>
<th>Meniscal Injury on Clinical Examination</th>
<th>Meniscal Injury on Arthroscopy</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detected</td>
<td>97 (82.9%)</td>
<td>117 (100%)</td>
</tr>
<tr>
<td>Not Detected</td>
<td>16 (26.2%)</td>
<td>61 (100%)</td>
</tr>
<tr>
<td>Total</td>
<td>113 (62.9%)</td>
<td>178 (100%)</td>
</tr>
</tbody>
</table>

Sensitivity = 86% Specificity = 69% PPV = 83% NPV = 74% Accuracy = 78%

DISCUSSION

Diagnostic arthroscopy is considered to be the only possible tool for giving an exact diagnosis in doubtful cases. It is costly and invasive technique. Its unyielding use leads to many additional complications like injury to intra-articular structures, neurovascular lesions and infection. With the advancement of surgical techniques and arthroscopy tools, arthroscopy has evolved as surgical modality rather than a diagnostic service. We noted a male predominance among patients with meniscal injuries of knee joint as 66.8% patients were male whereas 70% of the patients were aged between 20–40. The male predominance and majority having relatively young age shows that these injuries are more common among young males. Negative predictive value of MRI in this study is 74% meniscal tears. We had initially ruled out arthroscopy in 27/57 referred patients with the help of MRI. All this is depicting that pre-operative MRI can help preventing needless diagnostic arthroscopy among many of these cases. In another study, among these 69 cases waiting for arthroscopy, MRI ruled out lesions in 24 and helped
is removing these cases from waiting list. After nine months, only one patient was relisted for arthroscopy due to continued symptoms. Some other researchers have also noted similar observations. Contrary to that, some researchers have not found routine usage of MRI very effective among patients of meniscal injuries. Brooks and Colleagues concluded that MRI was not found to reduce negative arthroscopic procedures among patients of meniscal injuries. As we know that in a country like Pakistan, MRI is taken as an expensive tool for the majority but cost of arthroscopy is much higher. Some authors have also analyzed whether preoperative MRI could prove economical among patients waiting for arthroscopy and concluded that performing MRI could have saved around 680 US dollars for every single case. We also found MRI really helpful in ruling out arthroscopy which showing the worth of this tool as found by other local researchers as well.

Recent data also shows that clinical examination when done by an experienced examiner, can provide equal or even better diagnostic accuracy in comparison to MRI regarding evaluation of the meniscal lesions. We feel that as arthroscopy is an invasive and quite expensive procedure, thorough clinical examination needs to be done initially and if needed, MRI should be ordered. As for majority of the population, cost of MRI scan could be high, so clinical examination has almost equal sensitivity and specificity hence an additional financial burden of MRI can be avoided and patient can be directly offered arthroscopy. As far as limitations of this study are concerned, we had a comparatively smaller sample size so findings of this research cannot be generalized. More studies involving multiple centers and among different sets of population can further verify the findings of this study.

CONCLUSION

No significant difference was observed between the accuracy of clinical examination and MRI regarding the diagnosis of meniscal tears. MRI, other than specific circumstances, is an costly and avoidable diagnostic tool among cases having suspected meniscal pathology.

Acknowledgement: The authors are thankful to Muhammad Aamir (Research Consultant, Bahawalpur) for his volunteer support in statistical analysis of this research.

Author’s Contribution:

Concept & Design of Study: Muhammad Ammar, Naqvi

Drafting: M. Saif-ur-Rehman, Zahid Shafiq

Data Analysis: Muhammad Tahir Yusuf, Hafiz Muhammad Abid Hasan, Abdullah Tariq

Revisiting Critically: Muhammad Ammar

Final Approval of version: Muhammad Anmar Naqvi

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

REFERENCES


Frequency of Bacteria Causing Urinary Tract Infections During Pregnancy and Antimicrobial Sensitivity in Southern Punjab-Pakistan

S. M. Abbas Naqvi, M. Majid Rasheed, Shahbaz Anwar, Rubina Yaseen and Muhammad Nouman Iqbal

ABSTRACT

Objective: Urinary tract infections are common infection and incidence resistant strains causing UTI is also increasing. Bacteriuria results in serious complications in mother and fetus. The need of the hour is to aware the pregnant women of proper screening and improved treatment against resistant bacteria.

Study Design: Descriptive Cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Pathology in collaboration with the Gynecology department, Nishtar Medical College/Hospital, Multan from October 2018 to February 2019.

Materials and Methods: One hundred and sixty (n=160) pregnant women, presenting with signs and symptoms of UTI, were included in the study from Gynaecology outdoor of Nishtar Hospital, Multan. Midstream urine samples were collected in sterile containers and processed in microbiology section of that college. Complete urine examination and urine culture were done to diagnose UTI. Antimicrobial susceptibility testing of isolated bacteria were also done by standard Kirby-Bauer disk diffusion method using CLSI 2015 guidelines.

Results: Out of total 160 urine samples, 58 samples were culture positive. Of all isolates (100% i.e., 58), the highest number was of Staphylococcus aureus 41.38% (n=24) followed by E. coli 29.31% (n=17), S. saprophyticus 10.34% (n=6), Klebsiella enterica 5.18% (n=3), Pseudomonas spp 5.17% (n=3), Enterococcus fecalis 3.45% (n=2), Enterobacter spp 3.45% (n=2) and Staphylococcus epidermidis 1.69% (n=1). Moreover, 23.5% of Multi drug resistant E. coli were also isolated.

Conclusion: The study concluded that Staphylococcus aureus and Escherichia coli were the most frequent organisms isolated, with 23.5% of multidrug resistant E. coli. It is suggested, considering the complications of UTIs, that every pregnant women should have regular screening for bacteriuria followed by antibiotic susceptibility testing for improved therapy against resistant organisms.

Key Words: UTI. Pregnant women, Multidrug Resistant E. Coli, Staphylococcus Aureus.

INTRODUCTION

Urinary tract infection is one of the most frequent bacterial infections in pregnant and non-pregnant women and it may affect any part of the urinary tract. The total estimated yearly UTIs are about 150 million worldwide. Women are more prone to UTI due to proximity of urethra with the anus. Other risk factors are sexual contact, poor hygiene and indwelling catheters.

According to American Pregnancy Association women in 1st and 2nd trimester of pregnancy are at higher risk for a urinary tract infections. Pregnancy itself is a predisposing factor for UTI as it causes physiological and hormonal changes like relaxation of ureters and urinary stasis in bladder which favour development of UTI. The sign and symptoms of UTIs are urinary urgency, frequency, dysuria, suprapubic pain, nausea and vomiting. UTIs are not STIs, still type of organisms causing UTIs in pregnant and non-pregnant women are same. Organisms causing UTIs include Proteus species, Enterobacter species, Pseudomonas species, Klebsiella pneumonia, Staphylococcus saprophyticus, Enterococcus faecalis and Staphylococcus aureus. The prevalence of organisms causing UTI vary in different regions of world. The highly mutant E. coli strains that cause UTI have toxins like adhesins, pili, or fimbriae which help adherence to uroepithelium. Multidrug resistant E. coli is the strain that is resistant to more than three of the following classes of antibiotics i.e. pencillins third generation cephalosporins, aztreonam, aminoglycoside,
and quinolones\(^5\). The resistance of first line drugs like ampicillin, nitrofurantoin, and co-trimoxazole is increasing in community acquired strains. According to more recent studies, resistance to fluoroquinolones such as levofloxacin and ciprofloxacin is also increasing\(^10\). Therefore, considering the increased incidence of multidrug resistant UTIs, local antibiotic resistance profiles must be known to support empirical therapy for management of these serious infections. With this background the present study was conducted to find out frequency of bacteria plus Multi-Drug-Resistant (MDR) strains of E. coli causing symptomatic UTI in pregnant women.

**MATERIALS AND METHODS**

This Descriptive Cross-sectional study was carried out in the department of Pathology in collaboration with the Gynecology department, Nishtar Medical College/ Hospital, Multan from October 2018 to February 2019. A total number of 160 pregnant women of all ages having symptomatic urinary tract infection (UTI) were included. Midstream urine samples were taken in sterile containers after properly instructing every woman about sample collection. Specimens were first chemically tested for specific gravity, pH, albumin, glucose, leukocyte esterase and nitrites by urine dipstick. Then, by centrifuging urine at 3000 rpm for 5 minutes, microscopy of each sample was done to test out WBCs. All the samples were cultured on CLED agar media and incubated aerobically at 37°C for 24 hours\(^11\). On the next day growth of organism were identified morphologically by Gram stain and confirmed by biochemical analysis. Antimicrobial sensitivity (AST) testing of bacteria isolated was performed using standard Kirby-Bauer method\(^12\). A performa was employed for data collection and storage. The history of patients including name, socioeconomic status, education, gestational period, number of pregnancies result of tests on dipstick, culture positive bacteria and AST were all recorded. The data was analyzed through SPSS for Windows version 16. The nominal variables were reported as frequency and percentages. The age variable was reported as Mean.

**RESULTS**

The age of pregnant women was between 26-40 year, average age was 27 years; maximum were from lower socioeconomic status (83.04%). Out of 160 pregnant females included in this study, the most women showed multiple signs and symptoms. Urinary frequency (96%), urinary urgency (91%), dysuria (53%), fever (41%), supra-pubic pain (29%) and flank pain (7.5%) were seen. (Table-1) Maximum number of women 86 (53.8%) were in 2\(^{nd}\) trimester, 53 (33.1%) were in 3\(^{rd}\) trimester and 21 (13.1%) were in 1\(^{st}\) trimester of pregnancy. Of 160 samples, 58 samples were culture positive (36.25%). (Table-2)

Of all isolates (58), the highest number was of Staphylococcus aureus 24 (41.38%) followed by E. coli 17 (29.31%), S. saprophyticus 6 (10.34%), Klebsiella enterica 3 (5.17%), Pseudomonas spp. 3 (5.18%), Enterococcus fecalis 2 (3.45%), Enterobacter spp 2 (3.45%) and Staphylococcus epidermidis 1 (1.69%). (Table-3)

Of 160 samples, 46 (28.7%) samples showed a positive leukocyte esterase test and 114 (71.2%) samples showed negative leukocyte esterase test. Leukocyte esterase test was positive in those urine samples in which more than 13 WBCs/ HPF were seen. No organism was isolated from those urine samples in which insignificant WBCs (less than 6) were present. Of 160 samples, 22 (13.7%) samples showed a positive nitrate test and 138 (86.2%) showed negative nitrate test. Nitrate test was positive in E. coli, Enterobacter spp and Klebsiella enterica.

**Table No.1**: Signs and symptoms of UTI in pregnant women (n=160)

<table>
<thead>
<tr>
<th>Signs and Symptoms</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysuria</td>
<td>85</td>
<td>53%</td>
</tr>
<tr>
<td>Urine frequency</td>
<td>154</td>
<td>96%</td>
</tr>
<tr>
<td>Urine urgency</td>
<td>146</td>
<td>91%</td>
</tr>
<tr>
<td>Supra pubic pain</td>
<td>47</td>
<td>29%</td>
</tr>
<tr>
<td>Fever</td>
<td>66</td>
<td>41%</td>
</tr>
<tr>
<td>Flank tenderness</td>
<td>12</td>
<td>7.5%</td>
</tr>
</tbody>
</table>

**Table No.2**: Correlation of gestational period with the organisms isolated

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Gestational period</th>
<th>No. of patients</th>
<th>Organisms isolated</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1(^{st}) Trimester</td>
<td>21 (13.1%)</td>
<td>14.8%</td>
</tr>
<tr>
<td>2</td>
<td>2(^{nd}) Trimester</td>
<td>86 (53.8%)</td>
<td>31.3%</td>
</tr>
<tr>
<td>3</td>
<td>3(^{rd}) Trimester</td>
<td>53 (33.1%)</td>
<td>52.8%</td>
</tr>
<tr>
<td>4</td>
<td>Total</td>
<td>160 (100%)</td>
<td>36.2%</td>
</tr>
</tbody>
</table>

**Table No.3**: Frequency of Microorganisms Detected in Urine Samples (n=58)

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus (n=24)</td>
<td>41.38%</td>
</tr>
<tr>
<td>E. coli (n=17)</td>
<td>27.31%</td>
</tr>
<tr>
<td>Staphylococcus saprophyticus (n=6)</td>
<td>10.34%</td>
</tr>
<tr>
<td>Klebsiella enterica (n=3)</td>
<td>5.18%</td>
</tr>
<tr>
<td>Pseudomonas spp. (n=3)</td>
<td>5.18%</td>
</tr>
<tr>
<td>Enterococcus fecalis (n=2)</td>
<td>3.45%</td>
</tr>
<tr>
<td>Enterobacter spp (n=2)</td>
<td>3.45%</td>
</tr>
<tr>
<td>Staphylococcus epidermidis (n=1)</td>
<td>1.69%</td>
</tr>
</tbody>
</table>
Among 12 antibiotics tested, susceptibility pattern of E. coli was imipenem (82%), followed by nitrofurantoin (64%), amikacin (52%), cotrimoxazole (47%), ceftazidine (41%), ampicillin, norfloxacin, nalidixic acid and cefotaxime (29%), augmentin and cefaclor (23%) and pipemidic acid (17%). Out of 17 isolates of E. coli, 4 were multidrug resistant. (Figure-1)

**DISCUSSION**

According to various studies, it is also estimated that more than 50% of women will have UTI once during their lifetime. In childbearing women, the frequency of UTI can even be more than 8%. It is a serious health issue for women and more than 75% of all women experience it once or more at some stage of their life. In our study the frequency of UTI was 36.2%. The rate of incidence in our study was comparable with other studies reported. Furthermore, the percentage of UTI causing organisms in our study was higher than that reported by Leigh Brook et al., (2001) 1-10% and Onyemelukwe et al., (2003) 12.7%. The variation in above results may be because of the fact that we included only symptomatic pregnant woman as our targeted population or because geographical location is different.

In our study, the rate of UTI was more in the second trimester (53.8%) in comparison to the first and 3rd trimester. A study by Leigh (1989), did not match with our study that showed more cases of Urinary tract illness in the 3rd trimester. According to our study, S. aureus (41.32%) is the commonest organism identified in urine of pregnant mothers. According to results in Nigeria the commonest organisms was mainly E. coli (42.10%). This controversy might be due to the fact that all females included in our study were from outpatient department and not from indoor where there could be chance of spread of resistant E. coli strains that causes urinary tract infections.

**CONCLUSION**

Staphylococcus aureus 24 (41.4%) and Escherichia coli 17 (29.3%) were the commonest isolated organisms with 23.5% of multidrug resistant E. coli. Thus, every pregnant woman should undergo antenatal screening for bacteriuria followed by immediate treatment, to avoid any complications poses by UTI.

**Author's Contribution:**
- Concept & Design of Study: S. M. Abbas Naqvi
- Drafting: M. Majid Rasheed, Shahbaz Anwar
- Data Analysis: Rubina Yaseen, Muhammad Nouman Iqbal
- Revisiting Critically: S. M. Abbas Naqvi, M. Majid Rasheed
- Final Approval of version: S. M. Abbas Naqvi

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

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In this link write the goals of the study but avoid unqualified statements and conclusions not completely supported by data.

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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